AB Enzymes GmbH – Feldbergstrasse 78 , D-64293 Darmstadt

April 30, 2017

RE: GRAS Notification – Exemption Claim

Dear Sir or Madam:

Pursuant to the proposed 21C.F.R. § 170.36 (c)(1) AB Enzymes GmbH hereby claims that glucose oxidase enzyme preparation from *Trichoderma reesei* (*T.reesei)* strain expressing the glucose oxidase from *Penicillium* produced by submerged fermentation is Generally Recognized as Safe; therefore, they are exempt from statutory premarket approval requirements.

The following information is provided in accordance with the proposed regulation:
Proposed 21C.F.R. § 170.36 (c)(i) *The name and address of notifier.*
AB Enzymes GmbH
Feldbergstr. 78
D-64293 Darmstadt, Germany

Proposed 21C.F.R. § 170.36 (c)(ii) *The common or usual name of notified substance:*
Glucose oxidase enzyme preparation from *Trichoderma reesei* (*T.reesei)* strain expressing the glucose oxidase from *Penicillium.*

Proposed 21C.F.R. § 170.36 (c)(iii) *Applicable conditions of use:*
The glucose oxidase enzyme is to be used in baking processes. The enzyme preparation is used at minimum levels necessary to achieve the desired effect and according to requirements under current Good Manufacturing Practices. There are no maximal limits set, just suggested dosages.

Proposed 21C.F.R. § 170.36 (c)(iv) *Basis for GRAS determination:*
This GRAS determination is based upon scientific procedures.

Proposed 21C.F.R. § 170.36 (c)(v) *Availability of information:*
A notification package providing a summary of the information which supports this GRAS determination is enclosed with this letter. The package includes a safety evaluation of the production strain, the enzyme, and the manufacturing process, as well as an evaluation of dietary exposure. Complete data and information that are the basis for this GRAS determination are available to the Food and Drug Administration for review and copying at reasonable times (customary business hours) at a specific address set out in the notice or will be sent to FDA upon request (electronic format or on paper).

§170.225(c)(8) - FOIA (Freedom of Information Act):

AB Enzymes GmbH – Feldbergstrasse 78 , D-64293 Darmstadt

Parts 2 through 7 of this notification do not contain data or information that is exempt from disclosure under the FOIA (Freedom of Information Act).

§170.225(c)(9) – Information included in the GRAS notification:

To the best of our knowledge, the information contained in this GRAS notification is complete, representative and balanced. It contains both favorable and unfavorable information, known to AB Enzymes and pertinent to the evaluation of the safety and GRAS status of the use of this substance.

(b) (6)

April 30 2017

Candice Cryne
Regulatory Affairs Manager

Date

AB Enzymes GmbH – Feldbergstrasse 78 , D-64293 Darmstadt

GRAS NOTIFICATION FOR GLUCOSE OXIDASE FROM A GENETICALLY MODIFIED STRAIN OF *TRICHODERMA REESEI*

AB ENZYMES GmbH

April 30, 2017

1 PART 1 §170.225 – SIGNED STATEMENTS AND CERTIFICATIONS

§170.225(c)(1) – Submission of GRAS notice:
AB Enzymes GmbH hereby claims that glucose oxidase enzyme preparation from *Trichoderma reesei* (*T.reesei)* strain expressing the glucose oxidase from *Penicillium* produced by submerged fermentation is Generally Recognized as Safe; therefore, they are exempt from statutory premarket approval requirements.

§170.225(c)(2) -The name and address of the notifier:
AB Enzymes GmbH
Feldbergstr. 78
D-64293 Darmstadt, Germany

§170.225(c)(3) – Appropriately descriptive term:
Glucose oxidase enzyme preparation from *Trichoderma reesei* (*T.reesei)* strain expressing the glucose oxidase from *Penicillium*.

§170.225(b) – Trade secret or confidential:
This notification does not contain any trade secret or confidential information.

§170.225(c)(4) – Intended conditions of use:
The glucose oxidase enzyme is to be used in baking processes. The enzyme preparation is used at minimum levels necessary to achieve the desired effect and according to requirements under current Good Manufacturing Practices. There are no maximal limits set, just suggested dosages.

§170.225(c)(5) -Statutory basis for GRAS conclusion:
This GRAS determination is based upon scientific procedures.

§170.225(c)(6) – Premarket approval:
The notified substance is not subject to the premarket approval requirements of the FD&C Act based on our conclusion that the substance is GRAS under the conditions of the intended use.

Proposed 21C.F.R. § 170.36 (c)(v) *Availability of information:*
A notification package providing a summary of the information which supports this GRAS determination is enclosed with this letter. The package includes a safety evaluation of the production strain, the enzyme, and the manufacturing process, as well as an evaluation of dietary exposure. Complete data and information that are the basis for this GRAS determination are available to the Food and Drug Administration for review and copying at reasonable times (customary business hours) at a specific address set out in the notice or will be sent to FDA upon request (electronic format or on paper).

§170.225(c)(8) - FOIA (Freedom of Information Act):

Parts 2 through 7 of this notification do not contain data or information that is exempt from disclosure under the FOIA (Freedom of Information Act).

§170.225(c)(9) – Information included in the GRAS notification:

To the best of our knowledge, the information contained in this GRAS notification is complete, representative and balanced. It contains both favorable and unfavorable information, known to AB Enzymes and pertinent to the evaluation of the safety and GRAS status of the use of this substance.

(b) (6)

April 30 2017

Candice Cryne Date

Regulatory Affairs Manager

2 PART 2 §170.230 - IDENTITY, METHOD OF MANUFACTURE, SPECIFICATIONS AND PHYSICAL OR TECHNICAL EFFECT OF THE NOTIFIED SUBSTANCE

2.1 Identity of the notified substance

The dossier concerns a **glucose oxidase from a genetically modified *Trichoderma reesei***.

2.1.1 Common name of the enzyme

Name of the enzyme protein:	Glucose oxidase
Synonyms:	β-D-glucose oxidase, β-D-glucose: quinone oxidoreductase, D-glucose oxidase, D-glucose-1-oxidase, glucose oxyhydrase; deoxin-1, glucose aerodehydrogenase, aero-glucose dehydrogenase, glucose oxyhydrase, Notatin , corylophyline; penatin
EC (IUBMB) number:	EC 1.1.3.4
Production strain:	*Trichoderma reesei* RF11400

2.1.2 Classification of the enzyme

IUBMB #	1.1.3.4
CAS number	9001-37-0

2.2 Identity of the Source

2.2.1 Production Strain

The transformed production strain containing the glucose oxidase gene *is Trichoderma reesei* strain RF11400 which is deposited in the "Centraalbureau voor Schimmelcultures" (CBS) in the Netherlands with the deposit number CBS138879. The techniques used in transforming and handling *T. reesei* have been previously described *(Karhunen et al. 1993) (Penttilä et al. 1987)*. The production organism also meets the criteria for safe production microorganisms *(Pariza,*

Johnson 2001) (Decision Tree Analysis - *Appendix #1*). *T. reesei* strains are non-pathogenic and non-toxigenic and have been shown not to produce fungal toxins or antibiotics under harmless gene products *(Nevalainen et al. 1994; Olempska-Beer et al. 2006; Blumenthal 2004)*. The seed culture for the fermentation is inoculated with spores that have been stored at -80 0C. No additional growth cycles have been performed after the *T. reesei* RF11400 strain deposition to the culture collection.

2.2.2 Donor:

The strain RF11400 was constructed by transformation of the strain *T. reesei* RF10310 with a purified DNA fragment isolated from the plasmid pAB140SP-GOXPAMA. The techniques used in transforming and handling *T. reesei* were as described in Penttilä et al. (1987) and Karhunen et al. (1993).

2.2.3 Recipient Organism:

The recipient strain used for the genetic modification is *Trichoderma reesei* strain RF10310 which is derived from *Trichoderma reesei* RH4847, a classical mutant originating from QM6a. This strain has been shown to be genetically stable.

The *T. reesei* parental strain RF4847 was characterized by the Centraalbureau voor Schimmelcultures (CBS) in the Netherlands as *Trichoderma reesei*. It was identified based on the sequences of Internal Transcribed Spacer 1 and 2 and the 5.8S gene and Translation Elongation Factor 1a. *T. reesei* RF4847 was deposited as a CBS culture (safe deposit) as CBS 114041.

Therefore, the recipient can be described as followed:

Genus:	*Trichoderma*
Species:	*Trichoderma reesei*
Subspecies (if appropriate):	not applicable
Generic name of the strain:	RF10310
Commercial name:	Not applicable. The organism is not sold as such.

2.3 Genetic modification

Trichoderma reesei strain RF11400 was constructed for production of glucose oxidase, by transformation of the strain *T. reesei* RF10310 with a purified DNA fragment isolated from the plasmid consisting of the fungal expression cassette and a pUC19 vector backbone.

The plasmid was digested with *Not*I and the expression cassette containing the glucose oxidase gene was isolated. The purified expression cassette devoid of pUC19 elements was used for transformation of *T. reesei* RF10310.

The transformation of RF10310 strain with the glucose oxidase expression cassette was performed as described in Penttilä et al. (1987) with the modifications described in *Karhunen et al. (1993)*. The transformants were selected according to their ability to grow on acetamide plates. The expression cassette is integrated of at least one copy into the RF10310 genome.

Glucose oxidase expression cassette:

- *Penicillium glucose oxidase gene:* The glucose oxidase gene was chemically synthesized using the preferred codon usage for *Trichoderma reesei*. For the construction of the expression vector, the gene is fused at its 5´-end to a strong *Trichoderma* promoter. This promoter is used to drive *glucose oxidase* expression, to obtain high yields of glucose oxidase enzyme.
- terminator: To ensure termination of transcription a native *T. reesei* terminator is used.
- Linker: synthetic DNA sequence with *Stu*I restriction site
- *Aspergillus nidulans* amdS gene: the amdS gene was synthetized with optimized codon-usage, fewer restriction enzyme binding sites and without introns. The amdS gene sequence was from *Aspergillus nidulans* VH1-TRSX6 (Kelly, Hynes 1985). *Aspergillus nidulans* is closely related to *Aspergillus niger*, which is used in industrial production of food enzymes. The gene codes for an acetamidase that enables the strain to grow on acetamide as a sole nitrogen source (Kelly, Hynes 1985). This characteristic has been used for selecting the transformants, as it has been widely used as a selection marker in

fungal transformations without any disadvantage for more than 20 years. The expression cassette also contains the amdS promoter and terminator sequences.

The DNA fragments that have been transformed into *T. reesei* recipient strain RF10310 are well characterized, the sequences of the genes are known, and the fragments are free of any harmful sequences.

2.3.1 Stability of the Transformed Genetic Sequence

T. reesei strains are widely used in biotechnological processes because of their known stability. The transformed DNA does not contain any antibiotic resistance genes. The inserted DNA does not include any mobile genetic elements. Additionally, it should be highlighted that *T. reesei* genome lacks a significant repetitive DNA component and no extant functional transposable elements have been found in the genome *(Kubicek et al. 2011; Martinez et al. 2008)*. This results to low risk of transfer of genetic material.

The fermentation process starts always from the identical replica of the RF11400 seed ampoule. Production preserves at -80°C ("Working Cell Bank") are prepared from the "Master Cell Bank" (culture collection maintained at -150°C) in the following manner: A Petri dish is inoculated from the culture collection preserve (spore suspension) in such a way that single colonies deriving from one spore, each, can be selected upon germination. Altogether at least 20 individual colonies are inoculated into three parallel slants in which strains are grown and let to germinate. Spores from one parallel slant, representing each of the individual colonies, are inoculated into shake flasks. The shake flasks constitute the culture stage.

A so-called productivity test is performed, i.e. shake flask cultivation being completed; the enzymatic activity is measured, which must correspond to a given value. If this value is not reached, the culture is discarded. This test serves to determine the characteristic metabolic efficiency of each strain (isolate), i.e. to establish its identity. The productivity test is redone in fermenter cultivations for the chosen isolates (out of at least 20) that showed the best productivity in the shake flask cultivations. The working cell bank ampoules with glycerol solution are then prepared from those whose productivity tests show the highest results. The

suspensions thus obtained are frozen and stored divided into 0.5 ml aliquots at -80°C.

The annual production starts from these production preserves. Six of them are thawed for inoculation of six shake flasks and subsequent inoculation of the first process bioreactor is from these flasks. Mutations do not normally occur and if so only in the vegetative state during cell division. Owing to the above-described procedure, this vegetative state of the cultures is reduced to an inevitable minimum during production.

Potential changes in the genome of the production strain could theoretically occur during the propagation in the fermentation process. Therefore, Southern blot analysis was performed with genomic DNA isolated from the end of fermentation and genomic DNA prepared from the stock culture. The result revealed that the genome of *T. reesei* RF11400 stays genetically stable during the fermentation process.

Additionally, the stability is also followed as equal production of the glucose oxidase activity in a number of fermentation batches performed for the RF11400. The activity measurements from parallel successful fermentations showed that the productivity of the RF11400 strain remains unchanged. The data of the analysis of enzyme activities from preparations from three different fermentation batches of the recombinant RF11400 strain is presented in *Appendix #2*.

Therefore, the production strain RF11400 is stable in terms of genetic traits. The genetic materials in the expression cassettes have been integrated as part of the genome and are as stable as any natural gene. The integrated genetic materials are not acting as mobilisable elements and they do not contain mobilisable elements. Additionally, it should be highlighted that *T. reesei* genome lacks a significant repetitive DNA component and no extant functional transposable elements have been found in the genome *(Kubicek et al. 2011)*.

2.3.2 Good Industrial Large Scale Practice (GILSP)

The *T. reesei* RF11400 Glucose oxidase enzyme production strain complies with all criteria for a genetically modified GILSP organism.

In the USA, *Trichoderma reesei* is not listed as a Class 2 or higher Containment Agent under the

National Institute of Health (NIH, 1998) Guidelines for Recombinant DNA Molecules. Data submitted in Generally Recognized as Safe (GRAS) petitions to the Food and Drug Administration (FDA) for numerous enzyme preparations from *T. reesei* for human and animal consumption demonstrate that the enzymes produced by *T. reesei* are nontoxic. The Environmental Protection Institute (EPA) completed a risk assessment on *T. reesei* in 2011 resulting in a Proposed Rule in 2012, concluding that it is appropriate to consider *T. reesei* as a recipient microorganism eligible for exemptions from full reporting requirements[1], if this fungus was to be used in submerged standard industrial fermentation for enzyme production.

As a result, *T. reesei* can be used under the lowest containment level at large scale, GILSP, as defined by OECD *(ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT 1992)*.

The host organism is non-pathogenic, does not produce adventitious agents under the fermentation conditions employed and has an extended history of safe industrial use. Indeed, the *T. reesei* RF11400 strain originates from the wild type strain QM6a from which it was developed by conventional mutagenesis programs. The wild type *T. reesei* strains have been isolated only at low altitudes and within a narrow belt around the equator *(Kubicek et al. 2008)*. The mycoparasitism-specific genes have been shown to be lost in *T. reesei (Kubicek et al. 2011)*.

Overall, industrial microorganisms modified to produce high levels of enzymes, in fermentation conditions (e.g. no competitive microorganisms, optimal nutrients and aeration that are not present in the natural environment) are not expected to have any competitive advantage against other microorganisms in nature, which themselves are well-adapted in their natural environment. The fitness of the industrial strains to survive is very likely reduced by their high performance characteristic: most of the energy is needed for the production of proteins in high amounts.

The possible transfer of the recombinant DNA, if accidentally released into the environment, would not have any harmful or pathogenic effects on environmental processes. The DNA

[1] Reporting procedures in place under the Toxic Substances Control Act (TSCA) for new micro-organisms that are being manufactured for introduction into the commerce

fragments used in the construction of the expression cassette are well characterized and do not contain any undefined or harmful fragments. It can be concluded that the DNA fragments in the expression cassette or their corresponding gene products are not biologically harmful and are common in surroundings. Also, the recombinant DNA used for transformation does not contain any antibiotic resistance markers.

Therefore, the *T. reesei* RF11400 production organism is considered to be of low risk and can be produced with minimal controls and containment procedures in large-scale production. This is the concept of Good Industrial Large Scale Practice (GILSP), as endorsed by the OECD. The production organism has been approved by the Finnish competent authorities for large-scale productions, under containment conditions not exceeding the GILSP level of physical containment.

2.3.3 Structure and amount of vector and/or nucleic acid remaining in the GMM

Trichoderma reesei RF11400 strain does not harbor any replication competent vector DNA. The expression cassette used in the transformation was cleaved from the pUC19 vector backbone by restriction enzyme digestion followed by isolation of the expression cassette from agarose gels.

A Southern blot hybridization experiment using the pUC19 vector as a labeled probe and genomic DNA of the production strain RF11400 was performed to confirm that no vector DNA is included in the genome of RF11400. It produced negative results (no hybridization), demonstrating that no part of the plasmid vector removed to generate the linear transforming DNA fragment was carried over and introduced into the *Trichoderma* production host.

2.3.4 Demonstration of the absence of the GMM in the product

The down-stream process following the fermentation includes unit operations to separate the production strain. The procedures are executed by trained staff according to documented standard operating procedures complying with the requirements of the quality system.

The RF11400 enzyme production strain is recovered from the fermentation broth by a widely used process that results in a cell-free enzyme concentrate. The absence of the production strain

is confirmed for every production batch, using an internal Roal method. This method has been validated in-house. The sensitivity of the method is 1 cfu/20 ml in liquid and 1 cfu/0,2 gram in dried semifinals.

2.3.5 Inactivation of the GMM and evaluation of the presence of remaining physically intact cells

The RF11400 enzyme preparation is free from detectable, viable production organism. As the absence of the production strain is confirmed for every production batch, no additional information regarding the inactivation of the GMM cells is required.

It is also important to notice that the drying step gives an efficient way to kill *Trichoderma* strains, as the temperature is 75°C of the air leaving the dryer, and fungi are not very tolerant to heat.

2.3.6 Information on the possible presence of recombinant DNA

RF11400 Glucose oxidase enzyme preparation is produced by an aerobic submerged microbial fermentation using a genetically modified *Trichoderma reesei* strain. All viable cells of the production strain, RF11400, are removed during the down-stream processing: the fermentation broth is filtered with pressure filters and subsequent sheet filters, concentrated with ultra-filtration, and optionally followed by sheet filtration(s).

After this the final product does not contain any detectable number of fungal colony forming units or recombinant DNA. Two separate food enzyme samples (concentrates from industrial scale production) were tested for the presence of recombinant DNA using highly sensitive and specific PCR techniques. No recombinant DNA (recDNA) of the production strain was shown to be present above the detection limits. Please refer to appendix #2.

2.3.7 Absence of Antibiotic Genes and Toxic Compounds

As noted above, the transformed DNA does not contain any antibiotic resistance genes. Further, the production of known mycotoxins according to the specifications elaborated by the General Specifications for Enzyme Preparations Used in Food Processing Joint FAO/WHO Expert Committee on Food Additives, Compendium of Food Additive Specifications, FAO Food and

Nutrition Paper *(Food and Agriculture Organization of the United Nations 2006)* has been also tested from the fermentation products of the *T. reesei* strain RF11400. Adherence to specifications of microbial counts is routinely analysed. Several production batches produced by the production strain *T. reesei* RF11400 (2 dried fermentation concentrates) were analyzed and no antibiotic or toxic compounds were detected (*Appendix #2*).

2.4 ENZYME PRODUCTION PROCESS

2.4.1 Overview

The food enzyme is produced by ROAL Oy[2] by submerged fermentation of *Trichoderma reesei* RF11400 in accordance with current Good Manufacturing Practices for Food (GMP) and the principles of Hazard Analysis of Critical Control Points (HACCP). As it is run in the EU, it is also subject to the Food Hygiene Regulation (852/2004).

The enzyme preparation described herein is produced by controlled fed-batch submerged fermentation. The production process involves the fermentation process, recovery (downstream processing) and formulation and packaging. Finally, measures are taken to comply with cGMPs and HACCP. The manufacturing flow-chart is presented in Appendix #3.

It should be noted that the fermentation process of microbial food enzymes is substantially equivalent across the world. This is also true for the recovery process: in a vast majority of cases, the enzyme protein in question is only partially separated from the other organic material present in the food enzyme.

2.4.2 Fermentation

The production of food enzymes from microbial sources follows the process involving fermentation as described below. Fermentation is a well-known process that occurs in food and has been used for the production of food enzymes for decades. The main fermentation steps are:

- Inoculum
- Seed fermentation

[2] See footnote 1

- Main fermentation

2.4.3 Raw materials

The raw materials used in the fermentation and recovery processes are standard ingredients that meet predefined quality standards controlled by Quality Assurance for ROAL OY. The safety is further confirmed by toxicology studies. The raw materials conform to either specifications set out in the Food Chemical Codex, 10th edition, 2016 or The Council Regulation 93/315/EEC, setting the basic principles of EU legislation on contaminants and food, and Commission Regulation (EC) No 1881/2006 setting maximum limits for certain contaminants in food. The maximum use levels of antifoam and flocculants are ≤0.15% and ≤1.5% respectively.

2.4.4 Materials used in the fermentation process (inoculum, seed and main fermentation)

- Potable water
- A carbon source
- A nitrogen source
- Salts and minerals
- pH adjustment agents
- Foam control agents

2.4.5 Inoculum

A suspension of a pure culture of *T. reesei* RF11400 is aseptically transferred to a shake flask (1 liter) containing fermentation medium.

In order to have sufficient amount of biomass, the process is repeated several times. When a sufficient amount of biomass is obtained the shake flasks are combined to be used to inoculate the seed fermentor.

2.4.6 Seed fermentation

The inoculum is aseptically transferred to a pilot fermentor and then to the seed fermentor. The seed fermentation is run at a constant temperature and a fixed pH. At the end of fermentation, the inoculum is aseptically transferred to the main fermentation.

2.4.7 Main fermentation

Biosynthesis of the enzyme by the production strain occurs during the main fermentation.

The fermentation in the main fermentor is run as normal submerged fed-batch fermentation. The content of the seed fermentor is aseptically transferred to the main fermentor containing fermentation medium.

As in all processes, additional fermentation medium is added during the fermentation. In order to control the growth of the production organism and the enzyme production, the feed-rate of this medium is based upon a predetermined profile or on deviation from defined set points.

The fermentation process is continued for a predetermined time or until laboratory test data show that the desired enzyme production has been obtained or that the rate of enzyme production has decreased below a predetermined production rate. When these conditions are met, the fermentation is completed.

2.4.8 Recovery

The purpose of the recovery process is:

- to separate the fermentation broth into biomass and fermentation medium containing the desired enzyme protein,
- to concentrate the desired enzyme protein and to improve the ratio enzyme activity/Total Organic Substance (TOS).

During fermentation, the enzyme protein is excreted by the producing microorganism into the fermentation medium. During recovery, the enzyme-containing fermentation medium is separated from the biomass.

This Section first describes the materials used during recovery (downstream processing), followed by a description of the different recovery process steps:

- Pre-treatment
- Primary solid/ liquid separation

- Concentration
- Polish and germ filtration

The nature, number and sequence of the different types of unit operations described below may vary, depending on the specific enzyme production plant.

2.4.9 Materials

Materials used, if necessary, during recovery of the food enzyme include:

- Flocculants
- Filter aids
- pH adjustment agents

Potable water can also be used in addition to the above mentioned materials during recovery.

2.4.10 Pre-Treatment

Flocculants and/or filter aids are added to the fermentation broth, in order to get clear filtrates, and to facilitate the primary solid/liquid separation. Typical amount of filter aids is 2.5 %.

2.4.11 Primary solid/liquid separation

The purpose of the primary separation is to remove the solids from the enzyme containing fermentation medium. The primary separation is performed at a defined pH and a specific temperature range in order to minimize loss of enzyme activity.

The separation process may vary, depending on the specific enzyme production plant. This can be achieved by different operations like centrifugation or filtration.

2.4.12 Concentration

The liquid containing the enzyme protein needs to be concentrated in order to achieve the desired enzyme activity and/or to increase the ratio enzyme activity/TOS before formulation. Temperature and pH are controlled during the concentration step, which is performed until the desired concentration has been obtained. The filtrate containing the enzyme protein is collected for further recovery and formulation.

2.4.13 Polish and germ filtration

After concentration, for removal of residual cells of the production strain and as a general precaution against microbial contamination, filtration on dedicated germ filters is applied at various stages during the recovery process. Pre-filtration (polish filtration) is included if needed to remove insoluble substances and facilitate the germ filtration. The final polish and germ filtration at the end of the recovery process results in a concentrated enzyme solution free of the production strain and insoluble substances.

2.4.14 Formulation and Packaging

Subsequently, the food enzyme is formulated. The resulting product is defined as a 'food enzyme preparation'.

The glucose enzyme preparations from *T. reesei* RF11400 are sold mainly as solid preparations. For all kinds of food enzyme preparations, the food enzyme is adjusted to a declared activity, standardized and preserved with food ingredients or food additives (food grade quality).

The food enzyme preparation is tested by Quality Control for all quality related aspects, like expected enzyme activity and the general JECFA Specification for Food Enzyme Preparations, and released by Quality Assurance. The final product is packed in suitable food packaging material before storage. Warehousing and transportation are performed according to specified conditions mentioned on the accordant product label for food enzyme preparations.

2.4.15 General Production Controls and Specifications

In order to comply with cGMPs and HACCP principles for food production, the following potential hazards in food enzyme production are taken into account and controlled during production as described below:

Identity and purity of the producing microorganism:

The assurance that the production microorganism efficiently produces the desired enzyme protein is of utmost importance to the food enzyme producer. Therefore, it is essential that the identity and purity of the microorganism is controlled.

Production of the required enzyme protein is based on a well-defined Master (MCB) and Working Cell Bank (WCB). A Cell Bank is a collection of ampoules containing a pure culture. The cell line history and the production of a Cell Bank, propagation, preservation and storage is monitored and controlled. The MCB is prepared from a selected strain. The WCB is derived by sub-culturing of one or more ampoules of the MCB. A WCB is only accepted for production runs if its quality meets the required standards. This is determined by checking identity, viability, microbial purity and productivity of the WCB. The accepted WCB is used as seed material for the inoculum.

Microbiological hygiene:

For optimal enzyme production, it is important that hygienic conditions are maintained throughout the entire fermentation process. Microbial contamination would immediately result in decreased growth of the production organism, and consequently, in a low yield of the desired enzyme protein, resulting in a rejected product.

Measures utilized by ROAL OY to guarantee microbiological hygiene and prevent contamination with microorganisms ubiquitously present in the environment (water, air, raw materials) are as follows:

- Hygienic design of equipment:
    - all equipment is designed, constructed and used to prevent contamination by foreign micro-organisms
- Cleaning and sterilization:
    - Validated standard cleaning and sterilization procedures of the production area and equipment: all fermentors, vessels and pipelines are washed after use with a CIP-system (Cleaning in Place), where hot caustic soda and nitric acid are used as cleaning agents. After cleaning, the vessels are inspected manually; all valves and connections not in use for the fermentation are sealed by steam at more than 120°C; critical parts of down-stream equipment are sanitized with disinfectants approved for food industry

- Sterilization of all fermentation media:
    - all the media are sterilized with steam injection in fermentors or media tanks (at 121°C for at least 20 min at pH 4.3 – 4.8.).
- Use of sterile air for aeration of the fermentors:
    - Air and ammonia water are sterilized with filtration (by passing a sterile filter).
- Hygienic processing:
    - Aseptical transfer of the content of the WCB ampoule, inoculum flask or seed fermentor
    - Maintaining a positive pressure in the fermentor
- Germ filtration

In parallel, hygienic conditions in production are furthermore ensured by:

- Training of staff:
    - all the procedures are executed by trained staff according to documented procedures complying with the requirements of the quality system.
- Procedures for the control of personal hygiene
- pest control
- Inspection and release by independent quality organization according to version-controlled specifications
- Procedures for cleaning of equipment including procedures for check of cleaning efficiency (inspections, flush water samples etc.) and master cleaning schedules for the areas where production take place
- Procedures for identification and implementation of applicable legal requirements
- Control of labelling
- Requirements to storage and transportation

Chemical contaminants:

It is also important that the raw materials used during fermentation are of suitable quality and

do not contain contaminants which might affect the product safety of the food enzyme and/or the optimal growth of the production organism and thus enzyme yield.

It is ensured that all raw materials used in production of food enzymes are of food grade quality or have been assessed to be fit for their intended use and comply with agreed specifications.

In addition to these control measures in-process testing and monitoring is performed to guarantee an optimal and efficient enzyme production process and a high quality product (cGMPs). The whole process is controlled with a computer control system which reduces the probability of human errors in critical process steps.

These in-process controls comprise:

Microbial controls:
Absence of significant microbial contamination is analyzed by microscopy or plate counts before inoculation of both the seed and main fermentation and at regular intervals and at critical process steps during fermentation and recovery.

Monitoring of fermentation parameters may include:

- pH
- Temperature
- Aeration conditions

The measured values of these parameters are constantly monitored during the fermentation process. The values indicate whether sufficient biomass or enzyme protein has been developed and the fermentation process evolves according to plan.

Deviations from the pre-defined values lead to adjustment, ensuring an optimal and consistent process.

Enzyme activity and other relevant analyses (like dry matter, refraction index or viscosity):
This is monitored at regular intervals and at critical steps during the whole food enzyme

production process.

2.4.16 Stability of the enzyme during storage and prior to use

Food enzymes are formulated into various enzyme preparations in order to obtain standardized and stable products. The stability thus depends on the type of formulation, not on the food enzyme as such.

The date of minimum durability or use-by-date is indicated on the label of the food enzyme preparation. If necessary, special conditions of storage and/or use will also be mentioned on the label.

2.5 Composition and specifications

2.5.1 Characteristics of the enzyme preparation

The characteristics of the enzyme preparation are:

Property	Requirement	
Activity	min.	11500
Appearance	Solid, light beige	
Density	1.0 – 1.1 g/ml	

2.5.2 Formulation of the enzyme preparation

Composition	
Constituent	**%**
Glucose oxidase	32.8%
Sunflower oil	0.4
Wheat flour	remainder

2.5.3 Molecular mass and amino acid sequence of the enzyme

Depending on their physicochemical properties and on their origins, glucose oxidase often have molecular masses in a range of 72 - 80kDa *(* Kelley and Reddy, 1986; Zoldak *et al*., 2004*)*. The amino acid sequence has been verified.

2.5.4 Purity and identity specifications of the enzyme preparation

It is proposed that the food enzyme glucose oxidase should comply with the internationally accepted JECFA specifications for chemical and microbiological purity of food enzymes (Food and Agriculture Organization of the United Nations 2006):

Lead:	Not more than 5 mg/kg
Salmonella sp.:	Absent in 25 g of sample
Total coliforms:	Not more than 30 per gram
Escherichia coli:	Absent in 25 g of sample
Antimicrobial activity:	Not detected
Mycotoxins:	No significant levels[3]

The proof that the food enzyme lipase complies with these specifications is shown by the analyses on 2 different batches (see Appendix #2) and summarised below:

Batch #	**P160011l**	**161130700**
Lead (mg/kg)	<0.05	<0.05
Salmonella sp. (per 25 g)	Not detected	Not detected
Total coliforms (per g)	<10	<10
Escherichia coli (per 25 g)	Not detected	Not detected
Antimicrobial activity	Not detected*	Not detected*

[3] See JECFA specifications, ftp://ftp.fao.org/docrep/fao/009/a0675e/a0675e00.pdf, page 64: Although nonpathogenic and nontoxigenic microorganisms are normally used in the production of enzymes used in food processing, several fungal species traditionally used as sources of enzymes are known to include strains capable of producing low levels of certain mycotoxins under fermentation conditions conducive to mycotoxin synthesis. Enzyme preparations derived from such fungal species should not contain toxicologically significant levels of mycotoxins that could be produced by these species. Also see Section 3.2.1.2.4.

2.5.5 Composition of the enzyme preparation

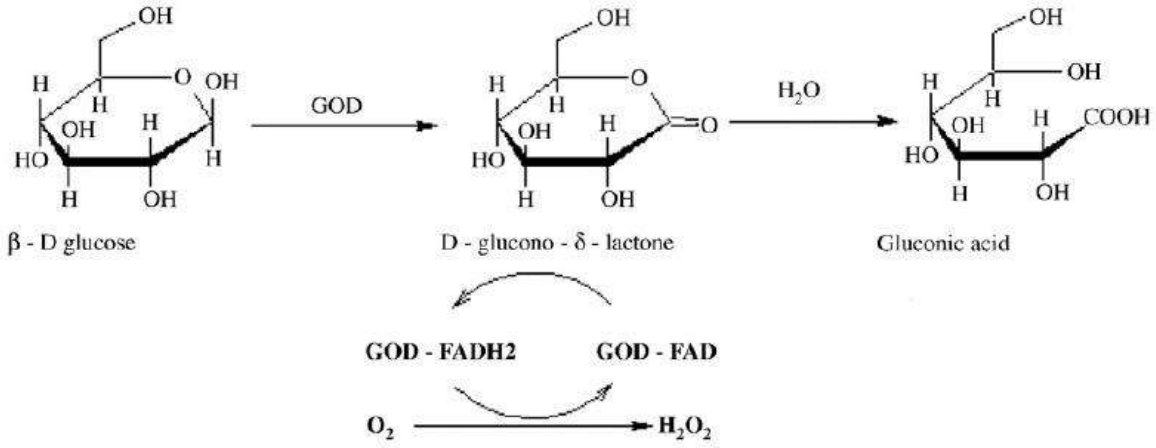
Batch Number	P160011l	161130700	Mean
Ash (%)	0.61	0.51	*0.56*
Water (%)	78.6	82.8	*80.7*
Protein (%)	15.8	11.7	*13.7*
TOS (%)	20.8	16.7	*18.75*
Activity (GOX/g concentrate)	14,100	13,100	*13,600*
Activity/mg TOS	**67.8**	**78.44**	***73.1***

The typical batch sizes range from 1 000 L to 150 000 L and are deeply depending on the market demand. Therefore, the frequency and the volume of production of the food enzyme vary. AB Enzymes is a small to mid-size company and this enzyme has only recently been developed. So far, the current market demand for this specific enzyme has not justified more than 2 full-scale fermentations and AB Enzymes is unfortunately not in the situation to have a wider range of batches available for comparisons. This explains the reduced number of samples that have been analysed for the purpose of this dossier.

TOS values were calculated using the following formula: % TOS = 100 % - (% Ash + % Moisture + % Diluents) as recommended by JECFA. The 2 samples do not contain any diluents.

2.6 Enzymatic Activity

The main activity of the enzyme preparation is glucose oxidase (IUB 1.1.3.4).



Glucose oxidase catalyses the oxidation of β-D-glucose to D-glucono-1,5-lactone and the reduction of oxygen to hydrogen peroxide. In the presence of water, D-glucono-1,5 -lactone is hydrolysed to gluconic acid.

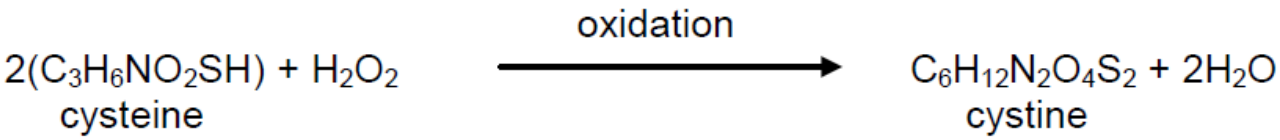
D-glucose is widespread in sweet fruits. But by far, the greatest part of glucose serves as monomer for the formation of oligo- and polysaccharides such as sucrose, dextrines, starch or cellulose (Online Encyclopedia ROEMPP Georg Thieme Verlag KG 2015). D-glucose can be found in various plant materials including the endosperm of cereals, such as wheat and barley, as monomer in small amount and in form of starch in large amount. During dough preparation endogenous amylases are able to release D-glucose from starch (Poutanen, 1997; Rosell et al., 2001).

Oxygen is naturally present in the dough making environment (air) and therefore incorporated into the dough as air bubbles during the process.

Consequently, the substrates for glucose oxidase occur naturally in nature and are therefore a natural part of the human diet.

Reaction products: as a result of the catalytic activity of glucose oxidase, glucon lacton / gluconic acid and hydrogen peroxide are formed. Gluconic acid can be found in plants, fruits and other foodstuffs and is used as food additive for several applications (Ramachandran et al.,

2006; Codex Alimentarius Commission, 2015). Hydrogen peroxide disappears either due to its oxidising reaction with the cysteine residues of proteins to form cystine and thus converting the sulfhydryl groups to a disulfide bond (see reaction below) or as substrate for endogeneous peroxidases for phenolic crosslink formation (Rasiah et al., 2005).



The method to analyse the activity of the enzyme is company specific and is capable of quantifying glucose oxidase activity as defined by its IUBMB classification. The enzyme activity is usually reported in GOX/g.

2.6.1 Side activities of the enzyme protein which might cause adverse effects

As far as AB Enzymes is aware, the glucose oxidase described in this dossier does not possess any enzymatic side activities which might cause adverse effects.

Apart from glucose oxidase, the food enzyme also contains other enzymatic side activities in small amount which are naturally and typically produced by the production organism *Trichoderma reesei,* mainly cellulases, xylanase and protease.

2.7 Allergenicity

As some enzymes manufactured for use in food have been reported to cause inhalation allergy in workers exposed to enzyme dust in manufacturing facilities, glucose oxidase may also cause such occupational allergy in sensitive individuals. However, the possibility of an allergic reaction to the glucose oxidase residues in food seems remote. In order to address allergenicity by ingestion, it may be taken into account that:

- The allergenic potential of enzymes was studied by *Bindslev-Jensen et al. (2006)* and reported in the publication: "*Investigation on possible allergenicity of 19 different commercial enzymes used in the food industry*". The investigation comprised enzymes produced by wild-type and genetically modified strains as well as wild-type enzymes and Protein Engineered variants and comprised 400 patients with a diagnosed allergy to inhalation allergens, food allergens, bee or wasp. It was concluded from this study that ingestion of food enzymes in general is not likely to be a concern with regard to food allergy.
- Previously, the AMFEP Working Group on Consumer Allergy Risk from Enzyme Residues in Food performed an in-depth analysis of the allergenicity of enzyme products (*Daurvin et al. 1998*). The overall conclusion was that – as opposed to exposure by inhalation – there are no scientific indications that the small amounts of enzymes in food can sensitize or induce allergy reactions in consumers.
- Enzymes when used as digestive *(Abad et al. 2010)* aids are ingested daily, over many years, at much higher amounts when compared to enzymes present in food (up to 1 million times more).

Thus, there are no scientific indications that small amounts of enzymes in food can sensitize or induce allergic reactions in consumers.

Additional considerations supporting the assumptions that the ingestion of an enzyme protein is not a concern for food allergy should also be taken into account:

- The majority of proteins are not food allergens and based on previous experience, the enzyme industry is not aware of enzyme proteins used in food being homologous to known food allergens[4].
- The food enzyme is used in small amounts during food processing resulting in very small amounts of the enzyme protein in the final food. A high concentration generally equals a

[4] The only enzyme protein used in food an known to have a weak allergenic potential is egg lysozyme

higher risk of sensitization, whereas a low level in the final food equals a lower risk *(Goodman et al. 2008)*.

- In the case where proteins are denatured which is the case for this glucose oxidase due to the food process conditions, the tertiary conformation of the enzyme molecule is destroyed. In general, these alterations in conformation are associated with decrease in the antigenic reactivity in humans: in the vast majority of investigated cases, denatured proteins are much less immunogenic than the corresponding native proteins *(Valenta 2002; Valenta, Kraft 2002; Takai et al. 1997; Takai et al. 2000; Nakazawa et al. 2005; Kikuchi et al. 2006)*.
- In addition, residual enzyme proteins still present in the final food will be subjected to digestion in the gastro-intestinal system, which reduces further the risk of enzyme allergenicity. While stability to digestion is considered as a potential risk factor of allergenicity, it is believed that small protein fragments resulting from digestion are less likely to be allergenic *(Food and Agriculture Organization of the United Nations January/2001; Goodman et al. 2008)*.
- Finally, enzymes have a long history of safe use in food processing, with no indication of adverse effects or reactions. Moreover, a wide variety of enzyme classes (and structures) are naturally present in food. This is in contrast with most known food allergens, which are naturally present in a narrow range of foods.

2.7.1 Allergenicity Search

In order to specifically evaluate the risk that the glucose oxidase enzyme would cross react with known allergens and induce a reaction in an already sensitized individual, sequence homology testing to known allergens was performed. This test used a 80 amino acid (aa) sliding window search as well as conventional FASTA alignment (overall homology), with the threshold of 35% homology as recommended in the most recent literature (*Food and Agriculture Organization of the United Nations January/2001; Goodman et al. 2008; Ladics et al. 2007*).

A sequence homology comparison test was then performed using a database of allergens from the Food Allergy Research and Resource Program (FARRP), University of Nebraska, Allergen Database (Version 16, January 27, 2016), which contains the amino acid sequences of known and putative allergenic proteins.

The resulting alignments of the full-length glucose oxidase protein to any allergenic proteins in the allergen database showed an identity of 30.7 % with Mala s 12 allergen precursors produced by the fungal species *Malassezia sympodialis*. Aalberse suggested "*cross-reactivity is rare below 50% amino acid identity and in most situations requires more than 70% identity*" (Aalberse 2000) making it unlikely that the glucose oxidase in question can be presumed to be allergenic based on full-length sequence relatedness to known allergens.

Using the 80-mer sliding window analysis the glucose oxidase protein sequence, one identity match of 41.2% with Mala s 12 allergen precursor produced by the fungal species *Malassezia sympodialis* was identified. As recommended by the FAO/WHO, a possible cross-reactivity has to be considered, when there is more than 35% identity in the amino acid sequence of the expressed protein using an 80 amino acids window and a suitable gap penalty (Food and Agriculture Organization of the United Nations January/2001). This recommendation was challenged however recently. According to Ladics et al. (2007) by comparing the predictive value of a full-length (conventional) FASTA search to the 80-mer analysis "*a conventional FASTA search provides more relevant identity to the query protein and better reflects the functional similarities between proteins. It is recommended that the conventional FASTA analysis be conducted to compare identities of proteins to allergens". This judgement on the predictive inferiority of the 80-mer (35% threshold) approach was supported recently by Goodman, Tetteh (2011) who suggested "because the purpose of the bioinformatics search is to identify matches that may require further evaluation by IgE binding, full-length sequence evaluation or an increase in the threshold from 35% identity toward 50% for the 80 amino acid alignment should be considered*" (Goodman, Tetteh 2011).

Using the latter recommendation the glucose oxidase in question would be below threshold

even using the 80-mer sliding window approach.

In addition, the glucose oxidase protein sequence showed no perfect match to any known allergen when searching for a straight stretch of eight amino acids that could serve as potential IgE binding sites.

In summary therefore the bioinformatics approach to estimate potential allergenicity based on relatedness to known allergens and taking into account the most recent scientific recommendations on the interpretation of such data leads us to conclude that the glucose oxidase produced by *Trichoderma reesei* RF11400 is of no concern.

Conclusion:

Based on the results obtained from the bioinformatics approach to estimate potential allergenicity on relatedness to known allergens and taking into account the most recent scientific recommendations on the interpretation of such data, and based on the fact that the enzyme is typically denatured during the food manufacturing process and that any residual enzyme still present in the final food will be subject to digestion in the gastro-intestinal system, it is not likely that the glucose oxidase produced by *Trichoderma reesei* RF11400 under evaluation will cause allergic reactions after ingestion of food containing the residues of these enzymes.

2.8 Technological purpose and mechanism of action of the enzyme in food

In principle, the enzymatic oxidation of glucose with the help of glucose oxidase can be of benefit in processing of all foods and food ingredients which naturally contain glucose.

When used in food applications glucose oxidase's function is to remove either glucose or oxygen (as reviewed by Wong *et al*., 2008 and Bankar *et al*., 2009). Typically, glucose oxidase is used to remove glucose, preventing product browning caused by Mailliard reaction which may occur during food processing (e.g. pateurisation of powdered eggs and fruit processing) and

other food processes involving high temperatures. Glucose oxidase is also used to lower alcohol content in wine production (through the removal of some of the glucose which would otherwise be converted into alcohol).

Other examples are the oxygen removal from the top of bottled beverages before sealing, or mayonnaise production and gluconic acid production (Wong *et al*., 2008; Bankar *et al*., 2009).

Finally, glucose oxidase is also currently used to strengthen the protein complexes contained in starch-based products through increased formation of cross-links between proteins, thereby improving the quality of such foods, as breads and other baked products (Vemulapalli and Hoseney, 1998; Bonet *et al*., 2006; Steffolani *et al*., 2012).

The glucose oxidase from *T. reesei* RF11400 object of this dossier is specifically intended to be used in baking (e.g. bread, biscuits, tortillas, cakes, steamed bread and croissants) and other cereal-based processes (e.g. pastas, noodles and snacks). In these processes, the glucose oxidase is used as a processing aid in food manufacturing and is not added directly to final foodstuffs.

Below, the benefits of the use of industrial glucose oxidase in those processes are described. The beneficial effects are of value to the food chain because they lead to better and/or more consistent product quality. Moreover, the applications lead to more effective production processes, resulting in better production economy and environmental benefits such as the use of less raw materials and the production of less waste.

Glucose oxidase has been used e.g. in baking and other cereal based processes for over 20 years and their use in the bakery industry is continuously increasing (Haarasilta and Pullinen, 1992; Mutsaers, 1997; Poulsen and Hostrup, 1998; Feng, 2000). Some of these applications have been specifically approved for a number of years in Denmark and France (baking, egg processing), which together with the extensive use for decades in a number of EU countries justifies the technological need of glucose oxidase in these food processes.

BAKING PROCESS

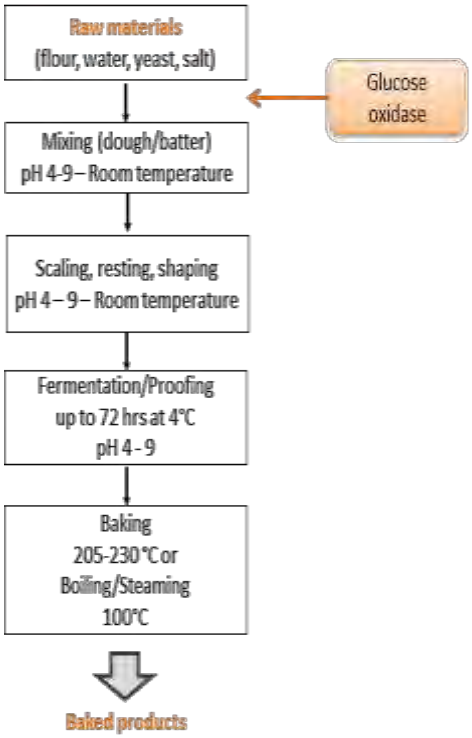
Glucose oxidase can be used in the manufacturing of bakery products such as, but not limited to, bread, biscuits, steamed bread, cakes, pancakes, tortillas, wafers and waffles.

Functional properties of bread dough greatly depend on the protein forming the gluten network. Protein crosslinking or the formation of covalent bonds between protein chains is a way of modifying the protein functionality and simultaneously increasing its applications in different processes.

The hydrogen peroxide produced during glucose oxidase reaction causes the oxidation of thiol groups of gluten proteins forming disulphide linkages It also produces dityrosine cross-linking and the gelation of water soluble pentosans (Steffolani *et al*., 2012 and references therein). The oxidation of bread dough induces therefore an important modification on the gluten proteins through the formation of both disulfide and non-disulfide crosslinks which results in significant improvement in the functional properties of the dough and leads to better bread making performance (Vemulapalli and Hoseney, 1998; Bonet *et al.,* 2006; Steffolani *et al*., 2012).

Glucose oxidase is normally not present in vegetable raw materials. This means that the enzyme has to be added to a food system in order to benefit from its functionality. Glucose oxidase is often used together with other enzymes (enzyme systems) which modify other components of the raw materials. In particular glucose oxidase is often applied together with endo-amylase, xylanase and cellulase (Primo-Martin et al., 2005; Steffolani *et al.,* 2012; Shafisoltani *et al.,* 2014).

The process flow chart is presented below and shows the conditions under which the food enzyme is used.



The benefits of the conversion of glucose and oxygen with the help of glucose oxidase in baking can be summarised as follows:

- Facilitate the handling of the dough
- Reduce dough stickiness which results in processing tolerance
- Improve dough stability and behaviour during the shaping or moulding step
- Improve dough machinability

Due to the better processing described above, the beneficial effects of the use glucose oxidase in the production of baked products may be the following:

- Ensure a uniform volume and an improved/uniformed crumb structure of the bakery product, which might otherwise be impaired by fluctuating processing of the dough;
- Support the creation of a more appealing crust surface of cutted bread types such as e.g. rolls or baguettes

- Possible effects are less product variation, ensuring uniform/standardised quality products.

Those beneficial effects may be associated with effects on the final food, which are however not exclusively obtainable by means of enzyme treatment: they can be achieved without the use of enzymes through e.g. modified, maybe more expensive, production processes, the use of chemicals or recipe changes.

The fate of the enzyme protein during baking process: In baking, glucose oxidase performs its technological function during dough or batter handling in order to contribute to an improved and consistent baking process. The glucose oxidase is denatured by heat during the baking or steaming step.

OTHER CEREAL-BASED FOOD PROCESSES

Glucose oxidase can also be used in the processing of other cereal based products such as, but not limited to, pasta, noodles and snacks.

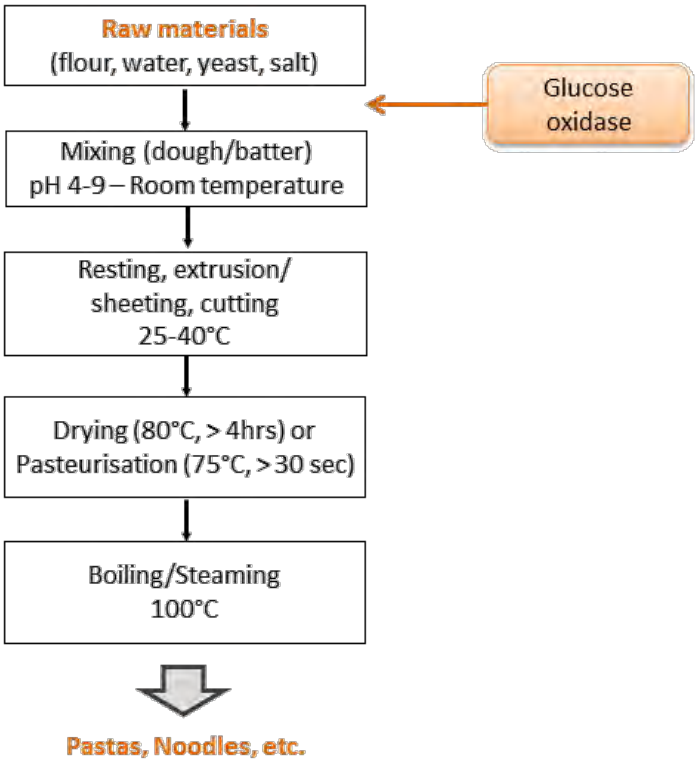
As mentioned above, the reaction products resulting from the conversion of the glucose with the help of glucose oxydase interact with the gluten proteins. Gluten proteins provide functional properties during pasta, noodle and snack making due to their ability to determine dough viscosity and dough stability. Modification of the gluten protein structure can improve the functional properties of the flour endogenous proteins as explained below.

Dried pasta has, among cereal derived foodstuffs, a very distinct microscopic structure. Starch granules are entrapped in an amorphous protein matrix. While cooking in hot water, physical competition between starch swelling and properties of polymerised and polymerising proteins determines whether the final cooked pasta is firm and elastic or rather sticky and soft. The first is the case when a strong gluten network is formed and starch particles are entrapped in this network. The second is the case when the gluten network is too week resulting in a significant

starch swelling (Resmini and Pagani, 1983; Bruneel *et al.*, 2010).

Because gluten has a predominant role in the pasta structure the use of glucose oxidase increases the gluten protein network resistance to cooking and decrease surface stickiness (Matsua, 1987; Fuad and Prabhasankar, 2010).

The process flow of other cereal based processes is presented below:



The benefits of the conversion of glucose and oxygen with the help of glucose oxidase in other cereal based processes can be summarised as follows:

- Facilitate the handling of the dough
- Reduce dough stickiness which results in processing tolerance

- Strengthen dough structure
- Improve cooking tolerance of pasta or noodle

Due to the better processing described above, the beneficial effects of the use glucose oxidase in the production of other cereal-based products may be the following:

- Firmer bite and better texture of pasta or noodle
- Possible effects are less product variation, ensuring uniform/standardised quality products.

The fate of the enzyme protein during the pasta and noodles production process: In other cereal based processes such as pasta and noodles, the glucose oxidase performs its function during dough handling. The enzyme is denatured by heat during the drying, boiling or steaming step.

To summarize, the use of glucose oxidase in baking and other cereal-based processes ensures a maximum compatibility with modern industrial processes (also leading to less product variations, hereby ensuring standardised quality products).

2.9 Use Levels

Commercial food enzyme preparations are generally used following the *Quantum Satis* (QS) principle, i.e. at a level not higher than the necessary dosage to achieve the desired enzymatic reaction – according to Good Manufacturing Practice. The amount of enzyme activity added to the raw material by the individual food manufacturer has to be determined case by case, based on the desired effect and process conditions.

Therefore, the enzyme manufacturer can only issue a recommended enzyme dosage range. Such a dosage range is the starting point for the individual food producer to fine-tune his process and determine the amount of enzyme that will provide the desired effect and nothing more. Consequently, from a technological point of view, there are no 'normal or maximal use levels' and glucose oxidase is used according to the QS principle. A food producer who would add

much higher doses than the needed ones would experience untenable costs as well as negative technological consequences.

The dosage of a food enzyme depends on the activity of the enzyme protein (in this case glucose oxidase) present in the final food enzyme preparation (i.e. the formulated food enzyme). However, the activity Units as such do not give an indication of the amount of food enzyme actually added.

Microbial food enzymes contain, apart from the enzyme protein in question, also some substances derived from the producing microorganism and the fermentation medium. The presence of all organic materials is expressed as Total Organic Solids (TOS). From a safety point of view, the dosage on basis of TOS is more relevant. It must also be noted that the methods of analysis and the expression of the Units are company specific. Consequently, in contrast to when the amount is expressed in TOS the activity Units of a certain enzyme cannot be compared when coming from different companies. Because of these reasons, the use levels are expressed in TOS in the Table below.

The Table below shows the range of recommended use levels for each application where the glucose oxidase is used:

Food Application	Raw material (RM)	Suggested recommended use levels (mg TOS/kg RM)
Baking and other cereal based processes	Flour	10

2.10 Effect of the presence of (residues of) the food enzyme on the final food

It is not the food enzyme itself, but the result of the enzymatic conversion that determines the effect in the food or food ingredient (including raw materials). This effect remains, irrespective of whether the food enzyme is still present or removed from the final food.

Glucose oxidase performs its technological function during food processing. In some cases, the

enzyme may no longer be present in the final food. In other cases, where the enzyme protein is still present in the final food, it does not perform any technological function in the final food, just like the endogenous glucose oxidase present in the cereal-based raw materials and ingredients.

In order to be able to perform a technological function in the final food, a number of conditions have to be fulfilled at the same time:

- the enzyme protein must be in its 'native' (non-denatured) form, AND
- the substrate must still be present, AND
- the enzyme must be free to move (able to reach the substrate), AND
- conditions like pH, temperature and water content must be favourable

The reasons why the glucose oxidase does not exert any (unintentional) enzymatic activity in the final food:

- the glucose oxidase is denatured by heat during the baking or steaming steps of the baking process and during the drying, boiling or steaming steps of processes of other cereal-based products: it is inactivated during regular baking processes, where temperatures inside the dough reach between 95° and 100°C for a period of at least 10-15 minutes.
- the remaining water content (water activity) within baked goods is much too low to support any hydrolytic enzymatic activity in the baking matrix.

Consequently, it can be concluded that the glucose oxidase does not exert any (unintentional) enzymatic activity in the final foods.

Based on the conditions of use and the activity of glucose oxidase under such conditions, it can be concluded the presence of (residues of) enzyme glucose oxidase in the final food does not lead to an effect in or on the final foods.

3 PART 3 § 170.325 - DIETARY EXPOSURE

The most appropriate way to estimate the human consumption in the case of food enzymes is using the so-called Budget Method *(Hansen 1966; Douglass et al. 1997)*. This method enables to calculate a Theoretical Maximum Daily Intake (TMDI) based on

conservative assumptions regarding physiological requirements for energy from food and the energy density of food rather than on food consumption survey data.

The Budget Method was originally developed for determining food additive use limits and is known to result in conservative estimations of the daily intake.

The Budget Method is based on the following assumed consumption of important foodstuffs and beverages (for less important foodstuffs, e.g. snacks, lower consumption levels are assumed):

Average consumption over the course of a lifetime/kg body weight/day 0.025	Total solid food (kg)	Total non-milk beverages (l)	Processed food (50% of total solid food) (kg)	Soft drinks (25% of total beverages) (l)
	0.025	0.1	0.0125	0.025

For the calculation of the TMDI, the maximum use levels are chosen. Furthermore, the calculation takes into account how much food or beverage is obtained per kg raw material (see below the table) and it is assumed that all the TOS will end up in the final product.

Applications		Raw material (RM)	Suggested recommended use level (mg TOS/kg RM)	Final food (FF)	Ratio RM/FF*	Suggested level in final food (mg TOS/kg food)
SOLID FOODS	Baking	Flour	10	Baked products, Pastas and noodles…	0.71	7.1

* *Assumptions behind ratios of raw material to final food:*

Baking:

Bakery products fall in the category of solid foods.

Flour is the raw material for bakery product and the yield will vary depending on the type of final food produced.

From 1 kg of flour you would have 4 kg of cakes, 1.4 kg of bread or 1.1 kg of cracker. Cracker may represent the most conservative input from the bakery processes. However, consumption of bread is higher than that of cracker, this is why bread is used as the assumption for the calculation of dietary exposure from bakery processes.

The yield of 1.4 kg of bread per 1 kg of flour correspond to a RM/FF ratio of 0.71 kg of flour per kg bakery product is used.

The Total TMDI can be calculated on basis of the maximal values found in food and beverage (in this case, the enzyme won't be used in a process leading to liquid food, so the maximal value is found in baked products) multiplied by the average consumption of food and beverage/kg body weight/day.

The Total TMDI will consequently be calculated as follows:

TMDI in food (mg TOS/kg body weight/day)	TMDI in beverage (mg TOS/kg body weight/day)	Total TMDI (mg TOS/kg body weight/day)
7 x 0.0125 = 0.088	0 x 0.025 = 0	**0.088**

It should be stressed that this Total TMDI is based on conservative assumptions and represents a highly exaggerated value because of the following reasons:

- It is assumed that ALL producers of the above mentioned foodstuffs use the specific enzyme glucose oxidase from *Trichoderma reesei* RF11400;
- It is assumed that ALL producers apply the HIGHEST use level per application;
- For the calculation of the TMDI's in food and in beverages, only THOSE foodstuffs and beverages were selected containing the highest theoretical amount of TOS.
- Thus, foodstuffs and beverages containing lower theoretical amounts were not taken into account;
- It is assumed that the amount of TOS does not decrease as a result of the food production process;
- It is assumed that the final food containing the calculated theoretical amount of TOS is consumed DAILY over the course of a lifetime;
- Assumptions regarding food and beverage intake of the general population are overestimates of the actual average levels *(Douglass et al. 1997)*.

The Margin of Safety (MoS) for human consumption can be calculated by dividing the NOAEL (see **Section** 6) by the Total Theoretical Maximal Daily Intake (TMDI). Total TMDI of the food enzyme is 0.088 mg TOS/kg body weight/day. Consequently, the MoS is:

- MoS = 1,000 / 0.088 = <u>11,429</u>

Total TMDI is highly exaggerated. Moreover, the NOAEL was based on the highest dose administered, and is therefore to be considered as a minimum value. Therefore, the actual Margin of Safety in practice will be some magnitudes higher. Consequently, there are no safety reasons for laying down maximum levels of use.

Conclusion:

The overall conclusion is that the use of the food enzyme glucose oxidase from *Trichoderma reesei* RF11400 in the production of food is absolutely safe. Considering the high safety factor – even when calculated by means of an overestimation of the intake via the Budget method – there is no need to restrict the use of the enzyme in food processing. The suggested dosage for food manufacturers is not a restrictive value and could be higher or lower depending on usage.

4 PART 4 §170.240 – Self-limiting levels of use

This part is not applicable to this notified substance, see **Section 2.9** for further details regarding use levels.

5 PART 5 § 170.245 – Experience based on common use in food before 1958

This part is not applicable to this notified substance

6 PART 6 § 170.250 – Part 6 of a GRAS notice: Narrative

The data and information contained in this GRAS notice provides a basis that the notified substance is safe under the conditions of its intended use described herein. In the following sub-sections, the safety of the enzyme, the genetic modification and toxicological studies are presented. The information is generally available and PART 6 § 170.250 does not contain any confidential information. This section provides the basis that the notified substance is generally recognized, among qualified experts, and study data, to be safe under the conditions of its intended use.

All available known information has been reviewed and AB Enzymes GmbH is not aware of any data or information that is, or may appear to be, consistent with our conclusion of the notified substance GRAS status.

6.1 Safety of the production strain

Production strain

The safety of *Trichoderma reesei* as an enzyme producer has been reviewed by *Nevalainen et al.; Olempska-Beer et al.; Blumenthal (1994; 2006; 2004)*. *T. reesei* is regarded as a safe organism for production of industrial enzymes.

The original *T. reesei* isolate, QM6a is the initial parental organism of practically all currently industrially relevant food enzyme production strains, including our strain RF11400. *Trichoderma reesei* has a long history (more than 30 years) of safe use in industrial-scale enzyme production *(Nevalainen et al. 1994; Olempska-Beer et al. 2006)*. Cellulases, hemicellulases, β-glucanases, pectinases and xylanases produced by this fungus are used in food, animal feed, pharmaceutical, textile, detergent, bioethanol and pulp and paper industries.

Food enzymes deriving from *Trichoderma reesei* strains (including recombinant *T. reesei* strains) have been evaluated by JECFA and many countries which regulate the use of food enzymes, such as the USA, France, Denmark, Australia and Canada, resulting in the approval of the use of food enzymes from *Trichoderma reesei* in the production of various foods, such as baking,

brewing, juice production, wine production and the production of dairy products.

Oy/Roal Oy starting from year 1987 and the parental strain RF4847 described here has been used from year 1995 on.

6.1.1 Pathogenicity and toxigenicity

Trichoderma reesei strains are non-pathogenic for healthy humans and animals (*Nevalainen et al. 1994)*. *Trichoderma reesei* is not present on the list of pathogens in the EU (Directive Council Directive2000/54/EC) and is present in major culture collections worldwide.

Trichoderma reesei is globally regarded as a safe microorganism:

- In the USA, *Trichoderma reesei* is not listed as a Class 2 or higher Containment Agent under the National Institute of Health (NIH, 1998) Guidelines for Recombinant DNA Molecules. Data submitted in Generally Recognized as Safe (GRAS) petitions to the Food and Drug Administration (FDA) for numerous enzyme preparations from *T. reesei* for human and animal consumption demonstrate that the enzymes are nontoxic. The Environmental Protection Institute (EPA) completed a risk assessment on *T. reesei* in 2011 resulting in a Proposed Rule in 2012, concluding that it is appropriate to consider *T. reesei* as a recipient microorganism eligible for exemptions from full reporting requirements[5], if this fungus was to be used in submerged standard industrial fermentation for enzyme production.

As a result, *Trichoderma reesei* can be used under the lowest containment level at large scale, GILSP, as defined by *(OECD, 1992)*.

The genus *Trichoderma* contains filamentous fungi which are frequently found on decaying wood and in soil. Industrial *T. reesei* strains have a long history of safe use and several of the

[5] reporting procedures in place under the Toxic Substances Control Act (TSCA) for new micro-organisms that are being manufactured for introduction into the commerce

Trichoderma based products have been approved for food and feed applications[6]. *T. reesei* is listed as a "Risk Group 1" organism according to German TRBA classification (Federal Institute for Occupational Safety and Health, www.baua.de) and as "Biosafety Level 1" organism by the American Type Culture Collection (www.atcc.org). *Trichoderma reesei* strains are non-pathogenic for healthy humans and animals. The DNA based identification methods have shown that *T. reesei* is taxonomically different from the other *Trichoderma* species of the section *Longibrachiatum (Druzhinina et al. 2005*).

Soome species belonging to *Trichoderma* genus are able to secrete various types of antibiotics in laboratory cultures. However, strains of *T. reesei* used in industrial applications are proven to be devoid of antibiotic activities (*Coenen et al. 1995; Hjortkjaer et al. 1986)*. The absence of antibiotic activities, according to the specifications recommended by JECFA (Food and Agriculture Organization of the United Nations 2006), was also confirmed for RF11400. The analyzed data are presented in appendix #2.

Additionally, the original host *T. reesei* RF4847 and the genetically modified strain do not carry any acquired antimicrobial resistance genes.

Conclusion: Based on the above mentioned available data, it is concluded that the organism *T. reesei*, has a long history of safe use in industrial-scale enzyme production and can be considered as a safe production organism for enzymes for food as well as feed processing and numerous other industrial applications. As an example, *T. reesei* strains have been cultivated in the production plant of Alko Oy/Roal Oy since 1987. During recent years, genetic engineering techniques have been used to improve the industrial production strains of *Trichoderma reesei* and considerable experience on the safe use of recombinant *Trichoderma reesei* strains at industrial scale has accumulated. From above, secondary metabolites are of no safety concern in fermentation products derived from *Trichoderma reesei*. Thus, *Trichoderma reesei* and its derivatives can be considered generally safe not only as a production organism of its natural enzymes, but also as a safe host for other safe gene products.

[6] AMFEP. 2009. Association of Manufacturers and Formulators of Enzyme Products List of enzyme products on markets; http://amfep.drupalgardens.com/sites/amfep.drupalgardens.com/files/Amfep-List-of-Commercial-Enzymes.pdf

6.1.1 Safety of the genetic modification

The genetic modification, e. g. integration into the genome of the recipient strain *T. reesei* RF10310 of the expression cassette results in the recombinant *Trichoderma reesei* strain RF11400. As described, the *T. reesei* RF11400 production strain differs from its original recipient strain (RF10310) in its high glucose oxidase production capability due to overexpression of the glucose oxidase gene driven by the improved *T.reesei* promoter.

Glucose oxidase (EC 1.1.3.4) catalyses the oxidation of β-D-glucose to D-glucono-1,5-lactone with the concomitant reduction of molecular oxygen to hydrogen peroxide.

Glucose oxidases have been used in the food and beverage industry for many years. When used in food applications glucose oxidase's function is to remove either glucose or oxygen. Typically, glucose oxidase is used to remove glucose, preventing product browning caused by Mailliard reaction which may occur during food processing (e.g. pasteurisation of powdered eggs and fruit processing) and other food processes involving high temperatures. Glucose oxidase is also used to lower alcohol content in wine production (through the removal of some of the glucose which would otherwise be converted into alcohol). Other examples are the oxygen removal from the top of bottled beverages before sealing, or mayonnaise production and gluconic acid production. Finally, glucose oxidase is also currently used to strenghten the protein complexes contained in starch-based products through increased formation of cross-links between proteins, thereby improving the quality of such foods as breads and other baked products.

The glucose oxidase described in this application was produced by submerged fermentation of a *Trichoderma reesei* RF11400 carrying the gene coding for glucose oxidase from *Penicillium*. The glucose oxidase gene was first synthesized using the preferred codon usage for *T. reesei* and placed under the control of the *Trichoderma reesei* modified *c*promoter and terminator.

The *Penicillium* glucose oxidase shows 81% identity with *P. chrysogenum* glucose oxidase and 63% identity with a glucose oxidase from *Aspergillus niger*. The *A. niger* glucose oxidase has been marketed as Gluzym by Novozymes and the glucose oxidase from *P. chrysogenum*

expressed in *A. niger* has been marketed as Bakezyme by DSM Food Specialities. These enzyme preparations are recognized as safe by the US FDA (GRAS Notice Inventory, GRN 106; GRAS Notice Inventory, GRN 509) and have been submitted to EFSA as well.

Based on the available information, it would be reasonable to conclude that the use of *P. amagasakiense* glucose oxidase gene for the production of glucose oxidase in *Trichoderma reesei* RF11400 does not lead to any particular safety concern.

The synthetic *acetamidase-encoding amdS gene* of *Aspergillus nidulans* is used as selectable marker. *A. nidulans* is closely related to *Aspergillus niger* which is used in industrial production of food enzymes. The product of the *amdS* gene, acetamidase (AmdS), can degrade acetamide which enables the strain to grow on media without any other nitrogen sources. The AmdS is not harmful or dangerous; the *amdS* marker gene has been widely used as a selection marker in fungal transformations without any disadvantage for more than 20 years.

The original host *T. reesei* RF4847 or the recipient strain RF10310 deriving from RF4847 does not carry any acquired antimicrobial resistance genes.

The transformed expression cassettes are fully characterized and free from potential hazards (as described above). The transformed DNAs are stably integrated into the fungal genome, and are no more susceptible to any further natural mutations than any other genes in the fungal genome. Also, the transformation does not increase the natural mutation frequency. The possibility of mutations is decreased to its minimum by inoculating the seed culture for the fermentation with controlled spore stocks that have been stored at -80°C and by keeping the vegetative state of the cultures to an inevitable minimum during production.

No additional growth/mutagenesis cycles have been performed after the RF11400 strain deposition in the culture collection. Therefore no reason can be seen that this genetic modification should have a negative effect on the safety properties.

Therefore, it can be concluded that *Trichoderma reesei* can be regarded as safe as the

recipient/parental organism to be used for production of enzymes for food and feed processing and that the *T. reesei* glucose oxidase enzyme preparation produced by *Trichoderma reesei* strain RF11400 is safe for use as a processing aid for food.

6.2 DATA FOR RISK ASSESSMENT

6.2.1 Toxicological testing

The following studies were performed:

— *In vitro* bacterial reverse mutation test Appendix #4

— *In vitro* mammalian micronucleus test Appendix #5

— 13-week oral toxicity study in rats Appendix #6

Glucose oxidase that has been tested is a dry ultra-filtrated concentrate, which is the most concentrated product before its formulation into a food enzyme preparation.

The batch that has been tested is batch No P14 0032J, which is representative of the commercial samples. All tests were performed according to the principles of Good Laboratory Practices (GLP) and the current OECD and EU guidelines.

Conclusions of the toxicity studies performed are given below.

AMES TEST

The test, based on OECD Guidelines No. 471 (OECD), was run at Eurofins BioPharma Product Testing Munich GmbH (Planegg/Munich) – Germany. The study was completed on July 13, 2015 and the report is summarized below.

This study was performed to investigate the potential of glucose oxydase produced with *Trichoderma reesei* RF11400 to induce gene mutations according to the plate incorporation test (experiment I) and the pre-incubation test (experiment II) using the *Salmonella typhimurium*

strains TA 1535, TA 1537, TA 98, TA 100, and TA 102.

Because the principal enzyme activity is a glucose oxidase that in the presence of glucose produces hydrogen peroxide, which is a well-known cytotoxic and mutagenic compound *in vitro* (causes cellular and sub-cellular oxidative damage, including damage to DNA), the glucose oxidase was inactivated by pH shift in order to ensure that secondary genetic mutations arising from potential hydrogen production would not occur.

The assay was performed in two independent experiments both with and without liver metabolic activation. The concentrations, including the controls, were tested in triplicate. The following concentrations of the test item were prepared and used in the experiments: 31.6; 100; 3.16; 1000; 2500; 5000 g/plate.

No precipitation of the test item was observed in any tester strain used in experiment I and II (with and without metabolic activation).
No toxic effect were noted in any of the five tester strains used up to the highest dose group evaluated (with and without metabolic activation) in experiment I and II.

No biological relevant increase in revertant colony numbers of any of the five tester strains were observed following treatment with glucose oxidase at any dose level, neither in the presence nor absence of metabolic activation in experiment I and II.

Appropriate reference mutagens were used as positive controls and induced a distinct increase of revertant colonies indicating the validity of the experiments.

In conclusion, it can be stated that during the described mutagenicity test and under the experimental conditions reported, the test item did not cause gene mutations by base pair changes or frameshifts in the genome of the tested strains used.

Therefore, the glucose oxidase from *Trichoderma reesei* RF11400 is considered to be non-mutagenic in this *Salmonella typhimurium* reverse mutation assay.

MAMMALIAN MICRONUCLEUS ASSAY IN HUMAN LYMPHOCYTES

The test, based on OECD Guidelines No. 487 (OECD, 2014), was run at Eurofins BioPharma Product Testing Munich GmbH (Planegg/Munich) – Germany. The study was completed on May 20th, 2015 and the report is summarized below.

The glucose oxidase from *Trichoderma reesei* RF11400 was assessed for its potential to induce structural micronuclei in human lymphocytes *in vitro* in two independent experiments. The following study design was performed:

	Without S9 mix		With S9 mix
	Experiment I	Experiment II	Experiment III
Exposure period	4 hrs	44 hrs	4 hrs
Cytochalasin B exposure	40 hrs	43 hrs	40 hrs
Preparation interval	44 hrs	44 hrs	44 hrs
Total culture period*	92 hrs	92 hrs	92 hrs

**exposure started 48h after culture initiation*

The selection of the concentrations was based on data from the pre-experiment. In experiment I without metabolic activation a concentration of 15 µg/mL and with metabolic activation a concentration of 275 µg/mL was selected as highest concentration for the microscopic analysis of micronuclei. In experiment II without metabolic activation a concentration of 2.5 µg/mL was selected as highest concentration for the microscopic analysis of micronuclei. The pH value detected with the test item solution was within the physiological range (7.0 ±0.4).

The following concentrations were evaluated for micronuclei frequencies:

Experiment I with short term exposure (4h):

- Without metabolic activation: 5, 10 and 15 µg/mL

- With metabolic activation: 50, 100, 200 and 275 µg/mL

Experiment II with long term exposure (44h):

- Without metabolic activation: 0.10, 0.25, 0.50, 1.0 and 2.5 µg/mL

No precipitate of the test item was noted in all concentrations groups evaluated in the main experiments at the end of the treatment (evaluated by unaided eye).

According to the OECD Guideline 487, the maximum of cytotoxicity should not exceed the limit of 55 ± 5%. Higher levels of cytotoxicity may induce chromosome damage as a secondary effect of cytotoxicity. According to laboratory experience a culture showing reduced cell viability (more than 30% rel. cytostasis) compared to the negative/solvent control displays cytotoxicity. Due to this, the limit of cytotoxicity is ≤70%. This corresponds to ≥30% of re. cytostasis.

In experiment I without metabolic activation no increase of the relative cytostasis above 30% was noted up to concentration of 10 g/mL. At a concentration of 15 µg/mL a relative cytostasis of 32% was noted. In experiment I with metabolic activation, no increase of the relative cytostasis above 30% was noted up to concentration of 50 µg/mL. At a concentration of 100 µg/mL a relative cytostasis of 33%, at a concentration of 200 µg/mL a relative cytostasis of 48% and at a concentration of 275 µg/mL a relative cytostasis of 60% was observed.

In experiment II without metabolic activation no increase of the relative cytostasis above 30% was noted up to concentration of 0.25 µg/mL. At a concentration of 0.50 µg/mL a relative cytostasis of 31%, at a concentration of 1.0 µg/mL a relative cytostasis of 50% and at a concentration of 2.5 µg/mL a relative cytostasis of 69% was noted.

In experiment I with and without metabolic activation and in experiment II without metabolic activation no biologically relevant increase of the micronucleus frequency was noted after treatment with the test item.

The non-parametric $_{\chi}2$ Test was performed to verify the results in both experiments. In

experiment I without metabolic activation a statistically significant enhancement (p=0.0191) of cells with micronuclei was noted at concentration of 10 µg/mL and in experiment I with metabolic activation a statistically significant enhancement (p=0.0011) of cells with micronuclei was noted at concentration of 275 µg/mL. However, the frequency of micronucleated cells was within the historical control limits of the negative control and significant cytotoxicity was observed for the concentration of 275 µg/mL with metabolic activation. Therefore, the increases were regarded as not biologically relevant. No statistically significant enhancement ($p<0.05$) of cells with micronuclei was noted in the concentration groups of the test item evaluated in experiment II.

The $_x2$ Test for trend was performed to test whether there is a concentration-related increase in the micronucleated cells frequency in the experiment conditions. No statistically significant increase was observed in experiment I and II without metabolic activation. In experiment I with metabolic activation a statistically significant increase of the micronucleated cells frequency was observed. However, since all values of the micronucleated cell frequency of this experimental condition were within the historical control limits of the negative control, this increase was regarded as not biologically relevant.

Appropriate clastogenic and aneugenic controls were applied. All induced distinct and statistically significant increases of the micronucleus frequency. This demonstrates the validity of the assay.

In conclusion, it can be stated that during the study described and under the experimental conditions reported, the test item did not induce structural and/or numerical chromosomal damage in human lymphocytes.

Therefore the glucose oxidase from *Trichoderma reesei* RF11400 is considered to be non-mutagenic with respect to clastogenicity and/or aneugenicity in the *in vitro* Mammalian Cell Micronucleus test.

Further *in vivo* tests were not performed, as there was no *in vitro* mutagenicity detected.

90 DAY ORAL TOXICITY STUDY

The test was performed according to the following guidelines: OECD No. 408 at Eurofins BSL Bioservice (Planegg/Munich) – Germany. The study was completed in July 2016 and the report is summarized below.

The aim of this study was to assess the possible health hazards which could arise from repeated exposure of Glucose oxidase produced with *Trichoderma reesei* via oral administration to rats over a period of 90 days.

The test item was administered daily in graduated doses to 3 groups of test animals, one dose level per group for a treatment period of 90 days. Animals of an additional control group were handled identically as the dose groups but received aqua ad injectionem (sterile water), the vehicle used in this study. The 4 groups comprised of 10 male and 10 female Wistar rats.

The following doses were evaluated:

- Control: 0 mg/kg body weight
- Low Dose: 100 mg/kg body weight
- Medium Dose: 300 mg/kg body weight
- High Dose: 1000 mg/kg body weight

The test item formulations were used not more than 10 days after preparation. The test item was dissolved in aqua ad injectionem and administered daily during a 90-day treatment period to male and female animals. Dose volumes were adjusted individually based on weekly body weight measurements.

During the period of administration, the animals were observed precisely each day for signs of toxicity. Animals no 54 and 71 that died was examined macroscopically and, surviving animals

were sacrificed at the conclusion of the test and observed macroscopically.

Body weight and food consumption were measured weekly. At the conclusion of the treatment period, all animals were sacrificed and subjected to necropsy. The wet weight of a subset of tissues was taken and a set of organs/tissues was preserved.

A full histopathological evaluation of the tissues was performed on high dose and control animals. Any gross lesion macroscopically identified will be examined microscopically in all animals.

Summary results:

The acceptance criteria for concentration of test item in dose formulations were met and homogeneity was confirmed.

No test item related mortality and no clinical signs of toxicity were observed in this study. Treatment with Glucose oxidase produced with *Trichoderma reesei* had no influence on neurobehavioural parameters examined at the end of the treatment period. Body weight developed normally in all groups independent of treatment and Glucose oxidase produced with Trichoderma reesei did not affect food consumption.

At the end of the treatment period parameters of haematology, blood coagulation and clinical biochemistry were not affected by Glucose oxidase produced with *Trichoderma reesei* in a biologically relevant way. Urinary parameters were not affected by Glucose oxidase produced with *Trichoderma reesei* in this study. At necropsy of the animals macroscopic findings observed in Glucose oxidase produced with *Trichoderma reesei* treated animals were either incidental or also present in control animals. None of them was considered toxicologically relevant.

Differences in organ weight between Glucose oxidase produced with *Trichoderma reesei* treated animals were slight and either not statistically significant or only present in one gender, but in any case not associated with any histopathological findings.

Moreover, Glucose oxidase produced with *Trichoderma reesei*, produced no histomorphologic evidence of toxicological properties in any organs and tissues examined.

Conclusion: On the basis of the present study, the 90-Day Repeated Dose Oral Toxicity study with Glucose oxidase produced with *Trichoderma reesei* in male and female Wistar rats, with dose levels of 100, 300, and 1000 mg/kg body weight day the following conclusions can be made:

There was no indicator for toxicity in any of the dose levels tested. Therefore, the NOEL may be established at 1000 mg/kg/day. Thus, the dose level of 1000 mg/kg/day also marks the NOAEL in this study.

Summarizing the results obtained from the several toxicity studies, the following conclusions can be drawn:

- No mutagenic or clastogenic activity under the given test conditions were observed;

The sub-chronic oral toxicity study showed a No Observed Adverse Effect Level (NOAEL) of at least 1,000 mg TOS/kg body weight/day.

7 PART 7 §170.255 – LIST OF SUPPORTING DATA AND INFORMATION

This section contains a list of all the data and literature discussed in this dossier to provide a basis that the notified substance is safe under the conditions of its intended use as described in accordance with §170.250 (a)(1). All information presented in this section are publically available.

Appendices

1. Decision Tree
2. Certificate of Analysis
3. Manufacturing Flow Chart
4. Reverse Mutation Test
5. Chromosome Aberration Test
6. 13 Week Oral Toxicity

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ANALYSIS OF SAFETY BASED ON PARIZA/JOHNSON DECISION TREE

Pariza and Johnson have published updated guidelines for the safety assessment of microbial enzyme preparations (2001)[1] from the 1991 IFBC Decision Tree[2]. The safety assessment of a given enzyme preparation is based upon an evaluation of the toxigenic potential of the production organism. The responses below follow the pathway indicated in the decision tree as outlined in Pariza and Johnson, 2001. The outcome of this inquiry is that glucose oxidase enzyme preparation from *Trichoderma reesei (T.reesei)* strain RF11400 expressing the gene encoding glucose oxidase from *Penicillium* is "ACCEPTED" as safe for its intended use.

Decision Tree:

1. **Is the production strain genetically modified?** *Trichoderma reesei* strain RF11400 was genetically modified to express glucose oxidase form *Penicillium*.
   Yes go to #2;

2. **Is the production strain modified using rDNA techniques?** Yes go to #3a;

3.

3a. Does the expressed enzyme product which is encoded by the introduced DNA have a history of safe use in food? Yes, Go to 3c;

3c. Is the test article free of transferable antibiotic resistance gene DNA? Yes, transferable DNA was not detected in the glucose oxidase enzyme preparation manufactured using *T. reesei* and production process described herein. Additionally, no antibiotic resistance gene has been integrated. Go to 3e;

3e. Is all other introduced DNA well characterized and free of attributes that would render it unsafe for constructing microorganisms to be used to produce food-grade products? Yes, inserted DNA is well characterized. Go to 4;

4. **Is the introduced DNA randomly integrated into the chromosome?** Yes, go to #5;

5. **Is the production strain sufficiently well characterized so that one may reasonably conclude that unintended pleiotropic effects which may result in the synthesis of**

[1] Pariza M.W. and Johnson E.A. Reg. Toxicol. Pharmacol. Vol. **33** (2001) 173-186

[2] IFBC (International Food Biotechnology Committee), Chapter 4: Safety Evaluation of Foods and Food Ingredients Derived from Microorganisms in Biotechnologies and Food: Assuring the Safety of Foods Produced by Genetic Modification, Regulatory Toxicology and Pharmacology. Vol. **12**:S1-S196 (1990).

toxins or other unsafe metabolites will not arise due to the genetic modification method that was employed? Yes, there is no concern for pleiotropic effects. Go to #6;

6. **Is the production strain derived from a safe lineage, as previously demonstrated by repeated assessment via this evaluation procedure?** Yes, *T. reesei* has been demonstrated as a safe production host and methods of modification have been well documented. Safety of this organism has been evaluated and confirmed through toxicological testing as described herein. **ACCEPTED**

Analytical report
RF11400
24.01.2017

Objective: **Chemical composition analysis of Glucose oxidase from *Trichoderma reesei* strain RF11400**

Sample: **1. Fermentation concentrate P160011I, LIMS ID 2016-635-1**
2. Fermentation concentrate 161130700, LIMS ID 2016-542-62

Table 1. Enzyme activity, presence of production strain and recombinant DNA and microbiological quality of the product

	P160011I	161130700
Glucose oxidase (GOX/g)	14100	13100
Presence of production strain (in 20 ml)	not detected	not detected
Recombinant DNA	not detected	not detected
Total viable count (cfu*/g)	<1000	<1000
Escherichia coli (in 25 g)	not detected	not detected
Salmonella (in 25 g)	not detected	not detected
Total coliforms (cfu*/g)	<1	<1
Lead (mg/kg)	<0,05	<0,05

GOX: Assay of glucose oxidase activity, Roal internal method B080
Production strain: Detection of production strain (Trichoderma, Aspergillus) M001, Roal internal
rDNA: Qualitative PCR for rDNA in food and feed enzymes, validated for the specific sequences
Total viable count: ISO 4833-1:2013
E. coli: SFS 4089:1998, mod.
Salmonella: NMKL 71:1999, mod.
Total coliforms: ISO 4832:2006, mod.
Lead: ISO 17294-2:2003
*cfu: colony forming units

Table 2. Nutritional analysis

	P160011I	161130700
Fat %	0,17	0,14
Protein %	15,8	11,7
Moisture %	78,6	82,8
Ash %	0,61	0,51
Carbohydrates %	4,82	4,85
Energy value (kJ/100 g)	357	287
TOS % Total organic solids [100-(moisture+ash)]	20,8	16,7

Fat: NMKL 131, Gravimetry
Protein: NMKL 6, Kjeldahl
Moisture: NMKL 23, Gravimetry
Ash: NMKL 173, Gravimetry
Carbohydrates: (EU) No 1169/2011, Calculation
Energy value: (EU) No 1169/2011, Calculation

Table 3. Mycotoxins (µg/kg)

	P160011I	161130700
Aflatoxin B1	<0,01	<0,01
Aflatoxin B2	<0,01	<0,01
Aflatoxin G1	<0,01	<0,01
Aflatoxin G2	<0,01	<0,01
Sum of aflatoxins B1+B2+G1+G2	<0,04	<0,04
Sterigmatocystin	<10	<10
Ochratoxin A	<2	<2
Deoxynivalenol	400	66
T2-Toxin	<10	<10
HT-2-Toxin	<10	<10
Fumonisin B1	<20	25
Fumonisin B2	<20	<20
Zearalenone	<10	110

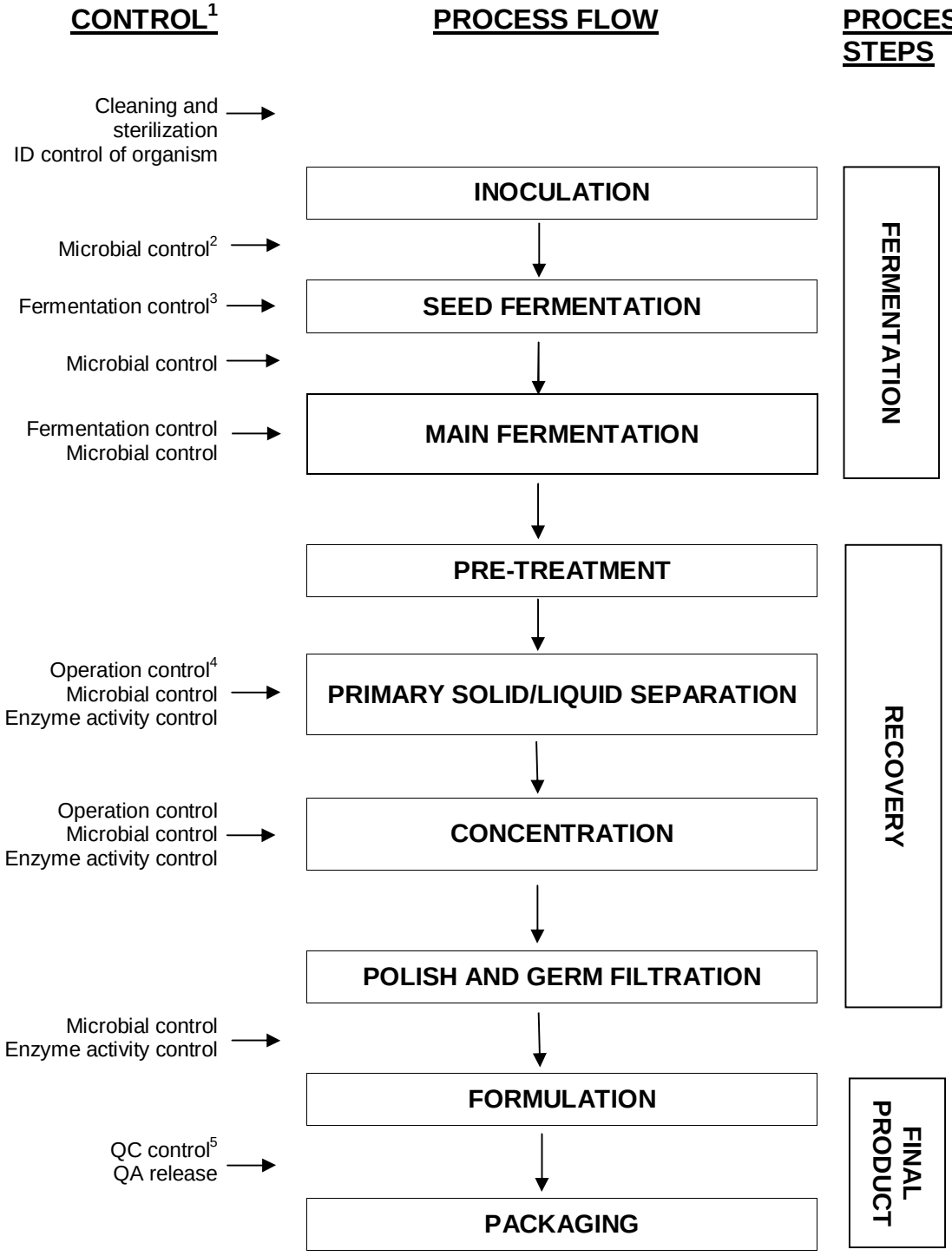
Aflatoxins: EN 15851, mod. IAC-LC-FLD
Sterigmatocystin: Internal Method LC-MS/MS
Ochratoxin A: Internal Method LC-MS/MS based on EN 14132 IAC-LC-FDL
Deoxynivalenol: Internal Method LC-MS/MS
T2- and HT-2Toxin: Internal Method LC-MS/MS
Fumonisin: Internal Method LC-MS/MS
Zearalenone: Internal Method LC-MS/MS

Rajamäki 24.01.2017

(b) (6)

Anni Honkanummi
Quality Management Coordinator
Roal Oy

Production Process of Food Enzymes from Fermentation



[1] The controls shown on the flow chart may vary depending on the production set-up. Controls are conducted at various steps throughout the production process as relevant.

[2] Microbial control: Absence of significant microbial contamination is analyzed by microscope or plate counts

[3] During fermentation parameters like e.g. pH, temperature, oxygen, CO_2, sterile air overflow are monitored / controlled.

[4] Operation control in downstream processes cover monitoring and control of parameters like e.g. pH, temperature

[5] Final QC control will check that product does live up to specifications like e.g. enzyme activity as well as chemical and microbial specification.

eurofins | BioPharma Product Testing

Reverse Mutation Assay using Bacteria (*Salmonella typhimurium*) with Glucose oxidase produced with *Trichoderma reesei*

Report

Version: Final

Study Completion Date: 21 JUL 2015

Eurofins Munich Study No.: 153281

Sponsor:
AB Enzymes GmbH
Feldbergstr. 78
64293 Darmstadt
Germany

Eurofins BioPharma Product Testing Munich GmbH
Behringstr. 6/8
D-82152 Planegg/Munich
Germany

Tel +49 (0)89 899 650-0
Fax +49 (0)89 899 650-11

GLP / GMP FDA approved

1. Copy of the GLP Certificate

Bayerisches Landesamt für
Gesundheit und Lebensmittelsicherheit

GLP-Bescheinigung/Statement of GLP Compliance
(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at

☒ Prüfeinrichtung/Test facility ☐ Prüfstandort/Test site

EUROFINS BIOPHARMA PRODUCT TESTING MUNICH GMBH
BEHRINGSTRAßE 6-8
82152 PLANEGG

(Unverwechselbare Bezeichnung und Adresse/Unequivocal name and address)

Prüfungen nach Kategorien/Areas of Expertise
(gemäß/according ChemVwV-GLP Nr. 5.3/OECD guidance)

Kategorie 2/ Category 2
Kategorie 3/ Category 3
Kategorie 8/ Category 8
Kategorie 9*/ Category 9*

*Sonstige Prüfungen:	*other tests:
biologische und mikrobiologische Sicherheitsprüfungen an Medizinprodukten und Arzneimitteln; Auftragsarchivierung	*biological an microbiological safety evaluation on medical devices and pharmaceuticals; contract archiving*

Datum der Inspektion/Date of Inspection
(Tag.Monat.Jahr/day.month.year)

18. bis 19.03.2015

Die/Der genannte Prüfeinrichtung/Prüfstandort befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility/test site is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung/diesem Prüfstandort die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.

Based on the inspection report it can be confirmed, that this test facility/test site is able to conduct the aforementioned studies in compliance with the Principles of GLP

Schwabach, 05.06.2015

(b) (6)

Dr. Peter Franke
Leiter der GLP-Landesleitstelle Bayern

GLP- Landesleitstelle Bayern
Bayerisches Landesamt für Gesundheit
und Lebensmittelsicherheit
Rathausgasse 4
91126 Schwabach

2. Contents

3. List of Tables

4. Preface

4.1. Abbreviations

2-AA	2-aminoanthracene
4-NOPD	4-nitro-o-phenylene-diamine
A. dest.	Aqua destillata *(purified water)*
Art.	Artikel *(article)*
BGBl.	Bundesgesetzblatt *(Federal Law Gazette)*
bio	biotin
cf.	confer
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
EC	European Community
e.g.	exempli gratia *(for example)*
EPA	Environmental Protection Agency
Eurofins Munich	Eurofins BioPharma Product Testing Munich GmbH
GLP	Good Laboratory Practice
GmbH	Gesellschaft mit beschränkter Haftung *(company with limited liability)*
his	histidine
mg/kg/bw	milligram/kilogram/body weight
MMS	methylmethanesulfonate
NaCl	sodium chloride
NADP	nicotinamide adenine dinucleotide phosphate
NaN_3	sodium azide
OECD	Organisation for Economic Cooperation and Development
OPPTS	Office of Prevention, Pesticides and Toxic Substances
QAU	Quality Assurance Unit
rfa	deep rough factor
RSD	relative standard deviation
S9	microsomal fraction of rat liver homogenate
SD	Standard Deviation
SOPs	Standard Operating Procedures
uvrB	repair mutant, UV light sensitive
v/v	volume per volume

4.2. General

Sponsor:	AB Enzymes GmbH Feldbergstr. 78 64293 Darmstadt Germany
Study Monitor:	Dr. Hans-Jürgen Schepers
Test Facility:	Eurofins BioPharma Product Testing Munich GmbH Behringstraße 6/8 82152 Planegg Germany
Eurofins Munich Study No.:	153281
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	Reverse Mutation Assay using Bacteria (*Salmonella typhimurium*) with Glucose oxidase produced with *Trichoderma reesei*

4.3. Project Staff

Study Director:	Dipl.-Biol. Gudrun Schreib
Management:	Dr. Angela Lutterbach Dr. Katrin Witschital
Head of GLP Quality Assurance Unit:	Dipl.-Biol. Carolin Schmidt

4.4. Schedule

Arrival of the Test Item:	11 June 2015
Study Initiation Date:	19 June 2015
Experimental Starting Date:	23 June 2015
Experimental Completion Date:	13 July 2015

5. Quality Assurance

5.1. GLP Compliance

This study was conducted to comply with:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

OECD Principles of Good Laboratory Practice (as revised in 1997); OECD Environmental Health and Safety Publications; Series on Principles of Good Laboratory Practice and Compliance Monitoring - Number 1. Environment Directorate, Organisation for Economic Co-operation and Development, Paris 1998 [3].

The OECD Principles of Good Laboratory Practice are accepted by regulatory authorities throughout the European Community, USA and Japan.

This study was assessed for compliance with the study plan and the Standard Operating Procedures of Eurofins Munich. The study and/or the test facility are inspected periodically by the Quality Assurance Unit according to the corresponding SOPs. These inspections and audits are carried out by the Quality Assurance Unit, personnel independent of staff involved in the study. A signed quality assurance statement, listing all performed audits, is included in the report.

5.2. Guidelines

This study followed the procedures indicated by internal Eurofins Munich SOPs and the following internationally accepted guidelines and recommendations:

Ninth Addendum to OECD Guidelines for Testing of Chemicals, Section 4, No. 471, "Bacterial Reverse Mutation Test", adopted 21st July, 1997. [4]

Commission Regulation (EC) No. 440/2008 B.13/14:"Mutagenicity – Reverse Mutation Test using Bacteria", dated May 30, 2008. [5]

EPA Health Effects Test Guidelines, OPPTS 870.5100 "Bacterial Reverse Mutation Assay" EPA 712-C-98-247, August 1998. [6]

5.3. Archiving

For a period of 15 years (or shorter if in compliance with the GLP regulations) Eurofins Munich will store the records, materials and specimens in their scientific archives according to the GLP regulations.

The following records have to be stored according to the GLP regulations:

A copy of the final report, the study plan and documentation of all raw data generated during the conduct of the study (documentation forms as well as any other notes of raw data, printouts of instruments and computers) and the correspondence with the sponsor concerning the study. Any document relating to the study will be discarded only with the prior consent of the sponsor.

The following materials and samples have to be stored according to the period of time specified in the GLP regulations:

A retained sample of the test item will be archived according to the GLP regulations, if possible, and will be discarded without the sponsor's prior consent.

Other materials and specimens have to be stored according to the GLP regulations and disposed of after the respective archiving period with the sponsor's prior consent.

As requested the remaining test item will be returned to the sponsor.

6. Statement of Compliance

Eurofins Munich Study No.:	153281
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	Reverse Mutation Assay using Bacteria (*Salmonella typhimurium*) with Glucose oxidase produced with *Trichoderma reesei*
Study Director:	Dipl.-Biol. Gudrun Schreib

This study performed in the test facility Eurofins Munich was conducted in compliance with Good Laboratory Practice Regulations:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

"OECD Principles of Good Laboratory Practice (as revised in 1997)", Paris 1998 [3].

There were no circumstances that may have affected the quality or integrity of the study.

Study Director: Dipl.-Biol. Gudrun Schreib

(b) (6)

Date: 21 JUL 2015

7. Statement of the Quality Assurance Unit

Eurofins Munich Study No.:	153281
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	Reverse Mutation Assay using Bacteria (*Salmonella typhimurium*) with Glucose oxidase produced with *Trichoderma reesei*
Study Director:	Dipl.-Biol. Gudrun Schreib

This report and the conduct of this study were inspected by the Quality Assurance Unit on the following dates:

Phase of QAU Inspection	Date of QAU Inspection	Date of Reporting to the Study Director and Management
Audit Final Study Plan:	19 June 2015	19 June 2015
Audit Experimental Phase (process-based):	16 February 2015	16 February 2015
Audit Final Report:	21 JUL 2015	21 JUL 2015

This report reflects the raw data.

Member of the
Quality Assurance Unit: (b) (6)

Print Name: Katrin Seidel

Date: 21 Jul 2015

8. Summary

8.1. Summary Results

In order to investigate the potential of Glucose oxidase produced with *Trichoderma reesei* for its ability to induce gene mutations the plate incorporation test (experiment I) and the pre-incubation test (experiment II) were performed with the *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 102.

In two independent experiments several concentrations of the test item were used. Each assay was conducted **with** and **without** metabolic activation. The concentrations, including the controls, were tested in triplicate. The following concentrations of the test item were prepared and used in the experiments:

31.6, 100, 316, 1000, 2500 and 5000 µg/plate

No precipitation of the test item was observed in any tester strain used in experiment I and II (**with** and **without** metabolic activation).

No toxic effects of the test item were noted in any of the five tester strains used up to the highest dose group evaluated (**with** and **without** metabolic activation) in experiment I and II.

No biologically relevant increases in revertant colony numbers of any of the five tester strains were observed following treatment with Glucose oxidase produced with *Trichoderma reesei* at any concentration level, neither in the presence nor absence of metabolic activation in experiment I and II.

The reference mutagens induced a distinct increase of revertant colonies indicating the validity of the experiments.

8.2. Conclusion

In conclusion, it can be stated that during the described mutagenicity test and under the experimental conditions reported, Glucose oxidase produced with *Trichoderma reesei* did not cause gene mutations by base pair changes or frameshifts in the genome of the tester strains used.

Therefore, Glucose oxidase produced with *Trichoderma reesei* is considered to be non-mutagenic in this bacterial reverse mutation assay.

9. Introduction

9.1. Aim of the Study

Bacterial reverse mutation assays use amino acid requiring strains of *Salmonella typhimurium* to detect point mutations, which involve substitution, addition or deletion of one or a few DNA base pairs. The principle of these bacterial reversion assays is that they detect mutations which functionally reverse mutations present in the tester strains and restore the capability to synthesise an essential amino acid [7], [9], [12].

The purpose of this study is to establish the potential of the test item to induce gene mutations in bacteria by means of a *S. typhimurium* reverse mutation assay. There is no requirement for verification of a clear positive response. Equivocal results should be clarified by further testing preferably using a modification of experimental conditions. Negative results need to be confirmed on a case-by-case basis. Modification of study parameters to extend the range of conditions assessed should be considered in follow-up experiments. Study parameters that might be modified include the concentrations spacing and / or the method of treatment (pre-incubation method). In case of severe toxicity of the test item or the use of ethanol as the most appropriate solvent, the confirmatory experiment is carried out according to the plate incorporation method with a different spacing between dose levels.

The *Salmonella typhimurium* histidine (his) reversion system measures $his^- \rightarrow his^+$ reversions. The *S. typhimurium* strains are constructed to differentiate between base pair (TA 100, TA 1535, TA 102) and frameshift (TA 98, TA 1537) mutations [12].

These assays directly measure heritable DNA mutations of a type which is associated with adverse effects [13], [14], [16], [17]. Point mutations are the cause of many human genetic diseases and there is substantial evidence that somatic cell point mutations in oncogenes and tumour suppressor genes are involved in cancer in humans and experimental systems [8].

The tester strains have several features that make them more sensitive for the detection of mutations. The specificity of the strains can provide useful information on the types of mutations that are induced by mutagenic agents.

According to the direct plate incorporation or the pre-incubation method the bacteria are exposed to the test item with and without metabolic activation and plated on selective medium. After a suitable period of incubation, revertant colonies are counted [12].

At least five different concentrations of the test item are tested with approximately half log (i.e. $\sqrt{10}$) intervals between test points for an initial test. More narrow spacing between dose levels may be appropriate when a dose response is investigated. For soluble, non-toxic test compounds the recommended maximum test concentration is 5 mg/plate or 5 µL/plate.

To validate the test, reference mutagens are tested in parallel to the test item [10].

9.2. Justification for the Selection of the Test System

The OECD Guideline for Testing of Chemicals, Section 4, No. 471 – Bacterial Reverse Mutation Test - recommends using a combination of *S. typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 102.

10. Materials and Methods

10.1. Characterisation of the Test Item

The identity of the test item was inspected upon delivery at the test facility (e.g. test item name, batch no. and additional data were compared with the label) based on the following specifications provided by the sponsor.

Name:	Glucose oxidase produced with *Trichoderma reesei*
Chemical Name:	Glucose oxidase (food enzyme)
State of Enzyme Activity:	inactivated
Batch No.:	P 140032 J
Expiry Date:	September 2016
Physical State at Room Temperature:	liquid
Colour:	light-brown
Purity:	9.2% TOS (Total Organic Substance, rounded; 1/10 of the powder) (see 16.2 Certificate of Analysis)
Storage Conditions:	if still in liquid form: 2 – 8°C if still frozen: ≤ -20°C, protected from light
Safety Precautions:	The routine hygienic procedures were sufficient to assure personnel health and safety.

10.2. Preparation of the Test Item

The test item was suspended in A. dest., processed by ultrasound for 5 min at 37 °C and diluted prior to treatment. The solvent was compatible with the survival of the bacteria and the S9 activity. All concentrations used were calculated based on the TOS value of the test item (9.2%). For this purpose a correction factor of 10.87 was applied.

10.3. Controls

Solvent and/or negative as well as positive controls were included in each experiment. Strain specific positive controls were included in the assay, which demonstrated the effective performance of the test.

Negative/Solvent Controls

Negative/solvent controls (A. dest., Eurofins Munich, Lot No. 150603) were treated in the same way as all dose groups.

Positive Controls

Without metabolic activation

Tester Strains:	*S. typhimurium*: TA 100, TA 1535
Name:	NaN_3; sodium azide
Supplier:	Sigma
Catalogue No.:	S2002
Batch No.:	BCBN6481V
Dissolved in:	A. dest.
Concentration:	10 µg/plate

Tester Strains:	*S. typhimurium*: TA 98, TA 1537
Name:	4-NOPD; 4-nitro-o-phenylene-diamine
Supplier:	Fluka
Catalogue No.:	73630
Batch No.:	MKBC3223
Dissolved in:	DMSO
Concentrations:	10 µg/plate for TA 98, 40 µg/plate for TA 1537

Tester Strain:	*S. typhimurium*: TA 102
Name:	MMS; methylmethanesulfonate
Supplier:	Sigma
Catalogue No.:	M 4016
Batch No.:	MKBL6789V
Dissolved in:	A. dest.
Concentration:	1 µL/plate

With metabolic activation

Tester Strains:	*S. typhimurium*: TA 98, TA 100, TA 1535, TA 1537 and TA 102
Name:	2-AA; 2-aminoanthracene
Supplier:	Aldrich
Catalogue No.:	A3, 880-0
Batch No.:	STBD3302V
Dissolved in:	DMSO
Concentrations:	2.5 µg/plate; 10 µg/plate for TA 102

The stability of the positive control substances in solution is unknown but a mutagenic response in the expected range is sufficient evidence of biological stability

10.4. Test System

10.4.1. Bacteria

Five strains of *S. typhimurium* with the following characteristics were used:

TA 98: his D 3052; rfa$^-$; uvrB$^-$; R-factor:	frame shift mutations
TA 100: his G 46; rfa$^-$; uvrB$^-$; R-factor:	base-pair substitutions
TA 1535: his G 46; rfa$^-$; uvrB$^-$:	base-pair substitutions
TA 1537: his C 3076; rfa$^-$; uvrB$^-$:	frame shift mutations
TA 102: his G 428 (pAQ1); rfa$^-$; R-factor:	base-pair substitutions

Tester strains TA 98, TA 1535 and TA 102 were obtained from MOLTOX, INC., NC 28607, USA. Tester strains TA 100 and TA 1537 were obtained from Xenometrix AG, Switzerland. They were stored as stock cultures in ampoules with nutrient broth (OXOID) supplemented with DMSO (approx. 8% v/v) over liquid nitrogen.

All Salmonella strains contain mutations in the histidine operon, thereby imposing a requirement for histidine in the growth medium. They contain the deep rough (rfa) mutation, which deletes the polysaccharide side chain of the lipopolysaccharides of the bacterial cell surface. This increases cell permeability of larger substances. The other mutation is a deletion of the uvrB gene coding for a protein of the DNA nucleotide excision repair system resulting in an increased sensitivity in detecting many mutagens. This deletion also includes the nitrate reductase (chl) and biotin (bio) genes (bacteria require biotin for growth).

The tester strains TA 98, TA 100 and TA 102 contain the R-factor plasmid, pkM101. These strains are reverted by a number of mutagens that are detected weakly or not at all with the non R-factor parent strains. pkM101 increases chemical and spontaneous mutagenesis by enhancing an error-prone DNA repair system which is normally present in these organisms [12], [15].

The properties of the *S. typhimurium* strains with regard to membrane permeability, ampicillin- and tetracycline-resistance as well as normal spontaneous mutation rates are checked regularly according to Ames *et al.* [7]. In this way it is ensured that the experimental conditions set up by Ames are fulfilled.

10.4.2. Preparation of Bacteria

Samples of each tester strain were grown by culturing for 12 h at 37 °C in Nutrient Broth to the late exponential or early stationary phase of growth (approx. 10^9 cells/mL). The nutrient medium consists per litre:

8 g	Nutrient Broth
5 g	NaCl

A solution of 125 µL ampicillin (10 mg/mL) (TA 98, TA 100, TA 102) was added in order to retain the phenotypic characteristics of the strain.

10.4.3. Agar Plates

The Vogel-Bonner Medium E agar plates with 2% glucose used in the Ames Test were prepared by Eurofins Munich or provided by an appropriate supplier. Quality controls were performed.

Vogel-Bonner-salts contain per litre:

10 g	$MgSO_4 \times 7\ H_2O$
100 g	citric acid
175 g	$NaNH_4HPO_4 \times 4\ H_2O$
500 g	K_2HPO_4

Sterilisation was performed for 20 min at 121 °C in an autoclave.

Vogel-Bonner Medium E agar plates contain per litre:

15 g	Agar Agar
20 mL	Vogel-Bonner salts
50 mL	glucose-solution (40%)

Sterilisation was performed for 20 min at 121 °C in an autoclave.

10.4.4. Overlay Agar

The overlay agar contains per litre:

7.0 g	Agar Agar
6.0 g	NaCl
10.5 mg	L-histidine x HCl x H_2O
12.2 mg	biotin

Sterilisation was performed for 20 min at 121 °C in an autoclave.

10.4.5. Mammalian Microsomal Fraction S9 Mix

The bacteria most commonly used in these reverse mutation assays do not possess the enzyme system which, in mammals, is known to convert promutagens into active DNA damaging metabolites. In order to overcome this major drawback an exogenous metabolic system was added in the form of mammalian microsome enzyme activation mixture.

10.4.6. S9 Homogenate

The S9 liver microsomal fraction was prepared at Eurofins Munich. Male Wistar rats were induced with phenobarbital (80 mg/kg bw) and β-naphthoflavone (100 mg/kg bw) for three consecutive days by oral route.

The following quality control determinations are performed:

a) Biological activity in the *Salmonella typhimurium* assay using 2-aminoanthracene and benzo[*a*]pyrene

b) Sterility Test

A stock of the supernatant containing the microsomes was frozen in aliquots of 2 and 4 mL and stored at ≤-75 °C.

The protein concentration in the S9 preparation (Lot: 060315B) was 34.0 mg/mL.

10.4.7. Preparation of S9 Mix

The S9 mix preparation was performed according to Ames *et al.* [7].

100 mM of sodium-ortho-phosphate-buffer, pH 7.4, was ice-cold added to the following pre-weighed sterilised reagents to give final concentrations in the S9 mix of:

8	mM	$MgCl_2$
33	mM	KCl
5	mM	glucose-6-phosphate
4	mM	NADP

This solution was mixed with the liver 9000 x g supernatant fluid in the following proportion:

co-factor solution	9.5 parts
liver preparation	0.5 parts

During the experiment the S9 mix was stored on ice.

10.4.8. S9 Mix Substitution Buffer

The S9 mix substitution buffer was used in the study as a replacement for S9 mix, without metabolic activation (-S9).

Phosphate-buffer (0.2 M) contains per litre:

0.2 M $NaH_2PO_4 \times H_2O$	120 mL
0.2 M Na_2HPO_4	880 mL

The two solutions were mixed and the pH was adjusted to 7.4. Sterilisation was performed for 20 min at 121 °C in an autoclave.

This 0.2 M phosphate-buffer was mixed with 0.15 M KCl solution (sterile) in the following proportion:

0.2 M phosphate-buffer	9.5 parts
0.15 M KCl solution	0.5 parts

This S9 mix substitution buffer was stored at 4 °C.

10.5. Experimental Design

10.5.1. Pre-Experiment for Toxicity

The toxicity of the test item was determined with tester strains TA 98 and TA 100 in a pre-experiment. Eight concentrations were tested for toxicity and induction of mutations with three plates each. The experimental conditions in this pre-experiment were the same as described below for the main experiment I (plate incorporation test).

Toxicity may be detected by a clearing or rather diminution of the background lawn or a reduction in the number of revertants down to a mutation factor of approximately ≤ 0.5 in relation to the solvent control.

The test item was tested in the pre-experiment with the following concentrations:

3.16, 10.0, 31.6, 100, 316, 1000, 2500 and 5000 µg/plate

10.5.2. Exposure Concentrations

The test item concentrations to be applied in the main experiments were chosen according to the results of the pre-experiment (see chapter 12.1.1 Pre-Experiment). 5000 µg/plate was selected as the maximum concentration. The concentration range covered two logarithmic decades. Two independent experiments were performed with the following concentrations:

31.6, 100, 316, 1000, 2500 and 5000 µg/plate

As the results of the pre-experiment were in accordance with the criteria described above, these were reported as a part of the main experiment I.

10.5.3. Experimental Performance

For the plate incorporation method the following materials were mixed in a test tube and poured over the surface of a minimal agar plate:

- 100 µL Test solution at each dose level, solvent control, negative control or reference mutagen solution (positive control),
- 500 µL S9 mix (for testing with metabolic activation) or S9 mix substitution buffer (for testing without metabolic activation),
- 100 µL Bacteria suspension (cf. Preparation of Bacteria, pre-culture of the strain),
- 2000 µL Overlay agar.

For the pre-incubation method 100 µL of the test item preparation was pre-incubated with the tester strains (100 µL) and sterile buffer or the metabolic activation system (500 µL) for 60 min at 37 °C prior to adding the overlay agar (2000 µL) and pouring onto the surface of a minimal agar plate.

For each strain and dose level, including the controls, three plates were used.

After solidification the plates were inverted and incubated at 37 °C for at least 48 h in the dark.

10.6. Data Recording

The colonies were counted using a ProtoCOL counter (Meintrup DWS Laborgeräte GmbH). If precipitation of the test item precluded automatic counting the revertant colonies were counted by hand. In addition, tester strains with a low spontaneous mutation frequency like TA 1535 and TA 1537 were counted manually.

10.7. Evaluation of Cytotoxicity

Cytotoxicity can be detected by a clearing or rather diminution of the background lawn (indicated as "N" or "B", respectively in the result tables) or a reduction in the number of revertants down to a mutation factor of approximately ≤ 0.5 in relation to the solvent control.

10.8. Criteria of Validity

A test is considered acceptable if for each strain:

- the bacteria demonstrate their typical responses to ampicillin (TA 98, TA 100, TA 102)
- the negative control plates (A. dest.) with and without S9 mix are within the following ranges (mean values of the spontaneous reversion frequency are within the historical control data range (2012 -2014)):

	- S9		+ S9	
	min	max	min	max
TA 98	13	48	13	61
TA 100	61	182	68	194
TA 1535	4	35	4	34
TA 1537	2	27	3	31
TA 102	136	415	91	495

- corresponding background growth on negative control, solvent control and test plates is observed
- the positive controls show a distinct enhancement of revertant rates over the control plate
- at least five different concentrations of each tester strain are analysable.

10.9. Evaluation of Mutagenicity

The Mutation Factor is calculated by dividing the mean value of the revertant counts by the mean values of the solvent control (the exact and not the rounded values are used for calculation).

A test item is considered as mutagenic if:

- a clear and dose-related increase in the number of revertants occurs and/or
- a biologically relevant positive response for at least one of the dose groups occurs

in at least one tester strain with or without metabolic activation.

A biologically relevant increase is described as follows:

- if in tester strains TA 98, TA 100 and TA 102 the number of reversions is at least twice as high
- if in tester strains TA 1535 and TA 1537 the number of reversions is at least three times higher

than the reversion rate of the solvent control [11].

According to OECD guidelines, the biological relevance of the results is the criterion for the interpretation of results, a statistical evaluation of the results is not regarded as necessary.

A test item producing neither a dose related increase in the number of revertants nor a reproducible biologically relevant positive response at any of the dose groups is considered to be non-mutagenic in this system.

11. Deviations from the Study Plan

There were no deviations from the study plan.

12. Results and Discussion

12.1. Results

12.1.1. Pre-Experiment

Toxicity may be detected by a clearing or rather diminution of the background lawn or a reduction in the number of revertants down to a mutation factor of approximately ≤ 0.5 in relation to the solvent control.

Table 1: Results Pre-Experiment

Substance	Dose (µg/plate)	TA 98 Mutation Factor [toxicity]*		TA 100 Mutation Factor [toxicity]*	
		without S9	with S9	without S9	with S9
Solvent Control (A. dest)		1.0	1.0	1.0	1.0
4-NOPD	10.0	11.9	-	-	-
NaN_3	10.0	-	-	5.8	-
2-AA	2.50	-	91.4	-	23.6
Test Item	3.16	1.4	1.2	1.1	1.0
	10.0	1.3	1.0	1.0	1.1
	31.6	1.0	1.1	0.9	1.0
	100	1.3	0.9	1.0	0.9
	316	1.3	1.1	0.9	0.9
	1000	1.5	1.2	1.1	1.0
	2500	1.2	1.4	1.2	1.2
	5000	1.3	1.1	1.1	1.0

* [toxicity parameter]: B = Background lawn reduced; N = No background lawn

12.1.2. Experiment I *(Plate-incorporation Test)*

Table 2: Results Experiment I

Tester Strain: TA 98 Experiment: 1

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		23 16 21	**20**	3.6	26 24 28	**26**	2.0	**1.0**	**1.0**
Test Item	31.6 µg	23 16 18	**19**	3.6	32 28 23	**28**	4.5	**1.0**	**1.1**
Test Item	100 µg	15 35 29	**26**	10.3	24 18 31	**24**	6.5	**1.3**	**0.9**
Test Item	316 µg	31 28 19	**26**	6.2	30 29 29	**29**	0.6	**1.3**	**1.1**
Test Item	1000 µg	23 38 28	**30**	7.6	15 36 44	**32**	15.0	**1.5**	**1.2**
Test Item	2500 µg	20 29 23	**24**	4.6	33 38 40	**37**	3.6	**1.2**	**1.4**
Test Item	5000 µg	26 28 26	**27**	1.2	27 27 32	**29**	2.9	**1.3**	**1.1**
4-NOPD	10 µg	242 231 243	**239**	6.7	/ / /	**/**	/	**11.9**	**/**
2-AA	2.5 µg	/ / /	**/**	/	2439 2484 2207	**2377**	148.6	**/**	**91.4**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 100

Experiment: 1

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		113 95 87	**98**	13.3	107 108 105	**107**	1.5	**1.0**	**1.0**
Test Item	31.6 µg	98 89 81	**89**	8.5	129 99 99	**109**	17.3	**0.9**	**1.0**
Test Item	100 µg	110 83 90	**94**	14.0	98 111 93	**101**	9.3	**1.0**	**0.9**
Test Item	316 µg	102 88 88	**93**	8.1	91 97 101	**96**	5.0	**0.9**	**0.9**
Test Item	1000 µg	120 113 94	**109**	13.5	104 106 108	**106**	2.0	**1.1**	**1.0**
Test Item	2500 µg	120 129 111	**120**	9.0	133 137 111	**127**	14.0	**1.2**	**1.2**
Test Item	5000 µg	110 111 99	**107**	6.7	103 129 102	**111**	15.3	**1.1**	**1.0**
NaN_3	10 µg	491 530 683	**568**	101.5	/ / /	/	/	**5.8**	/
2-AA	2.5 µg	/ / /	/	/	2656 2491 2408	**2518**	126.2	/	**23.6**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 1535

Experiment: 1

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		3 10 15	**9**	6.0	9 8 12	**10**	2.1	**1.0**	**1.0**
Test Item	31.6 µg	5 6 10	**7**	2.6	8 10 16	**11**	4.2	**0.8**	**1.2**
Test Item	100 µg	4 8 9	**7**	2.6	0 2 8	**3**	4.2	**0.8**	**0.3**
Test Item	316 µg	9 11 13	**11**	2.0	6 6 11	**8**	2.9	**1.2**	**0.8**
Test Item	1000 µg	8 9 12	**10**	2.1	8 10 12	**10**	2.0	**1.0**	**1.0**
Test Item	2500 µg	6 10 12	**9**	3.1	6 12 14	**11**	4.2	**1.0**	**1.1**
Test Item	5000 µg	9 11 14	**11**	2.5	5 8 12	**8**	3.5	**1.2**	**0.9**
NaN_3	10 µg	359 379 400	**379**	20.5	/ / /	**/**	/	**40.6**	**/**
2-AA	2.5 µg	/ / /	**/**	/	79 75 123	**92**	26.6	**/**	**9.6**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn

P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 1537

Experiment: 1

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		12 15 26	**18**	7.4	7 8 10	**8**	1.5	**1.0**	**1.0**
Test Item	31.6 µg	9 12 13	**11**	2.1	14 19 20	**18**	3.2	**0.6**	**2.1**
Test Item	100 µg	16 16 19	**17**	1.7	8 11 20	**13**	6.2	**1.0**	**1.6**
Test Item	316 µg	13 15 17	**15**	2.0	10 13 14	**12**	2.1	**0.8**	**1.5**
Test Item	1000 µg	10 14 20	**15**	5.0	6 22 25	**18**	10.2	**0.8**	**2.1**
Test Item	2500 µg	22 22 24	**23**	1.2	26 26 28	**27**	1.2	**1.3**	**3.2**
Test Item	5000 µg	19 24 33	**25**	7.1	18 20 27	**22**	4.7	**1.4**	**2.6**
4-NOPD	40 µg	131 92 109	**111**	19.6	/ / /	**/**	/	**6.3**	**/**
2-AA	2.5 µg	/ / /	**/**	/	264 243 262	**256**	11.6	**/**	**30.8**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 102

Experiment: 1

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		217 198 194	**203**	12.3	268 224 234	**242**	23.1	**1.0**	**1.0**
Test Item	31.6 µg	276 245 233	**251**	22.2	256 252 245	**251**	5.6	**1.2**	**1.0**
Test Item	100 µg	179 182 165	**175**	9.1	234 200 220	**218**	17.1	**0.9**	**0.9**
Test Item	316 µg	147 137 166	**150**	14.7	188 179 182	**183**	4.6	**0.7**	**0.8**
Test Item	1000 µg	160 164 177	**167**	8.9	214 193 212	**206**	11.6	**0.8**	**0.9**
Test Item	2500 µg	210 204 220	**211**	8.1	274 231 220	**242**	28.5	**1.0**	**1.0**
Test Item	5000 µg	201 176 206	**194**	16.1	195 221 260	**225**	32.7	**1.0**	**0.9**
MMS	1 µL	536 1032 1141	**903**	322.5	/ / /	/	/	**4.4**	/
2-AA	10 µg	/ / /	/	/	858 859 939	**885**	46.5	/	**3.7**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

12.1.3. Experiment II *(Pre-incubation Test)*

Table 3: Results Experiment II

Tester Strain: TA 98 Experiment: 2

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		36 26 23	**28**	6.8	37 39 39	**38**	1.2	**1.0**	**1.0**
Test Item	31.6 µg	24 23 25	**24**	1.0	31 34 36	**34**	2.5	**0.8**	**0.9**
Test Item	100 µg	19 33 23	**25**	7.2	32 34 40	**35**	4.2	**0.9**	**0.9**
Test Item	316 µg	20 22 34	**25**	7.6	35 27 27	**30**	4.6	**0.9**	**0.8**
Test Item	1000 µg	50 18 26	**31**	16.7	23 27 32	**27**	4.5	**1.1**	**0.7**
Test Item	2500 µg	31 28 21	**27**	5.1	35 29 33	**32**	3.1	**0.9**	**0.8**
Test Item	5000 µg	30 16 17	**21**	7.8	50 41 43	**45**	4.7	**0.7**	**1.2**
4-NOPD	10 µg	242 304 260	**269**	31.9	/ / /	**/**	/	**9.5**	**/**
2-AA	2.5 µg	/ / /	**/**	/	1422 1544 1808	**1591**	197.3	**/**	**41.5**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 100

Experiment: 2

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		93 94 95	**94**	1.0	89 99 87	**92**	6.4	**1.0**	**1.0**
Test Item	31.6 µg	95 82 87	**88**	6.6	102 103 90	**98**	7.2	**0.9**	**1.1**
Test Item	100 µg	106 93 102	**100**	6.7	90 91 91	**91**	0.6	**1.1**	**1.0**
Test Item	316 µg	100 91 112	**101**	10.5	71 95 78	**81**	12.3	**1.1**	**0.9**
Test Item	1000 µg	103 98 117	**106**	9.8	99 88 113	**100**	12.5	**1.1**	**1.1**
Test Item	2500 µg	107 84 113	**101**	15.3	144 119 111	**125**	17.2	**1.1**	**1.4**
Test Item	5000 µg	90 93 98	**94**	4.0	126 94 139	**120**	23.2	**1.0**	**1.3**
NaN_3	10 µg	313 369 358	**347**	29.7	/ / /	**/**	/	**3.7**	**/**
2-AA	2.5 µg	/ / /	**/**	/	652 846 688	**729**	103.2	**/**	**7.9**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 1535

Experiment: 2

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		9 11 12	**11**	1.5	8 11 11	**10**	1.7	**1.0**	**1.0**
Test Item	31.6 µg	12 13 16	**14**	2.1	11 12 14	**12**	1.5	**1.3**	**1.2**
Test Item	100 µg	11 13 17	**14**	3.1	6 12 12	**10**	3.5	**1.3**	**1.0**
Test Item	316 µg	10 11 11	**11**	0.6	8 8 12	**9**	2.3	**1.0**	**0.9**
Test Item	1000 µg	19 20 23	**21**	2.1	6 8 9	**8**	1.5	**1.9**	**0.8**
Test Item	2500 µg	15 18 24	**19**	4.6	11 12 15	**13**	2.1	**1.8**	**1.3**
Test Item	5000 µg	20 20 26	**22**	3.5	9 10 13	**11**	2.1	**2.1**	**1.1**
NaN_3	10 µg	479 515 628	**541**	77.7	/ / /	**/**	/	**50.7**	**/**
2-AA	2.5 µg	/ / /	**/**	/	66 79 94	**80**	14.0	**/**	**8.0**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 1537

Experiment: 2

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		6 10 12	**9**	3.1	8 9 17	**11**	4.9	**1.0**	**1.0**
Test Item	31.6 µg	4 5 6	**5**	1.0	6 7 13	**9**	3.8	**0.5**	**0.8**
Test Item	100 µg	5 7 9	**7**	2.0	6 7 11	**8**	2.6	**0.8**	**0.7**
Test Item	316 µg	4 4 6	**5**	1.2	6 9 10	**8**	2.1	**0.5**	**0.7**
Test Item	1000 µg	9 9 10	**9**	0.6	12 13 14	**13**	1.0	**1.0**	**1.1**
Test Item	2500 µg	9 10 12	**10**	1.5	6 15 17	**13**	5.9	**1.1**	**1.1**
Test Item	5000 µg	10 10 14	**11**	2.3	10 12 16	**13**	3.1	**1.2**	**1.1**
4-NOPD	40 µg	71 105 92	**89**	17.2	/ / /	**/**	/	**9.6**	**/**
2-AA	2.5 µg	/ / /	**/**	/	100 103 103	**102**	1.7	**/**	**9.0**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

Tester Strain: TA 102

Experiment: 2

Treatment	Dose/plate	REVERTANT COLONIES PER PLATE						MUTATION FACTOR	
		Without activation (-S9)			With activation (+S9)				
		Counts	Mean	SD	Counts	Mean	SD	-S9	+S9
A. dest.		185 177 154	**172**	16.1	218 175 208	**200**	22.5	**1.0**	**1.0**
Test Item	31.6 µg	273 236 211	**240**	31.2	323 281 276	**293**	25.8	**1.4**	**1.5**
Test Item	100 µg	150 179 119	**149**	30.0	231 232 268	**244**	21.1	**0.9**	**1.2**
Test Item	316 µg	119 151 142	**137**	16.5	186 157 152	**165**	18.4	**0.8**	**0.8**
Test Item	1000 µg	112 125 158	**132**	23.7	218 213 220	**217**	3.6	**0.8**	**1.1**
Test Item	2500 µg	243 198 215	**219**	22.7	300 243 221	**255**	40.8	**1.3**	**1.3**
Test Item	5000 µg	205 207 217	**210**	6.4	268 265 231	**255**	20.6	**1.2**	**1.3**
MMS	1 µL	1125 1064 1090	**1093**	30.6	/ / /	/	/	**6.4**	/
2-AA	10 µg	/ / /	/	/	453 602 531	**529**	74.5	/	**2.6**

SD: Standard-deviation
B: Background lawn reduced
N: No background lawn
P: Precipitation
C: Contamination

$$\text{Mutation factor} = \frac{\text{mean revertants (test item)}}{\text{mean revertants (vehicle control)}}$$

12.2. Discussion

The test item Glucose oxidase produced with *Trichoderma reesei* was investigated for its potential to induce gene mutations according to the plate incorporation test (experiment I) and the pre-incubation test (experiment II) using *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 102.

In two independent experiments several concentrations of the test item were used. Each assay was conducted **with** and **without** metabolic activation. The concentrations, including the controls, were tested in triplicate. The following concentrations of the test item were prepared and used in the experiments:

31.6, 100, 316, 1000, 2500 and 5000 µg/plate

No precipitation of the test item was observed in any tester strain used in experiment I and II (**with** and **without** metabolic activation).

No toxic effects of the test item were noted in any of the five tester strains used up to the highest dose group evaluated **with** and **without** metabolic activation in experiment I and II. The reduction in the number of revertants down to a mutation factor of 0.3 found in experiment I in tester strain TA 1535 at a concentration of 100 µg/plate (**with** metabolic activation) was regarded as not biologically relevant due to lack of a dose-response relationship.

No biologically relevant increases in revertant colony numbers of any of the five tester strains were observed following treatment with Glucose oxidase produced with *Trichoderma reesei* at any concentration level, neither in the presence nor absence of metabolic activation in experiment I and II. In experiment I in tester strain TA 1537 a mutation factor of 3.2 was observed at a concentration of 2500 µg/plate (**with** metabolic activation). However, the corresponding revertant colony number was within the range of the historical negative control data, no dose-response relationship was observed and the effect could not be reproduced in experiment II. Thus, the effect was considered as not biologically relevant.

The reference mutagens induced a distinct increase of revertant colonies indicating the validity of the experiments.

13. Conclusion

In conclusion, it can be stated that during the described mutagenicity test and under the experimental conditions reported, Glucose oxidase produced with *Trichoderma reesei* did not cause gene mutations by base pair changes or frameshifts in the genome of the tester strains used.

Therefore, Glucose oxidase produced with *Trichoderma reesei* is considered to be non-mutagenic in this bacterial reverse mutation assay.

14. Distribution of the Report

1 original (paper):	Sponsor
1 copy (paper):	Eurofins Munich
1 copy (electronic):	Sponsor

15. References

15.1. Guidelines

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[4] Ninth Addendum to OECD Guidelines for Testing of Chemicals, Section 4, No. 471, "Bacterial Reverse Mutation Test", adopted 21st July, 1997

[5] Commission Regulation (EC) No. 440/2008 B.13/14. "Mutagenicity – Reverse Mutation Test using Bacteria", dated May 30, 2008.

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15.2. Literature

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15.3. Internal Eurofins Munich SOPs

Standard Operating Procedures (SOPs), No. 15-1-1, No. 15-1-2, No. 15-2-2, No. 15-2-3, No. 4-6-6, No. 4-6-7

16. Appendix: Historical Laboratory Control Data

16.1. Appendix 1: Historical Laboratory Control Data

Table 4: Historical Laboratory Control Data of the Negative Control (in 2012 - 2014) without S9 (-S9)

	TA 98	TA 100	TA 1535	TA 1537	TA 102
Mean	22.3	95.5	10.9	7.5	230.5
SD	4.8	18.1	5.1	2.4	47.8
Min	13	61	4	2	136
Max	48	182	35	27	415
RSD [%]	21.6	18.9	46.8	31.4	20.8
n	1159	1281	1043	1043	684

S9: metabolic activation
Mean: mean of revertants/plate
Min.: minimum of revertants/plate
Max.: maximum of revertants/plate
SD: Standard Deviation
RSD: Relative Standard Deviation
n: Number of control values

Table 5: Historical Laboratory Control Data of the Positive Control (in 2012 - 2014) without S9 (-S9)

	TA 98	TA 100	TA 1535	TA 1537	TA 102
Substance	4-NOPD	NaN_3	NaN_3	4-NOPD	MMS
Conc./plate	10 µg	10 µg	10 µg	40 µg	1 µL
Mean	443.7	704.8	858.3	93.2	1733.5
SD	183.1	272.7	320.2	27.3	408.3
Min	192	132	34	30	162
Max	2213	1498	1472	273	3181
RSD [%]	41.3	38.7	37.3	29.3	23.6
n	1172	1285	1042	1054	688

S9: metabolic activation
Conc.: concentration
Mean: mean of revertants/plate
Min.: minimum of revertants/plate
Max.: maximum of revertants/plate
SD: Standard Deviation
RSD: Relative Standard Deviation
n: Number of control values

Table 6: Historical Laboratory Control Data of the Negative Control (in 2012 - 2014) with S9 (+S9)

	TA 98	TA 100	TA 1535	TA 1537	TA 102
Mean	29.9	103.4	9.1	7.6	290.9
SD	6.2	17.4	3.3	2.7	65.3
Min	13	68	4	3	91
Max	61	194	34	31	495
RSD [%]	20.9	16.8	36.1	35.3	22.4
n	1157	1286	1042	1040	683

S9: metabolic activation
Mean: mean of revertants/plate
Min.: minimum of revertants/plate
Max.: maximum of revertants/plate
SD: Standard Deviation
RSD: Relative Standard Deviation
n: Number of control values

Table 7: Historical Laboratory Control Data of the Positive Control (in 2012 - 2014) with S9 (+S9)

	TA 98	TA 100	TA 1535	TA 1537	TA 102
Substance	2-AA	2-AA	2-AA	2-AA	2-AA
Conc./plate	2.5 µg	2.5 µg	2.5 µg	2.5 µg	10 µg
Mean	2318.0	1839.6	100.0	218.6	663.9
SD	573.6	455.1	60.6	85.2	176.6
Min	128	169	19	28	137
Max	3606	3132	1011	489	2001
RSD [%]	24.7	24.7	60.6	39.0	26.6
n	1156	1284	1041	1039	688

S9: metabolic activation
Conc.: concentration
Mean: mean of revertants/plate
Min.: minimum of revertants/plate
Max.: maximum of revertants/plate
SD: Standard Deviation
RSD: Relative Standard Deviation
n: Number of control values

16.2. Appendix 2: Certificate of Analysis

NOVALAB OY

ANALYSIS REPORT

Order: 1404846 1(2)
Date: 28.11.2014

ROAL Oy
Vilma Ikonen
Tykkimäentie 15
PL 57, 05201 Rajamäki

FINAS
Finnish Accreditation Service
T071 (EN ISO/IEC 17025)

Order name: **Enzyme sample,P140032J, nutritional analysis**
Sample: 14MU0883 Glukoosi-oksidaasi, P140032J
Sampling time: 10.11.2014
Sample arrived: 11.11.2014
Analysis started: 13.11.2014

Analysis		Result	Method
Dry matter	%	94.9	Novalab 010*
Ash	%	3.5	Novalab 009*
Moisture	%	5.1	Novalab 010*
Protein	%	68.3	Novalab 001.A, kjeldahl*
Carbohydrate, calculated	%	23.1	
Energy value, calculated	kJ/100 g	1554	
Fat	%	<0.1	Novalab 076*

* Accredited method. Statement is not accredited. Results apply only samples analyzed

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Bank
Länsi-Uudenmaan Op
Karkkila
FI43 5297 2820 0007 16

Business ID 0733227-8
Location Karkkila
VAT reg.

NOVALAB OY

ANALYSIS REPORT

Order: 1404846 2(2)
Date: 28.11.2014

ROAL Oy
Vilma Ikonen
Tykkimäentie 15
PL 57, 05201 Rajamäki

FINAS
Finnish Accreditation Service
T071 (EN ISO/IEC 17025)

Novalab Oy
(b) (6)

Eeva Luoma
Head of Quality
The certificate has been signed electronically.

Add.details Methods:
Moisture: AOAC 2002 950.46 (39.1.02) modified
Protein: AOAC 2002 2001.11 (4.2.11) modified
Fat: NMKL 131:1989 modified
Ash: NMKL 173:2005 modified
Carbohydrate: By difference 100 % - (moisture+protein+fat+ash)%
Energy value: Calculated on the basis of contents of protein, fat and carbohydrate. Factors protein and carbohydrate 17 kJ/g, fat 37 kJ/g

Measurement uncertainty:
Moisture: ± 3 relative-%
Ash: ± 10 relative-%
Fat: under the limit of measurement
Protein: ± 5 relative-%
Carbonhydrates, calculated: ± 5 relative-%
Energy, calculated: ± 5 relative-%

Distribute vilma.ikonen@roal.fi

* Accredited method. Statement is not accredited. Results apply only samples analyzed

eurofins | BioPharma Product Testing

In vitro Mammalian Micronucleus Assay in Human Lymphocytes with Glucose oxidase produced with *Trichoderma reesei*

Report

Version: Final

Study Completion Date: 02 JUL 2015

Eurofins Munich Study No.: 150137

Sponsor:
AB Enzymes GmbH
Feldbergstr. 78
64293 Darmstadt
Germany

Eurofins BioPharma Product Testing Munich GmbH
Behringstr. 6/8
D-82152 Planegg/Munich
Germany

Tel +49 (0)89 899 650-0
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GLP / GMP FDA approved

1. Copy of the GLP Certificate

Bayerisches Landesamt für
Gesundheit und Lebensmittelsicherheit

GLP-Bescheinigung/Statement of GLP Compliance
(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at:

☒ Prüfeinrichtung/Test facility ☐ Prüfstandort/Test site

EUROFINS BIOPHARMA PRODUCT TESTING MUNICH GMBH
BEHRINGSTRAßE 6-8
82152 PLANEGG

(Unverwechselbare Bezeichnung und Adresse/Unequivocal name and address)

Prüfungen nach Kategorien/Areas of Expertise
(gemäß/according ChemVwV-GLP Nr. 5.3/OECD guidance)

Kategorie 2/ Category 2
Kategorie 3/ Category 3
Kategorie 8/ Category 8
Kategorie 9*/ Category 9*

**Sonstige Prüfungen:*
biologische und mikrobiologische Sicherheitsprüfungen an Medizinprodukten und Arzneimitteln; Auftragsarchivierung

**other tests:*
biological an microbiological safety evaluation on medical devices and pharmaceuticals; contract archiving

Datum der Inspektion/Date of Inspection
(Tag.Monat.Jahr/day.month.year)

18. bis 19.03.2015

Die/Der genannte Prüfeinrichtung/Prüfstandort befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility/test site is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung/diesem Prüfstandort die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.

Based on the inspection report it can be confirmed, that this test facility/test site is able to conduct the aforementioned studies in compliance with the Principles of GLP.

(b) (6)

Schwabach, 05.06.2015

Dr. Peter Franke
Leiter der GLP-Landesleitstelle Bayern

GLP- Landesleitstelle Bayern
Bayerisches Landesamt für Gesundheit
und Lebensmittelsicherheit
Rathausgasse 4
91126 Schwabach

2. Contents

3. List of Tables and Figures

3.1. List of Tables

3.2. List of Figures

4. Preface

4.1. Abbreviations

Art.	Artikel *(article)*
ATCC	American Type Culture Collection
BGBl.	Bundesgesetzblatt *(Federal Law Gazette)*
CBPI	cytokinesis block proliferation index
CPA	cyclophosphamide
DNA	desoxyribonucleic acid
e.g.	exempli gratia *(for example)*
EC	European Commission
ECVAM	European Centre for the Validation of Alternative Methods
EMS	ethylmethanesulfonate
EPA	Environmental Protection Agency
ESAC	ECVAM Scientific Advisory Committee
Eurofins Munich	Eurofins BioPharma Product Testing Munich GmbH
FBS	fetal bovine serum
GLP	Good Laboratory Practice
GmbH	Gesellschaft mit beschränkter Haftung *(company with limited liability)*
i.e.	id est *(that is)*
KCl	potassium chloride
MNvit	*in vitro* micronuclei
NADP	nicotinamide adenine di-phosphate
No	number
Nr.	Nummer *(number)*
OECD	Organisation for Economic Cooperation and Development
PBS	phosphate buffered saline
PHA	phytohemagglutinin
QA	Quality Assurance
QAU	Quality Assurance Unit
RPMI	Roswell Park Memorial Institute medium
S9	microsomal fraction of rat liver homogenate
SOPs	Standard Operating Procedures
v/v	volume per volume

4.2. General

Sponsor:	AB Enzymes GmbH Feldbergstr. 78 64293 Darmstadt Germany
Study Monitor:	Dr. Hans-Jürgen Schepers
Test Facility:	Eurofins BioPharma Product Testing Munich GmbH Behringstraße 6/8 82152 Planegg Germany
Eurofins Munich Study No.:	150137
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	*In vitro* Mammalian Micronucleus Test in Human Lymphocytes with Glucose oxidase produced with *Trichoderma reesei*

4.3. Project Staff

Study Director:	Dr. Claudia Donath
Management:	Dr. Angela Lutterbach Dr. Katrin Witschital
Head of GLP Quality Assurance Unit:	Dipl.-Biol. Carolin Schmidt

4.4. Schedule

Arrival of the Test Item:	09 January 2015
Study Initiation Date:	20 January 2015
Experimental Starting Date:	26 January 2015
Experimental Completion Date:	20 May 2015

5. Quality Assurance

5.1. GLP Compliance

This study was conducted to comply with:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

OECD Principles of Good Laboratory Practice (as revised in 1997); OECD Environmental Health and Safety Publications; Series on Principles of Good Laboratory Practice and Compliance Monitoring - Number 1. Environment Directorate, Organisation for Economic Co-operation and Development, Paris 1998 [3].

The OECD Principles of Good Laboratory Practice are accepted by regulatory authorities throughout the European Community, USA and Japan.

This study was assessed for compliance with the study plan and the Standard Operating Procedures of Eurofins Munich. The study and/or the test facility are inspected periodically by the Quality Assurance Unit according to the corresponding SOPs. These inspections and audits are carried out by the Quality Assurance Unit, personnel independent of staff involved in the study. A signed quality assurance statement, listing all performed audits, is included in the report.

5.2. Guidelines

This study followed the procedures indicated by internal Eurofins Munich SOPs and the following internationally accepted guidelines and recommendations:

Ninth Addendum to OECD Guidelines for Testing of Chemicals, Section 4, No. 487, "*In Vitro* Mammalian Cell Micronucleus Test", adopted 26 September, 2014 [4].

5.3. Archiving

For a period of 15 years (or shorter if in compliance with the GLP regulations) Eurofins Munich will store the records, materials and specimens in their scientific archives according to the GLP regulations.

The following records have to be stored according to the GLP regulations:

A copy of the final report, the study plan and documentation of all raw data generated during the conduct of the study (documentation forms as well as any other notes of raw data, printouts of instruments and computers) and the correspondence with the sponsor concerning the study. Any document relating to the study will be discarded only with the prior consent of the sponsor.

The following materials and samples have to be stored according to the period of time specified in the GLP regulations:

A retained sample of the test item will be archived according to the GLP regulations, if possible, and will be discarded without the sponsor's prior consent.

Other materials and specimens have to be stored according to the GLP regulations and disposed of after the respective archiving period with the sponsor's prior consent.

As requested the remaining test item will be returned to the sponsor.

6. Statement of Compliance

Eurofins Munich Study No.:	150137
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	*In vitro* Mammalian Micronucleus Test in Human Lymphocytes with Glucose oxidase produced with *Trichoderma reesei*
Study Director:	Dr. Claudia Donath

This study performed in the test facility Eurofins Munich was conducted in compliance with Good Laboratory Practice Regulations:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

"OECD Principles of Good Laboratory Practice (as revised in 1997)", Paris 1998 [3].

There were no circumstances that may have affected the quality or integrity of the study.

Study Director: Dr. Claudia Donath

(b) (6)

Date: 02 Jul 2015

7. Statement of the Quality Assurance Unit

Eurofins Munich Study No.:	150137
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	*In vitro* Mammalian Micronucleus Test in Human Lymphocytes with Glucose oxidase produced with *Trichoderma reesei*
Study Director:	Dr. Claudia Donath

This report and the conduct of this study were inspected by the Quality Assurance Unit on the following dates:

Phase of QAU Inspection	Date of QAU Inspection	Date of Reporting to the Study Director and Management
Audit Final Study Plan:	21 January 2015	21 January 2015
Audit Experimental Phase (study-based):	25 February 2015	25 February 2015
Audit Final Report:	30 JUN 2015	30 JUN 2015

This report reflects the raw data.

Member of the Quality Assurance Unit: (b) (6)

Print Name: Gwendolyn Beckmann, M.Sc.

Date: 02 JUL 2015

8. Summary

8.1. Summary Results

In order to investigate a possible potential of Glucose oxidase produced with *Trichoderma reesei* for its ability to induce micronuclei in human lymphocytes an *in vitro* micronucleus assay was carried out. The following study design was performed:

	Without S9		With S9
	Exp. I	Exp. II	Exp. I
Exposure period	4 h	44 h	4 h
Cytochalasin B exposure	40 h	43 h	40 h
Preparation interval	44 h	44 h	44 h
Total culture period*	92 h	92 h	92 h

*Exposure started 48 h after culture initiation

The selection of the concentrations was based on data from the pre-experiment. In experiment I **without** metabolic activation a concentration of 15 µg/mL and **with** metabolic activation a concentration of 275 µg/mL was selected as highest concentration for the microscopic analysis of micronuclei. In experiment II **without** metabolic activation a concentration of 2.5 µg/mL was selected as highest concentration for the microscopic analysis of micronuclei. The pH value detected with the test item solution was within the physiological range (7.0 ± 0.4).

The following concentrations were evaluated for micronuclei frequencies:

Experiment I with short-term exposure (4 h):

without metabolic activation: 5, 10 and 15 µg/mL

with metabolic activation: 50, 100, 200 and 275 µg/mL

Experiment II with long-term exposure (44 h):

without metabolic activation: 0.10, 0.25, 0.50, 1.0 and 2.5 µg/mL

No precipitate of the test item was noted in all concentration groups evaluated in the main experiments at the end of treatment (evaluated by unaided eye).

Table 1: Summary: Experiment I and II, without metabolic activation

	Dose Group	Concentration [µg/mL]	Number of cells evaluated	Cytostasis [%]	Relative CBPI [%]	Micro-nucleated Cells Frequency [%]	Historical Control Limits Negative Control	Precipitation	Statistical Significant Increase[a]
Exp. I 4 h treatment, 44 h fixation interval	**C**	0	4000	0	**100**	**0.45**	0.44% - 1.56%	/	/
	1	5	4000	2	**98**	**0.58**		-	-
	2	10	4000	9	**91**	**0.88**		-	+
	3	15	4000	32	**68**	**0.45**		-	-
	EMS	1200	2000	22	**78**	**2.40**		-	+
	Colc	0.8	1564	77	**23**	**2.33**		-	+
Exp. II 44 h treatment, 44 h fixation interval	**C**	0	2000	0	**100**	**0.50**	0.44% - 1.56%	/	/
	8	0.10	2000	0	**100**	**0.60**		-	-
	9	0.25	4000	21	**79**	**0.38**		-	-
	10	0.50	2000	31	**69**	**0.45**		-	-
	11	1.0	4000	50	**50**	**0.75**		-	-
	12	2.5	1848	69	**31**	**0.79**		-	-
	EMS	900	1620	68	**32**	**2.40**		-	+
	Colc	0.04	1377	80	**20**	**3.20**		-	+

C: Negative Control (Culture medium)
a: statistical significant increase compared to negative control (χ^2 test , $p<0.05$).
+: significant; -: not significant
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [900 and 1200 µg/mL]
Colc: Colcemid, Positive Control (without metabolic activation) [0.04 and 0.8 µg/mL]
CBPI: Cytokinesis Block Proliferation Index, CBPI = $((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
c_1: mononucleate cells
c_2: binucleate cells
c_x: multinucleate cells
n: total number of cells

Table 2: Summary: Experiment I, with metabolic activation

	Dose Group	Concentration [µg/mL]	Number of cells evaluated	Cytostasis [%]	Relative CBPI [%]	Micro-Nucleated Cells Frequency [%]	Historical Control Limits Negative Control	Precipitation	Statistical Significant Increase[a]
Exp. I 4 h treatment, 44 h fixation interval	**C**	0	4000	0	**100**	**0.53**	0.44% - 1.69%	/	/
	2	50	2000	18	**82**	**0.45**		-	-
	3	100	4000	33	**67**	**0.80**		-	-
	5	200	2000	48	**52**	**0.90**		-	-
	7	275	4000	60	**40**	**1.20**		-	+
	CPA	15	2000	11	**89**	**3.00**		-	+

C: Negative Control (Culture medium)
a: statistical significant increase compared to negative control (χ^2 test , $p<0.05$).
+: significant; -: not significant
CPA: Cyclophosphamide, Positive Control (with metabolic activation) [15 µg/mL]
CBPI: Cytokinesis Block Proliferation Index, CBPI = $((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
c_1: mononucleate cells
c_2: binucleate cells
c_x: multinucleate cells
n: total number of cells

According to the OECD guideline 487 the maximum of cytotoxicity should not exceed the limit of 55 ± 5%. Higher levels of cytotoxicity may induce chromosome damage as a secondary effect of cytotoxicity. According to laboratory experience a culture showing reduced cell viability (more than 30% rel. cytostasis) compared to the negative/solvent control displays cytotoxicity. Due to this, the limit of cytotoxicity is ≤ 70%. This corresponds to ≥ 30% of rel. cytostasis

In experiment I **without** metabolic activation no increase of the relative cytostasis above 30 % was noted up to a concentration of 10 µg/mL. At a concentration of 15 µg/mL a relative cytostasis of 32% was noted. In experiment I **with** metabolic activation no increase of the relative cytostasis above 30 % was noted up to a concentration of 50 µg/mL. At a concentration of 100 µg/mL a relative cytostasis of 33%, at a concentration of 200 µg/mL a relative cytostasis of 48% and at a concentration of 275 µg/mL a relative cytostasis of 60% was observed.
In experiment II **without** metabolic activation no increase of the relative cytostasis above 30 % was noted up to a concentration of 0.25 µg/mL. At a concentration of 0.50 µg/mL a relative cytostasis of 31%, at a concentration of 1.0 µg/mL a relative cytostasis of 50% and at a concentration of 2.5 µg/mL a relative cytostasis of 69% was noted.

In experiment I **without** and **with** metabolic activation and in experiment II **without** metabolic activation no biologically relevant increase of the micronucleus frequency was noted after treatment with the test item.

The nonparametric χ^2 Test was performed to verify the results in both experiments. In experiment I **without** metabolic activation a statistically significant enhancement ($p = 0.0191$) of cells with micronuclei was noted at a concentration of 10 µg/mL (Table 11) and in experiment I **with** metabolic activation a statistically significant enhancement ($p = 0.0011$) of cells with micronuclei was noted at a concentration of 275 µg/mL (Table 12). However, the frequency of micronucleated cells was within the historical control limits of the negative control and significant cytotoxicity was observed for the concentration of 275 µg/mL **with** metabolic activation. Therefore, these increases were regarded as not biologically relevant. No statistically significant enhancement ($p<0.05$) of cells with micronuclei was noted in the concentration groups of the test item evaluated in experiment II.

The χ^2 Test for trend was performed to test whether there is a concentration-related increase in the micronucleated cells frequency in the experimental conditions. No statistically significant increase was observed in experiment I and II **without** metabolic activation. In experiment I **with** metabolic activation a statistically significant increase of the micronucleated cells frequency was observed. However, since all values of the micronucleated cell frequency of this experimental condition were within the historical control limits of the negative control, this increase was regarded as not biologically relevant.

Ethylmethanesulfonate (EMS, 900 and 1200 µg/mL) and cyclophosphamide (CPA, 15 µg/mL) were used as clastogenic controls. Colcemid (0.04 and 0.8 µg/mL) was used as aneugenic control. All induced distinct and statistically significant increases of the micronucleus frequency. This demonstrates the validity of the assay.

8.2. Conclusion

In conclusion, it can be stated that during the study described and under the experimental conditions reported, the test item Glucose oxidase produced with *Trichoderma reesei* did not induce structural and/or numerical chromosomal damage in human lymphocytes.

Therefore, Glucose oxidase produced with *Trichoderma reesei* is considered to be non-mutagenic with respect to clastogenicity and/or aneugenicity in the *in vitro* Mammalian Cell Micronucleus Test.

9. Introduction

9.1. Aim of the Study

The *in vitro* micronucleus assay detects the activity of clastogenic and aneugenic chemicals in cells that have undergone cell division during or after exposure to the test substance. The micronuclei may originate from acentric fragments (chromosome fragments lacking a centromer) or whole chromosomes which are unable to migrate with the rest of the chromosomes during the anaphase of the cell division. Micronuclei formation may also result at the level of proteins directly or indirectly involved in chromosome segregation (e.g. tubulin). The addition of the actin polymerisation inhibitor Cytochalasin B prior to the targeted mitosis, allows the identification and analysis of micronucleus frequency only in those cells, which have complete mitosis. These cells are binucleate [6], [7]. The *in vitro* micronucleus test is an *in vitro* test which is able to detect both numerical and chromosomal aberrations, two mechanisms involved in genetic and carcinogenic risk [5], [6]. Clastogenic or aneugenic incidents are critical lesions for the cell that could cause alterations in protooncogens and tumor suppressor genes. These alterations could result in oncogenesis. However the *in vitro* micronucleus assay did not allow the identification of polyploidy cells.

Human peripheral blood lymphocytes should be obtained from healthy, non-smoking donors. The most efficient approach is to test human lymphocytes 44 - 48 h after PHA stimulation, when the cell cycle synchronisation will have declined. It is recommended to perform the first experiment with a 3 - 6 h (short-term) treatment in presence and absence of metabolic activation, with sampling occurring at a time equivalent to about two normal cell cycle lengths after the beginning of treatment. If the first experiment gives negative or equivocal results a second experiment with modified conditions should be done. In absence of metabolic activation the cells should be exposed continuously to the test substance (long-term treatment) [4].

At least three analysable concentrations of the test item with concentration intervals of approximately 2 to 3 fold should be tested. For soluble, non-toxic test items the highest concentration should correspond to 10 mM, 2 µL/mL or 2 mg/mL, whichever is the lowest. When the test chemical is not of defined composition, e.g. substance of unknown or variable composition, the top concentration may need to be higher (e.g. 5 mg/mL) in the absence of sufficient cytotoxicity. For poorly soluble compounds, one concentration with precipitate visible by the unaided eye at the end of treatment should be used as highest concentration. The precipitate should not interfere with scoring. If toxicity is found, the highest concentration evaluated should induce approximately 55 ± 5% toxicity [4], [8], [9]. If possible, the concentration tested should exhibit substantial toxicity, intermediate toxicity and/or no toxicity [4], [9].

Assessment of cytotoxicity should be performed by determining cell proliferation in both treated and control cultures. The proliferation rate is determined by calculation of the cytokinesis-block proliferation index (CBPI) and the cytostasis [7].

As validity criterion for the test, reference mutagens are tested in parallel to the test item.

9.2. Justification for the Selection of the Test System

The OECD Guideline for Testing of Chemicals Section 4, No 487 – "*In Vitro* Mammalian Cell Micronucleus Test, adopted 26 September, 2014" – recommends using a variety of cell lines or primary cell cultures (e.g. Chinese hamster fibroblasts, human or other mammalian peripheral blood lymphocytes) in the presence or absence of cytochalasin B.

10. Materials and Methods

10.1. Characterisation of the Test Item

The identity of the test item was inspected upon delivery at the test facility (e.g. test item name, batch no. and additional data were compared with the label) based on the following specifications provided by the sponsor.

Name:	Glucose oxidase produced with *Trichoderma reesei*
Chemical Name:	Glucose oxidase (food enzyme)
Batch No.:	P 140032 J
Expiry Date:	September 2016
Physical State at Room Temperature:	powder
Colour:	brownish
Purity:	91.5% TOS (Total Organic Substance) (Certificate of Analysis will be included in final report)
Storage Conditions:	at room temperature, protected from light
Safety Precautions:	The routine hygienic procedures were sufficient to assure personnel health and safety

10.2. Preparation of the Test Item

A solubility test was performed with different solvents and vehicles up to the maximum recommended concentration of 5 mg/mL. Based on the results of the solubility test RPMI cell culture medium was used as solvent. The test item was dissolved and diluted in cell culture medium (RPMI) within 1 hour prior to treatment. The solvent was compatible with the survival of the cells and the S9 activity.

All concentrations used were calculated based on the TOS value of the test item (91.5%). For this purpose a correction factor of 1.09 was applied.

For the maximum concentration without metabolic activation the osmolality (in comparison to negative (solvent) control) and pH value were determined:

		Concentration (µg/mL)	Osmolality (mOsm/kg)	pH value
Exp. I	Solvent control	-	299	-
	Test item	35,4	303	7,4
Exp. II	Solvent control	-	291	-
	Test item	10,9	291	7,0

10.3. Controls

Negative and positive controls were included in each experiment.

Negative Controls

Negative controls (cell culture medium) were treated in the same way as all dose groups.

Positive Controls

Positive controls should employ a known inducer of micronuclei formation at exposure levels expected to give a reproducible and detectable increase over background, which demonstrates the sensitivity of the test system.

Clastogenic Controls

Without metabolic activation

Name	EMS, ethylmethanesulfonate
CAS No.	62-50-0
Supplier	Sigma
Catalogue No.	M0880
Batch No.	BCBL0357V / BCBN1209V
Dissolved in	RPMI
Final concentrations	900 and 1200 µg/mL

With metabolic activation

Name	CPA, cyclophosphamide
CAS No.	50-18-0
Supplier	Sigma
Catalogue No.	C0768
Batch No.	SLBC0666V
Dissolved in	RPMI
Final concentration	15 µg/mL

CPA displays a good stability at room temperature. At 25 °C only 3.5% of its potency is lost after 24 h [15]. The solution was aliquoted and stored at ≤ -15 °C. Additionally, the stability of CPA in solution was proven by the clastogenic response in the expected range.

Aneugenic Control

Name	Colcemid
CAS No.	477-30-5
Supplier	Sigma
Catalogue No.	C 9754
Batch No.	091M1528V
Dissolved in	RPMI
Final concentrations	0.04 and 0.8 µg/mL

The dilutions of the stock solutions of the positive controls were prepared on the day of the experiment and used immediately.

The stability of both positive control substances in solution is proven by the mutagenic response in the expected range.

10.4. Test System

10.4.1. Blood Collection

Human peripheral blood lymphocytes from healthy and non-smoking donors with no known recent exposure to genotoxic chemicals and radiation were used to examine the ability of chemicals to induce cytogenetic damage and thus to identify potential carcinogens or mutagens *in vitro*. For this study (in each experiment) blood was collected only from a single donor to reduce inter-individual variability.

Blood samples were drawn by venous puncture and collected in heparinized tubes. Before use the blood was stored under sterile conditions at 4 °C for a maximum of 4 h. Whole blood samples treated with an anti-coagulant (e. g. heparin) were pre-cultured in the presence of mitogen (phyto-haematogglutinin, PHA).

10.4.2. Mammalian Microsomal Fraction S9 Homogenate

An advantage of using *in vitro* cell cultures is the accurate control of the concentration and exposure time of cells to the test item under study. However, due to the limited capacity of cells growing *in vitro* for metabolic activation of potential mutagens, an exogenous metabolic activation system is necessary. Many substances only develop mutagenic potential when they are metabolized by the mammalian organism. Metabolic activation of substances can be achieved by supplementing the cell cultures with liver microsome preparations (S9 mix).

The S9 liver microsomal fraction was prepared at Eurofins Munich. Male Wistar rats were induced with phenobarbital (80 mg/kg bw) and ß-naphthoflavone (100 mg/kg bw) [12], [13] for three consecutive days by oral route.

The following quality control determinations were performed:

a) Biological activity in:
   - the *Salmonella typhimurium* assay using 2-aminoanthracene
   - the mouse lymphoma assay using benzo[*a*]pyrene
   - the chromosome aberration assay using cyclophosphamide.

b) Sterility Test

A stock of the supernatant containing the microsomes was frozen in aliquots of 2 and 4 mL and stored at ≤ -75°C.

The protein concentration in the S9 preparation (Lot: 110414A) was 38 mg/mL.

10.4.3. S9 Mix

An appropriate quantity of the S9 supernatant was thawed and mixed with S9 cofactor solution to result in a final protein concentration of 0.75 mg/mL in the cultures. Cofactors were added to the S9 mix to reach the concentrations below:

8	mM	$MgCl_2$
33	mM	KCl
5	mM	Glucose-6-phosphate
5	mM	NADP

in 100 mM sodium-phosphate-buffer pH 7.4. During the experiment the S9 mix was stored on ice. The final concentration of S9 mix in the cultures was 5%.

10.4.4. Culture Medium

Complete Culture Medium

RPMI 1640 medium supplemented with:

15	%	fetal bovine serum (FBS)
100 U/100	µg/mL	penicillin/streptomycin solution
2	mM	L-glutamine
2.4	µg/mL	phytohaemagglutinin (PHA)

Treatment Medium (short-term exposure)

Complete culture medium without FBS.

After Treatment Medium / Treatment Medium (long-term exposure)

Complete culture medium with FBS (15%) and cytochalasin B (6 µg/mL)

10.5. Experimental Design

10.5.1. Pre-Experiment for Toxicity

A pre-experiment was conducted under identical conditions as described for the main experiment I (4 h incubation). The following concentrations were tested **without** and **with** S9 mix:

without S9: 2.0, 3.9, 7.8, 15.6, 31.3, 62.5, 125, 250, 500, 1000, 2500 and 5000 µg/mL

with S9: 7.8, 15.6, 31.3, 62.5, 125, 250, 500, 1000, 2500 and 5000 µg/mL

The concentration of 5000 µg/mL was considered to be the highest test concentration to be used in this test system following the recommendation of the corresponding OECD testing guideline 487 [4].

10.5.2. Exposure Concentrations

Duplicate cultures were treated at each concentration. The selection of the concentrations used in experiment I and II based on data from the pre-experiment. The following concentrations were used in the main experiments:

Experiment I:

without metabolic activation: 5, 10, 15, 17.5, 20, 22.5, 25, 27.5, 30, 32.5 µg/mL

with metabolic activation: 25, 50, 100, 150, 200, 250, 275, 300, 325, 350, 375 and 400 µg/mL

Experiment II:

without metabolic activation: 0.0005, 0.0010, 0.0025, 0.005, 0.010, 0.025, 0.05, 0.10, 0.25, 0.50, 1.0, 2.5, 5 and 10 µg/mL

The following concentrations were selected in the main experiments for the microscopic analyses:

Experiment I with short-term exposure (4 h):

without metabolic activation: 5, 10 and 15 µg/mL

with metabolic activation: 50, 100, 200 and 275 µg/mL

Experiment II with long-term exposure (44 h):

without metabolic activation: 0.10, 0.25, 0.50, 1.0 and 2.5 µg/mL

10.5.3. Experimental Performance

Experiment I

Whole blood samples were treated with anti-coagulant (Heparin) and were pre-cultured (48 h) in presence of PHA prior to exposure to the test item. It is recommended to test human lymphocytes 44 to 48 h after PHA stimulation, when the cell cycle synchronisation is disappeared. The lymphocytes were incubated with the test item for 4 h in presence or absence of metabolic activation. At the end of the incubation, the treatment medium was removed and the cells were washed twice with PBS + 10% FBS. Subsequently the cells were incubated in complete culture medium + 6 µg/mL cytochalasin B for 40 h at 37°C and 5% CO_2 [7].

Experiment II

If negative or equivocal results are obtained, they should be confirmed using continuous treatment or modified conditions as appropriate. In the experiment **without** metabolic activation, cells were exposed continuously (long-term treatment) to the test item. The whole blood cultures were pre-cultured in presence of PHA for 48 h prior to exposure to the test item. Then the test item was added in complete culture medium. 1 h later 6 µg/mL cytochalasin B were added and the cells were incubated for further 43 h at 37 °C. At the end of the treatment the cell culture medium was removed and the cells were prepared for microscopic analysis.

10.5.4. Number of Cultures

Duplicate cultures were performed at each concentration level.

10.5.5. Preparation of the Cultures

At the end of the cultivation, the complete culture medium was removed. Subsequently, the cells were treated with cold hypotonic solution (0.075 M KCl) for some minutes at room temperature and immediately centrifuged. The pellet was resuspended with a solution consisted of fixation solution + NaCl 0.9% (1+1) and centrifuged. After that the cells were fixed with methanol + glacial acetic acid (3+1). The cells were resuspended gently and the suspension was dropped onto clean glass slides. Consecutively, the cells were dried on a heating plate. The cells were stained with acridine orange solution.

10.5.6. Analysis of Micronuclei

All slides, including those of positive and negative controls were independently coded before microscopic analysis. For each dose group at least 2000 binucleated cells (if possible) per concentration (1000 binucleated cells per slide) were analysed for micronuclei according to the criteria of Fenech [6], i.e. clearly surrounded by a nuclear membrane, having an area of less than one-third of that of the main nucleus, being located within the cytoplasm of the cell and not linked to the main nucleus via nucleoplasmic bridges. Mononucleated and multinucleated cells and cells with more than six micronuclei were not considered [7].

10.5.7. Cytokinesis Block Proliferation Index

As an assessment of the cytotoxicity, a cytokinesis block proliferation index (CBPI) was determined from 500 cells according to the following formula:

$$CBPI = \frac{(c_1 \times 1) + (c_2 \times 2) + (c_x \times 3)}{n}$$

c_1: mononucleate cells

c_2: binucleate cells

c_x: multinucleate cells

n: total number of cells

The CBPI was used to calculate the % cytostasis, which indicates the inhibition of cell growth of treated cultures in comparison to control cultures:

$$\% \text{ Cytostasis} = 100 - 100 \times ((CBPI_T - 1) / (CBPI_C - 1))$$

$CBPI_T$: Cytokinesis Block proliferation index of treated cultures

$CBPI_C$: Cytokinesis Block proliferation index of control cultures

10.6. Data Recording

The data generated are recorded in the raw data. The results are presented in tables, including experimental groups with the test item, negative and positive controls. The experimental unit is the cell and therefore, the percentage of cells with micronuclei is evaluated. A concurrent measurement of cytotoxicity is also recorded.

10.7. Acceptability of the Assay

A mutation assay is considered acceptable if it meets the following criteria:

- The concurrent negative/solvent control is considered acceptable for addition to the laboratory historical negative/solvent control database.
- Concurrent positive controls should induce responses that are compatible with those generated in the laboratory's historical positive control data base and produce a statistically significant increase compared with the concurrent negative/solvent control.
- Cell proliferation criteria in the negative/solvent control should be fulfilled.
- All experimental conditions are tested unless one resulted in positive results.
- Adequate number of cells and concentrations are analysable.
- Criteria for the selection of top concentration are fulfilled.

10.8. Evaluation of Results

A test item is considered to be clearly positive if, in any of the experimental conditions examined:

- at least one of the test concentrations exhibits a statistically significant increase compared with the concurrent negative control
- the increase is concentration-related in at least one experimental condition when evaluated with an appropriate trend test
- any of the results are outside the distribution of the historical negative/solvent control data (e.g. Poisson-based 95% control limits).

When all of these criteria are met, the test item is considered able to induce chromosome breaks and/or gain or loss in this test system.

A test item is considered to be clearly negative if in all experimental conditions examined none of the criteria mentioned above are met.

11. Deviations from the Study Plan

There were the following deviations from the study plan:

- **Concerning:**

  Name of Test Facility

  The name of the test facility has changed from BSL BIOSERVICE Scientific Laboratories GmbH to Eurofins BioPharma Product Testing Munich GmbH.

- **Concerning:**

  Controls, study plan, p. 10

  Study Plan:

  With metabolic activation

Name:	CPA, cyclophosphamide
CAS No.:	50-18-0
Supplier:	Sigma
Catalogue No.:	C0768
Batch No.:	will be added in the report
Dissolved in:	RPMI
Final concentration:	7.5 – 12.5 µg/mL

  Report:

  With metabolic activation

Name	CPA, cyclophosphamide
CAS No.	50-18-0
Supplier	Sigma
Catalogue No.	C0768
Batch No.	SLBC0666V
Dissolved in	RPMI
Final concentration	15 µg/mL

  Reason:

  Technical reason.

  Due to biological variability the final concentration of the clastogenic control CPA was increased to 15 µg/mL in experiment I to achieve a detectable increase of the micronuclei frequency above the background and to demonstrate the sensitivity of the test system.

These deviations did not influence the quality or integrity of the present study.

12. Results and Discussion

12.1. Results

12.1.1. Pre-Experiment

According to the corresponding OECD testing guideline [8] the highest recommended dose is 5000 µg/mL. The test item was prepared in cell culture medium. No precipitate of the test item was noted in the cultures at the end of treatment (evaluated by unaided eye). The highest concentration group evaluated in the pre-experiment was 15.6 µg/mL (**without** metabolic activation) and 250 µg/mL (**with** metabolic activation). The cytokinesis block proliferation index (CBPI) was used to calculate the cytostasis (cytostasis [%] = 100 - CBPI relative [%]). The cytostasis will be used to describe cytotoxicity. The selection of concentrations used in the main experiment based on the results obtained in the pre-experiment.

Table 3: Test for Cytotoxicity, *without* and *with* metabolic activation

Dose Group	Concentration [µg/mL]	CBPI	CBPI relative [%]	Cytostasis relative [%]
without metabolic activation				
C	0	1.53	100	0
1	2.0	1.60	114	0*
2	3.9	1.63	120	0*
3	7.8	1.60	114	0*
4	15.6	1.51	97	3
5	31.3	ne	ne	ne
6	62.5	ne	ne	ne
7	125	ne	ne	ne
8	250	ne	ne	ne
9	500	ne	ne	ne
10	1000	ne	ne	ne
11	2500	ne	ne	ne
12	5000	ne	ne	ne
with metabolic activation				
C	0	1.40	100	0
1	7.8	1.35	86	14
2	15.6	1.46	114	0*
3	31.3	1.33	82	18
4	62.5	1.31	78	22
5	125	1.24	59	41
6	250	1.26	64	36
7	500	ne	ne	ne
8	1000	ne	ne	ne
9	2500	ne	ne	ne
10	5000	ne	ne	ne

The CBPI was determined in 500 cells per culture of each test group.
The relative values of the CBPI are related to the negative control.

C: Negative Control (Culture medium)
CBPI: Cytokinesis Block Proliferation Index, $CBPI = ((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
CBPI rel.: $100 \times ((CBPI_{\text{Test conc}} - 1) / (CBPI_{\text{control}} - 1))$
c_1: mononucleate cells
c_2: binucleate cells
c_x: multinucleate cells
n: total number of cells
ne: not evaluable

Cytostasis [%] = 100 - CBPI relative [%]
*: the cytostasis is defined 0, when the relative CBPI exceeds 100%

12.1.2. Experiment I

Table 4: Experiment I - CBPI: 4 h treatment (*without* and *with* metabolic activation), 44 h fixation interval

Dose Group	Concentration [µg/mL]	CBPI 1/2	CBPI 2/2	CBPI relative [%]	Cytostasis relative [%]
without metabolic activation					
C	0	1.43	1.43	100	0
1	5	1.45	1.38	98	2
2	10	1.46	1.31	91	9
3	15	1.32	1.26	68	32
EMS	1200	1.39	1.27	78	22
Colcemid	0.8	1.13	1.06	23	77
with metabolic activation					
C	0	1.57	1.54	100	0
2	50	1.45	1.46	82	18
3	100	1.36	1.39	67	33
5	200	1.26	1.32	52	48
7	275	1.20	1.24	40	60
CPA	15	1.55	1.44	89	11

The CBPI was determined in 500 cells per culture of each test group.
The relative values of the CBPI are related to the negative control.

C:	Negative Control (Culture medium)
EMS:	Ethylmethanesulfonate, Positive Control (without metabolic activation) [1200 µg/mL]
Colcemid:	Positive Control (without metabolic activation) [0.8 µg/mL]
CPA:	Cyclophosphamide, Positive Control (with metabolic activation) [15 µg/mL]
CBPI:	Cytokinesis Block Proliferation Index, CBPI = $((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
CBPI rel.:	$100 \times ((CBPI_{Test\ conc} - 1) / (CBPI_{control} - 1))$
c_1:	mononucleate cells
c_2:	binucleate cells
c_x:	multinucleate cells
n:	total number of cells
CBPI 1/2	Slide 1 of 2
CBPI 2/2	Slide 2 of 2

Cytostasis [%] = 100- CBPI relative[%]

Table 5: Experiment I - Micronucleus induction in human lymphocytes, 4 h treatment, 44 h fixation interval, *without* metabolic activation

Dose Group	Concentration [µg/mL]	Culture	Scored binucleated Cells	Micronuclei	Micronucleated Cells Frequency
C	0	1	2000	10	0.50
		2	2000	8	0.40
		total	**4000**	**18**	**0.45**
1	5	1	2000	15	0.75
		2	2000	8	0.40
		total	**4000**	**23**	**0.58**
2	10	1	2000	18	0.90
		2	2000	17	0.85
		total	**4000**	**35**	**0.88**
3	15	1	2000	10	0.50
		2	2000	8	0.40
		total	**4000**	**18**	**0.45**
EMS	1200	1	1000	31	3.10
		2	1000	17	1.70
		total	**2000**	**48**	**2.40**
Colcemid	0.8	1	590	13	2.20
		2	974	24	2.46
		total	**1564**	**37**	**2.33**

The micronucleated cell frequency was determined where possible in 1000 binucleated cells in each of the two separate cultures per test group, except for the positive control colcemid (590 for the 1st and 974 for the 2nd culture). In case of significant difference between both slides (generally factor > 2) additional 1000 binucleated cells of the same concentration were screened to verify this analysis. Only the final count of all analyzed binucleated cells per culture and concentration is given in this table.

C: Negative Control (Culture medium)
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [1200 µg/mL]
Colcemid: Positive Control (without metabolic activation) [0.8 µg/mL]

Table 6: Experiment I - Micronucleus induction in human lymphocytes, 4 h treatment, 44 h fixation interval, *with* metabolic activation

Dose Group	Concentration [µg/mL]	Culture	Scored binucleated Cells	Micronuclei	Micronucleated Cells Frequency
C	0	1	2000	12	0.60
		2	2000	9	0.45
		total	**4000**	**21**	**0.53**
2	50	1	1000	4	0.40
		2	1000	5	0.50
		total	**2000**	**9**	**0.45**
3	100	1	2000	13	0.65
		2	2000	19	0.95
		total	**4000**	**32**	**0.80**
5	200	1	1000	9	0.90
		2	1000	9	0.90
		total	**2000**	**18**	**0.90**
7	275	1	2000	18	0.90
		2	2000	30	1.50
		total	**4000**	**48**	**1.20**
CPA	15	1	1000	39	3.90
		2	1000	21	2.10
		total	**2000**	**60**	**3.00**

The micronucleated cell frequency was determined where possible in 1000 binucleated cells in each of the two separate cultures per test group. In case of significant difference between both slides (generally factor > 2) additional 1000 binucleated cells of the same concentration were screened to verify this analysis. Only the final count of all analyzed binucleated cells per culture and concentration is given in this table.

C: Negative Control (Culture medium)
CPA: Cyclophosphamide, Positive Control (with metabolic activation) [15 µg/mL]

12.1.3. Experiment II

Table 7: Experiment II - CBPI: 44 h treatment (*without* metabolic activation), 44 h fixation interval

Dose Group	Concentration [µg/mL]	CBPI 1/2	CBPI 2/2	CBPI relative [%]	Cytostasis relative [%]
without metabolic activation					
C	0	1.42	1.55	100	0
8	0.10	1.43	1.53	100	0
9	0.25	1.39	1.37	79	21
10	0.50	1.33	1.34	69	31
11	1.0	1.23	1.25	50	50
12	2.5	1.15	1.15	31	69
EMS	900	1.15	1.16	32	68
Colcemid	0.04	1.09	1.10	20	80

The CBPI was determined in 500 cells per culture of each test group.
The relative values of the CBPI are related to the negative control.

C: Negative Control (Culture medium)
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [900 µg/mL]
Colcemid: Positive Control (without metabolic activation) [0.04 µg/mL]
CBPI: Cytokinesis Block Proliferation Index, CBPI = $((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
CBPI rel.: $100 \times ((CBPI_{Test\ conc} - 1) / (CBPI_{control} - 1))$
c_1: mononucleate cells
c_2: binucleate cells
c_x: multinucleate cells
n: total number of cells
CBPI 1/2 Slide 1 of 2
CBPI 2/2 Slide 2 of 2

Cytostasis [%] = 100- CBPI relative[%]

Table 8: Experiment II - Micronucleus induction in human lymphocytes, 44 h treatment, 44 h fixation interval, *without* metabolic activation

Dose Group	Concentration [µg/mL]	Culture	Scored binucleated Cells	Micronuclei	Micronucleated Cells Frequency
C	0	1	1000	4	0.40
		2	1000	6	0.60
		total	**2000**	**10**	**0.50**
8	0.10	1	1000	4	0.40
		2	1000	8	0.80
		total	**2000**	**12**	**0.60**
9	0.25	1	2000	9	0.45
		2	2000	6	0.30
		total	**4000**	**15**	**0.38**
10	0.50	1	1000	4	0.40
		2	1000	5	0.50
		total	**2000**	**9**	**0.45**
11	1.0	1	2000	9	0.45
		2	2000	21	1.05
		total	**4000**	**30**	**0.75**
12	2.5	1	848	5	0.59
		2	1000	10	1.00
		total	**1848**	**15**	**0.79**
EMS	900	1	620	18	2.90
		2	1000	19	1.90
		total	**1620**	**37**	**2.40**
Colcemid	0.04	1	689	13	1.89
		2	688	31	4.51
		total	**1377**	**44**	**3.20**

The micronucleated cell frequency was determined where possible in 1000 binucleated cells in each of the two separate cultures per test group, except for concentration group 12 (848 for the 1st and 1000 for the 2nd culture), the positive control EMS (620 for the 1st and 1000 for the 2nd) and the positive control colcemid (689 for the 1st and 688 for the 2nd). In case of significant difference between both slides (generally factor > 2) additional 1000 binucleated cells of the same concentration were screened to verify this analysis. Only the final count of all analyzed binucleated cells per culture and concentration is given in this table.

C: Negative Control (Culture medium)
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [900 µg/mL]
Colcemid: Positive Control (without metabolic activation) [0.04 µg/mL]

12.1.4. Micronuclei Effects

Table 9: Summary of Micronuclei Effects: Experiment I *without* and *with* metabolic activation

Dose Group	Concentration [µg/mL]	Treatment Time	Fixation Interval	Micronucleated Cells Frequency
without metabolic activation				
C	0	4 h	44 h	**0.45**
1	5	4 h	44 h	**0.58**
2	10	4 h	44 h	**0.88**
3	15	4 h	44 h	**0.45**
EMS	1200	4 h	44 h	**2.40**
Colcemid	0.8	4 h	44 h	**2.33**
with metabolic activation				
C	0	4 h	44 h	**0.53**
2	50	4 h	44 h	**0.45**
3	100	4 h	44 h	**0.80**
5	200	4 h	44 h	**0.90**
7	275	4 h	44 h	**1.20**
CPA	15	4 h	44 h	**3.00**

The micronucleated cell frequency was determined where possible in 1000 binucleated cells in each of the two separate cultures per test group , except for the positive control colcemid (590 for the 1st and 974 for the 2nd culture). In case of significant difference between both slides (generally factor > 2) additional 1000 binucleated cells of the same concentration were screened to verify this analysis. Only the final count of all analyzed binucleated cells per culture and concentration is given in this table.

C: Negative Control (Culture medium)
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [1200 µg/mL]
Colcemid: Positive Control (without metabolic activation) [0.8 µg/mL]
CPA: Cyclophosphamide, Positive Control (with metabolic activation) [15 µg/mL]

Table 10: Summary of Micronuclei Effects: Experiment II *without* metabolic activation

Dose Group	Concentration [µg/mL]	Treatment Time	Fixation Interval	Micronucleated Cells Frequency
without metabolic activation				
C	0	44 h	44 h	**0.50**
8	0.10	44 h	44 h	**0.60**
9	0.25	44 h	44 h	**0.38**
10	0.50	44 h	44 h	**0.45**
11	1.0	44 h	44 h	**0.75**
12	2.5	44 h	44 h	**0.79**
EMS	900	44 h	44 h	**2.40**
Colcemid	0.04	44 h	44 h	**3.20**

The micronucleated cell frequency was determined where possible in 1000 binucleated cells in each of the two separate cultures per test group, except for concentration group 12 (848 for the 1st and 1000 for the 2nd culture), the positive control EMS (620 for the 1st and 1000 for the 2nd) and the positive control colcemid (689 for the 1st and 688 for the 2nd). In case of significant difference between both slides (generally factor > 2) additional 1000 binucleated cells of the same concentration were screened to verify this analysis. Only the final count of all analyzed binucleated cells per culture and concentration is given in this table.

C: Negative Control (Culture medium)
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [900 µg/mL]
Colcemid: Positive Control (without metabolic activation) [0.04 µg/mL]

12.1.5. Biometry

Table 11: Biometry - Experiment I *without* metabolic activation

Statistical significance at the 5% level ($p < 0.05$) was evaluated by the non-parametric χ^2 test. The p value was used as a limit in judging for significance levels in comparison with the concurrent negative control.

Control versus Test Group	Concentration [µg/mL]	Treatment Time	Micronuclei Frequencies [%]	Significance	P Value
EMS	1200	4	2.40	+	<0.0001
Colcemid	0.8	4	2.33	+	<0.0001
1	5	4	0.58	-	0.4337
2	10	4	0.88	+	0.0191
3	15	4	0.45	-	1.0000

+: significant
-: not significant
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [1200 µg/mL]
Colcemid: Positive Control (without metabolic activation) [0.8 µg/mL]

Statistical significance: statistical significant difference in micronucleated cells frequency compared to negative control (nonparametric $\chi 2$ test, $p < 0.05$).

Table 12: Biometry - Experiment I *with* metabolic activation

Statistical significance at the 5% level ($p < 0.05$) was evaluated by the non-parametric χ^2 test. The p value was used as a limit in judging for significance levels in comparison with the concurrent negative control.

Control versus Test Group	Concentration [µg/mL]	Treatment Time [h]	Micronuclei Frequencies [%]	Significance	P Value
CPA	15	4	3.00	+	<0.0001
2	50	4	0.45	-	0.6978
3	100	4	0.80	-	0.1295
5	200	4	0.90	-	0.0884
7	275	4	1.20	+	0.0011

+: significant
-: not significant
CPA: Cyclophosphamide, Positive Control (with metabolic activation) [15 µg/mL]

Statistical significance: statistical significant difference in micronucleated cells frequency compared to negative control (nonparametric $\chi 2$ test, $p < 0.05$).

Table 13: Biometry - Experiment II *without* metabolic activation

Statistical significance at the 5% level ($p < 0.05$) was evaluated by the non-parametric χ^2 test. The p value was used as a limit in judging for significance levels in comparison with the concurrent negative control.

Control versus Test Group	Concentration [µg/mL]	Treatment Time [h]	Micronuclei Frequencies [%]	Significance	P Value
EMS	900	44	2.40	+	<0.0001
Colcemid	0.04	44	3.20	+	<0.0001
8	0.10	44	0.60	-	0.6690
9	0.25	44	0.38	-	0.4786
10	0.50	44	0.45	-	0.8181
11	1.0	44	0.75	-	0.2620
12	2.5	44	0.79	-	0.2292

+: significant
-: not significant
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [900 µg/mL]
Colcemid: Positive Control (without metabolic activation) [0.04 µg/mL]

Statistical significance: statistical significant difference in micronucleated cells frequency compared to negative control (nonparametric $\chi 2$ test, $p < 0.05$).

Table 14: Biometry – Trend test

Statistical significance at the 5% level ($p < 0.05$) was evaluated by the χ^2 test for trend. The p value was used as a limit in judging for significance levels.

Experiment	Treatment Time [h]	Significance	P Value
Exp. I without metabolic activation	4	-	0.4810
Exp. I with metabolic activation	4	+	0.0031
Exp. II without metabolic activation	44	-	0.1270

+: significant
-: not significant

Statistical significance: statistical significant concentration-related increase in micronucleated cells frequency ($\chi 2$ test for trend, $p < 0.05$).

12.2. Discussion

The test item Glucose oxidase produced with *Trichoderma reesei* was investigated for a possible potential to induce micronuclei in human lymphocytes *in vitro* in the absence and presence of metabolic activation with S9.

The selection of the concentrations used in main experiment I and II was based on data from the pre-experiment according to the guidelines.

In experiment I **without** metabolic activation a concentration of 15 µg/mL and **with** metabolic activation a concentration of 275 µg/mL was selected as highest concentration for the microscopic analysis of micronuclei. In experiment I **without** metabolic activation the highest concentration selected for microscopic analysis (15 µg/mL) showed a relative cytostasis of 32% and thus did not reach the toxicity of 50-60% compared to the concurrent negative control as demanded by OECD 487. However the next concentration tested (17.5 µg/mL) already showed such a strong cytotoxic effect that no analysable cells could be observed on the slides. Due to this steep toxicity gradient the analysis of a concentration of 15 µg/mL as highest concentration was considered acceptable.
In experiment II **without** metabolic activation a concentration of 2.5 µg/mL was selected as highest concentration for the microscopic analysis of micronuclei.

The cells were prepared 44 h after start of treatment with the test item. The treatment intervals were 4 h **without** and **with** metabolic activation (experiment I) and 44 h **without** metabolic activation (experiment II). Parallel cultures were set up and 1000 binucleated cells per culture were scored for micronuclei.

The following concentrations were evaluated for micronuclei frequencies:

Experiment I with short-term exposure (4 h):

without metabolic activation: 5, 10 and 15 µg/mL

with metabolic activation: 50, 100, 200 and 275 µg/mL

Experiment II with long-term exposure (44 h):

without metabolic activation: 0.10, 0.25, 0.50, 1.0 and 2.5 µg/mL

12.2.1. Precipitation

The test item was dissolved and diluted in cell culture medium (RPMI medium). No precipitate of the test item was noted in all concentrations evaluated at the end of treatment.

12.2.2. Cytotoxicity

According to the OECD guideline 487 the maximum of cytotoxicity should not exceed the limit of 55 ± 5%. Higher levels of cytotoxicity may induce chromosome damage as a secondary effect of cytotoxicity. According to laboratory experience a culture showing reduced cell viability (more than 30% rel. cytostasis) compared to the negative/solvent control displays cytotoxicity. Due to this, the limit of cytotoxicity is ≤ 70%. This corresponds to ≥ 30% of rel. cytostasis.

In experiment I **without** metabolic activation no increase of the relative cytostasis above 30 % was noted up to a concentration of 10 µg/mL. At a concentration of 15 µg/mL a relative cytostasis of 32% was noted. In experiment I **with** metabolic activation no increase of the relative cytostasis above 30 % was noted up to a concentration of 50 µg/mL. At a concentration of 100 µg/mL a relative cytostasis of 33%, at a concentration of 200 µg/mL a relative cytostasis of 48% and at a concentration of 275 µg/mL a relative cytostasis of 60% was observed.

In experiment II **without** metabolic activation no increase of the relative cytostasis above 30 % was noted up to a concentration of 0.25 µg/mL. At a concentration of 0.50 µg/mL a relative cytostasis of 31%, at a concentration of 1.0 µg/mL a relative cytostasis of 50% and at a concentration of 2.5 µg/mL a relative cytostasis of 69% was noted.

12.2.3. Clastogenicity / Aneugenicity

In experiment I **without** metabolic activation the micronucleated cell frequency of the negative control (0.45%) was within the historical control limits of the negative control (0.44% – 1.56%, Table 15). The mean values of micronucleated cell frequencies found after treatment with the test item were 0.58% (5 µg/mL), 0.88% (10 µg/mL) and 0.45% (15 µg/mL). The number of micronucleated cells found in the groups treated with the test item was within the historical control limits of the negative control and did not show a biologically relevant increase compared to the concurrent negative control.

In experiment I **with** metabolic activation the micronucleated cell frequency of the negative control (0.53%) was within the historical control limits of the negative control (0.44% – 1.69%, Table 15). The mean values of micronucleated cell frequencies found after treatment with the test item were 0.45% (50 µg/mL), 0.80% (100 µg/mL), 0.90% (200 µg/mL) and 1.20% (275 µg/mL). The number of micronucleated cells found in the groups treated with the test item was within the historical control limits of the negative control and did not show a biologically relevant increase compared to the concurrent negative control.

In experiment II **without** metabolic activation the micronucleated cell frequency of the negative control (0.50%) was within the historical control limits of the negative control (0.44% – 1.56, Table 15). The mean values of micronucleated cell frequencies found after treatment with the test item were 0.60% (0.10 µg/mL), 0.38% (0.25 µg/mL), 0.45% (0.50 µg/mL), 0.75% (1.0 µg/mL) and 0.79% (2.5 µg/mL). The number of micronucleated cells found in the groups treated with the test item was within or below the historical control limits of the negative control and did not show a biologically relevant increase compared to the concurrent negative control.

The nonparametric χ^2 Test was performed to verify the results in both experiments. In experiment I **without** metabolic activation a statistically significant enhancement ($p = 0.0191$) of cells with micronuclei was noted at a concentration of 10 µg/mL (Table 11) and in experiment I **with** metabolic activation a statistically significant enhancement ($p = 0.0011$) of cells with micronuclei was noted at a concentration of 275 µg/mL (Table 12). However, the frequency of micronucleated cells was within the historical control limits of the negative control and significant cytotoxicity was observed for the concentration of 275 µg/mL **with** metabolic activation. Therefore, these increases were regarded as not biologically relevant. No statistically significant enhancement ($p<0.05$) of cells with micronuclei was noted in the concentration groups of the test item evaluated in experiment II.

The χ^2 Test for trend was performed to test whether there is a concentration-related increase in the micronucleated cells frequency in the experimental conditions. No statistically significant increase was observed in experiment I and II **without** metabolic activation. In experiment I **with** metabolic activation a statistically significant increase of the micronucleated cells frequency was observed. However, since all values of the micronucleated cell frequency of this experimental condition were within the historical control limits of the negative control, this increase was regarded as not biologically relevant.

EMS (900 and 1200 µg/mL) and CPA (15 µg/mL) were used as clastogenic controls and colcemid as aneugenic control (0.04 and 0.8 µg/mL). They induced distinct and statistically significant increases of the micronucleus frequency, demonstrating the validity of the assay.

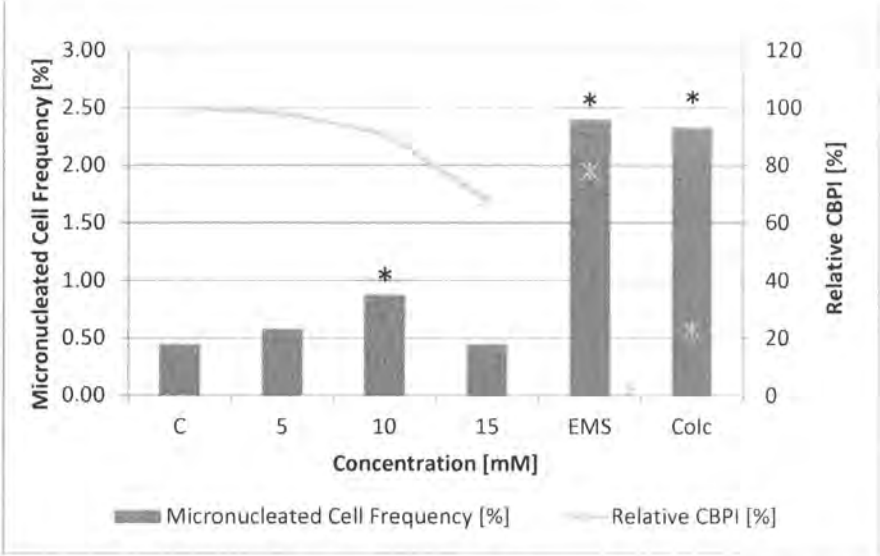

Figure 1: Micronucleus Frequency and Growth rate for Experiment I *without* metabolic activation

The CBPI was determined in 500 cells per culture of each test group.
The relative values of the CBPI are related to the negative control.

Micronucleated Cell Frequency was determined in 4000 cells (2000 cells per slide), except for the positive controls EMS (2000 cells) and colcemid (1564 cells).

C: Negative Control (Culture medium)
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [1200 µg/mL]
Colc: Colcemid, Positive Control (without metabolic activation) [0.8 µg/mL]
CBPI: Cytokinesis Block Proliferation Index, CBPI = $((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
CBPI rel.: $100 \times ((CBPI_{\text{Test conc}} - 1) / (CBPI_{\text{control}} - 1))$
c_1: mononucleate cells
c_2: binucleate cells
c_x: multinucleate cells
n: total number of cells
*: statistically significant increase of micronucleated cells

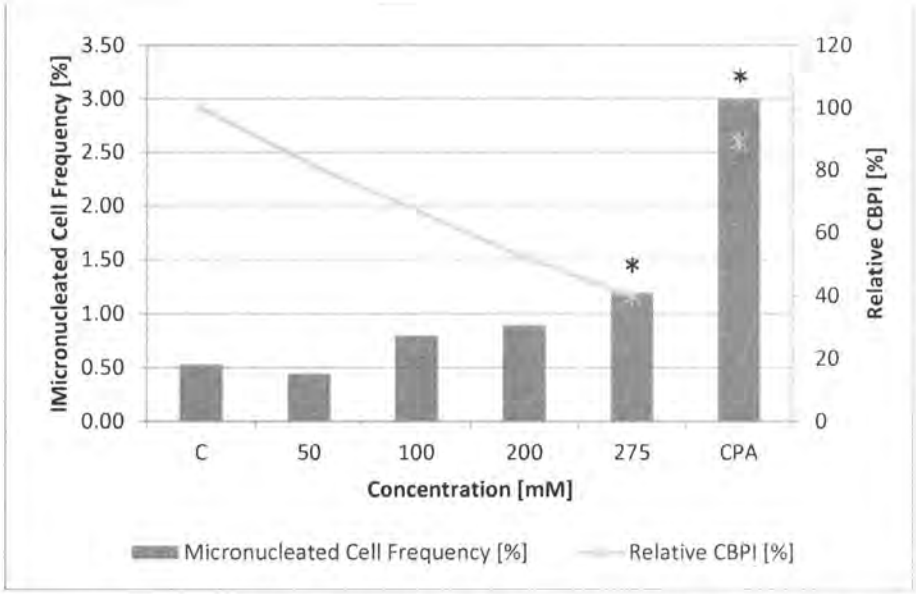

Figure 2: Micronucleus Frequency and Growth rate for Experiment I *with* metabolic activation

The CBPI was determined in 500 cells per culture of each test group.
The relative values of the CBPI are related to the negative control.

Micronucleated Cell Frequency was determined in 2000 cells (1000 cells per slide), except for the negative control and at concentrations of 100 and 275 µg/mL (4000 cells).

C: Negative Control (Culture medium)
CPA: Cyclophosphamide, Positive Control (with metabolic activation) [15 µg/mL]
CBPI: Cytokinesis Block Proliferation Index, CBPI = $((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
CBPI rel.: $100 \times ((CBPI_{\text{Test conc}} - 1) / (CBPI_{\text{control}} - 1))$
c_1: mononucleate cells
c_2: binucleate cells
c_x: multinucleate cells
n: total number of cells
*: statistically significant increase of micronucleated cells

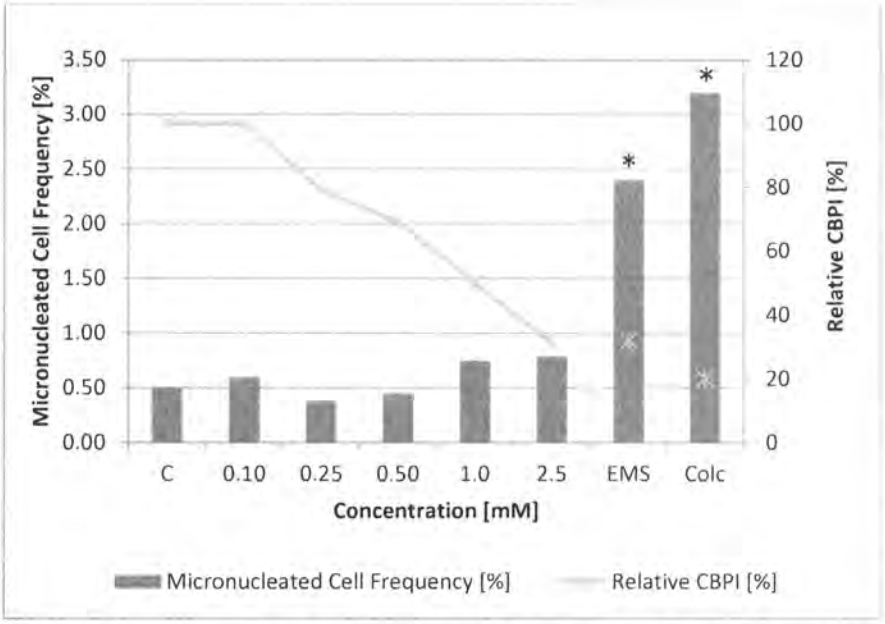

Figure 3: Micronucleus Frequency and Growth rate for Experiment II *without* metabolic activation

The CBPI was determined in 500 cells per culture of each test group.
The relative values of the CBPI are related to the negative control.

Micronucleated Cell Frequency was determined in 2000 cells (1000 cells per slide), except at concentrations 0.25 and 1.0 µg/mL (4000 cells), at concentration 2.5 µg/mL (1848 cells) and for the positive control EMS (1620 cells) and colcemid (1377 cells).

C: Negative Control (Culture medium)
EMS: Ethylmethanesulfonate, Positive Control (without metabolic activation) [900 µg/mL]
Colc: Colcemid, Positive Control (without metabolic activation) [0.04 µg/mL]
CBPI: Cytokinesis Block Proliferation Index, CBPI = $((c_1 \times 1) + (c_2 \times 2) + (c_x \times 3))/n$
CBPI rel.: $100 \times ((CBPI_{\text{Test conc}} - 1) / (CBPI_{\text{control}} - 1))$
c_1: mononucleate cells
c_2: binucleate cells
c_x: multinucleate cells
n: total number of cells
*: statistically significant increase of micronucleated cells

13. Conclusion

In conclusion, it can be stated that during the study described and under the experimental conditions reported, the test item Glucose oxidase produced with *Trichoderma reesei* did not induce structural and/or numerical chromosomal damage in human lymphocytes.

Therefore, Glucose oxidase produced with *Trichoderma reesei* is considered to be non-mutagenic with respect to clastogenicity and/or aneugenicity in the *in vitro* Mammalian Cell Micronucleus Test.

14. Distribution of the Report

1 original (paper):	Sponsor
1 copy (paper):	Eurofins Munich
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15. References

15.1. Guidelines

[1] Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498)

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[4] Ninth Addendum to OECD Guidelines for Testing of Chemicals, Section 4, No. 487, "In Vitro Mammalian Cell Micronucleus Test", adopted 26 September, 2014

15.2. Literature

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15.3. Internal Eurofins Munich SOP

Standard Operating Procedures (SOPs), No. 15-2-14

16. Appendix: Historical Laboratory Control Data

Table 15: Historical Laboratory Control Data of the negative and solvent control in human lymphocytes (negative control: in 2009-2013, solvent control: in 2008-2013)

	Negative Control	
	metabolic activation	
	without	**with**
Mean	1.00	1.06
SD	0.28	0.31
RSD	27.85	29.50
Min	0.50	0.65
Max	1.55	1.60
LCL	0.44	0.44
UCL	1.56	1.69
n	28	12

	Solvent Control	
	metabolic activation	
	without	**with**
Mean	1.19	1.09
SD	0.33	0.33
RSD	27.39	29.77
Min	0.70	0.60
Max	1.60	1.70
LCL	0.54	0.44
UCL	1.84	1.74
n	11	8

Negative Control: Cell culture medium
Solvent Control: DMSO or ethanol 1% v/v in cell culture medium
Mean: Mean number of micronucleated cells (%)
SD: Standard Deviation
RSD: Relative Standard Deviation (%)
Min: Minimum number of micronucleated cells (%)
Max: Maximum number of micronucleated cells (%)
LCL: Lower control limit (95%, mean-2SD)
UCL: Upper control limit (95%, mean+2SD)
n: Number of assays

Table 16: Historical Laboratory Control Data of the positive control in human lymphocytes (in 2009-2013)

	Positive Control		
	metabolic activation		
	without		with
	EMS	Colcemid	CPA
Mean	3.80	6.12	4.09
SD	1.22	4.12	1.68
RSD	32.10	67.24	41.14
Min	2.15	2.20	3.07
Max	7.00	21.60	8.65
LCL	1.36	0.00	0.73
UCL	6.23	14.36	7.45
n	28	28	12

EMS:	Positive Control-clastogenicity without metabolic activation: Ethylmethanesulfonate
Colcemid:	Positive Control- aneugenicity without metabolic activation
CPA:	Positive Control-clastogenicity with metabolic activation: Cyclophosphamide
Mean:	Mean number of micronucleated cells (%)
SD:	Standard Deviation
RSD:	Relative Standard Deviation (%)
Min:	Minimum number of micronucleated cells (%)
Max:	Maximum number of micronucleated cells (%)
LCL:	Lower control limit (95%, mean-2SD)
UCL:	Upper control limit (95%, mean+2SD)
n:	Number of assays

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in cooperation with BIOSERVICE SCIENTIFIC LABORATORIES

90-Day Repeated Dose Oral Toxicity Study in Wistar Rats

with

Glucose oxidase produced with *Trichoderma reesei*

Report

Version: Final

Study Completion Date: 16 SEP 2016

Eurofins Munich / BSL Munich Study No.: 154307

Sponsor:

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1. Copies of the GLP Certificates

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GLP-Bescheinigung/Statement of GLP Compliance
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Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

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Kategorie 3/ Category 3
Kategorie 8/ Category 8
Kategorie 9*/ Category 9*

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other tests:
biological an microbiological safety evaluation on medical devices and pharmaceuticals; contract archiving

Datum der Inspektion/Date of Inspection
(Tag.Monat.Jahr/day.month.year)

18. bis 19.03.2015

Die/Der genannte Prüfeinrichtung/Prüfstandort befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility/test site is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung/ diesem Prüfstandort die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.

Based on the inspection report it can be confirmed, that this test facility/test site is able to conduct the aforementioned studies in compliance with the Principles of GLP.

(b) (6)

Schwabach, 05.06.2015

Dr. Peter Franke
Leiter der GLP-Landesleitstelle Bayern

GLP- Landesleitstelle Bayern
Bayerisches Landesamt für Gesundheit
und Lebensmittelsicherheit
Rathausgasse 4
91126 Schwabach

Bayerisches Landesamt für
Gesundheit und Lebensmittelsicherheit

GLP-Bescheinigung/Statement of GLP Compliance

(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at:

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Kategorie 9*/ Category 9*
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Bioaktivitätsprüfungen / Bioactivity testing

Datum der Inspektion/Date of Inspection
(Tag.Monat.Jahr/day.month.year)

18. bis 19.03.2015

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Based on the inspection report it can be confirmed, that this test facility/test site is able to conduct the aforementioned studies in compliance with the Principles of GLP.

(b) (6)

Schwabach, 05.06.2015

Dr. Peter Franke
Leiter der GLP-Landesleitstelle Bayern

GLP- Landesleitstelle Bayern
Bayerisches Landesamt für Gesundheit
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2. Contents

3. List of Tables

4. Preface

4.1. Abbreviations

ALAT	alanine aminotransferase
Alb	albumin
ANOVA	Analysis of Variance
AP	alkaline phosphatise
approx.	approximately
aPTT	activated partial thromboplastin time
Art.	Artikel *(article)*
ASAT	aspartate-aminotransferase
Baso	basophils
BGBl.	Bundesgesetzblatt *(Federal Law Gazette)*
BIL	bilirubin
BSL Munich	BSL BIOSERVICE Scientific Laboratories Munich GmbH
bw	body weight
C	control
Ca	calcium
Chol	cholesterol
Crea	creatinine
Dipl.-Biol.	Diplom Biologe (*Biology Diploma*)
e.g.	exempli gratia *(for example)*
EC	European Commission
EDTA	ethylen diamine tertraacetic acid
Eos	eosinophils
Ery	erythrocytes
Eurofins Munich	Eurofins BioPharma Product Testing Munich GmbH
GGT	gamma-glutamyl-transferase
GLP	Good Laboratory Practice
Gluc	glucose
GmbH	Gesellschaft mit beschränkter Haftung *(company with limited liability)*
H&E	hematoxylin & eosin
Hb	haemoglobin
Hct	haematocrit
HD	high dose
IVC	individually ventilated cages

K	potassium
Ket	ketone bodies
LD	low dose
Leu	leukocytes
Lym	lymphocytes
Luc	large unstained cells
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MD	medium dose
Mono	monocytes
N	number
Na	sodium
Neu	neutrophils
NOAEL	No-Observed-Adverse-Effect Level
Nr.	Nummer *(number)*
OECD	Organisation for Economic Cooperation and Development
P	phosphate
PLT	platelet count
PT	prothrombin time
QA	Quality Assurance
QAU	Quality Assurance Unit
RBC	red blood cell count
Re	reticulocytes
SD	standard deviation
SOP	Standard Operating Procedure
SPF	specific-pathogen free
TBIL	total bilirubin
TP	total protein
UBG	urobilinogen
WBC	white blood cells
WI	Wistar

4.2. General

Sponsor:	AB Enzymes GmbH Feldbergstr. 78 64293 Darmstadt Germany
Study Monitor:	Mrs Marianne Dessen-Mugniot
Test Facility:	BSL BIOSERVICE Scientific Laboratories Munich GmbH Behringstr. 6/8 82152 Planegg Germany
Eurofins Munich / BSL Munich Study No.:	154307
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*

4.3. Project Staff

Study Director:	Dr. Philip Allingham BSL BIOSERVICE Scientific Laboratories Munich GmbH Behringstr. 6/8 82152 Planegg Germany
Management:	Dr. Angela Lutterbach / Dr. Katrin Witschital BSL BIOSERVICE Scientific Laboratories Munich GmbH Behringstr. 6/8 82152 Planegg Germany
Head of GLP Quality Assurance Unit:	Dipl.-Biol. Carolin Schmidt Eurofins BioPharma Product Testing Munich GmbH Behringstr. 6/8 82152 Planegg Germany
Head of Quality Assurance Unit for Test Site 1 and 2:	Mrs Nina Häuselmann AnaPath GmbH Quality Assurance GLP Buchsweg 56 4625 Oberbuchsiten Switzerland

Test Site 1: (Histopathological Tissue Processing)	AnaPath GmbH AnaPath Services Hammerstrasse 49 4410 Liestal Switzerland
Principal Investigator:	Ms Katja Scharbert
Test Site 2: (Histological Evaluation)	AnaPath GmbH Buchsweg 56 4625 Oberbuchsiten Switzerland
Principal Investigator:	Dr. Yoshimasa Okazaki
Test Site 3: (Formulation Analysis)	IBACON GmbH Institut für Biologische Analytik und Consulting IBACON GmbH Arheilger Weg 17 64380 Rossdorf Germany
Principal Investigator:	Dr. Volker Wydra

4.4. Schedule

Arrival of the Test Item:	09 January 2015
Study Initiation Date:	06 November 2015
Amendment to Study Plan:	11 March 2016
2nd Amendment to Study Plan:	04 April 2016
3rd Amendment to Study Plan:	10 May 2016
Delivery of Animals:	05 November 2015
Acclimatisation Period:	05 November 2015 – 10 November 2015
Experimental Starting Date:	10 November 2015
Treatment Period:	17 November 2015- 17 February 2016
Necropsies:	15 February 2016 – 18 February 2016
Experimental Completion Date:	18 February 2016
Completion Date of Delegated Phase (Histopathology):	07 July 2016
Completion Date of Delegated Phase (Formulation Analysis):	04 July 2016

5. Quality Assurance

5.1. GLP Compliance

This study was conducted to comply with:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

OECD Principles of Good Laboratory Practice (as revised in 1997); OECD Environmental Health and Safety Publications; Series on Principles of Good Laboratory Practice and Compliance Monitoring – Number 1. Environment Directorate, Organisation for Economic Co-operation and Development, Paris 1998 [3].

The OECD Principles of Good Laboratory Practice are accepted by regulatory authorities throughout the European Community, USA and Japan.

'OECD Series on principles of Good Laboratory Practice and compliance monitoring' Document No 13 ENV/JM/MONO (2002) 9 [4].

This study was assessed for compliance with the study plan and the Standard Operating Procedures of Eurofins Munich and BSL Munich. The Quality Assurance Unit of Eurofins Munich was the lead QA. The study and/or the test facility were periodically inspected by the Quality Assurance Unit according to the corresponding SOPs. These inspections and audits were carried out by the Quality Assurance Unit of Eurofins Munich, personnel independent of staff involved in the study. A signed quality assurance statement, listing all performed audits, is included in the report.

5.2. Guidelines

This study followed the procedures indicated by internal Eurofins Munich and BSL Munich SOPs and the following internationally accepted guidelines and recommendations:

OECD Guidelines for Testing of Chemicals, Section 4, No. 408, "Repeated Dose 90 day Oral Toxicity Study in Rodents" adopted 21 September 1998 [5]

Commission Regulation (EC) No. 440/2008, L 142, Annex Part B, May 30, 2008 [6]

Commission Directive 2001/59/EC of 6 August 2001 [7]

Procedures and facilities comply with the requirements of Directive 2010/63/EU [8] and the national legislation defined in the animal protection law concerning the protection of animals used for experimental and other scientific procedures [9].

5.3. Archiving

For a period of 15 years (or shorter if in compliance with the GLP regulations) Eurofins Munich will store the records, materials and specimens in their scientific archives according to the GLP regulations.

The following records have to be stored according to the GLP regulations:

A copy of the final report, the study plan and documentation of all raw data generated during the conduct of the study (documentation forms as well as any other notes of raw data, printouts of instruments and computers) and the correspondence with the sponsor concerning the study. With exceptions, data were captured using the validated departmental computerised system Ascentos (Pathology Data Systems Ltd.) and these raw data will be archived electronically by E-WorkBook (version 9.4.0, ID Business Solutions Ltd.). For non electronic raw data archiving will be performed in paper form according to appropriate SOPs. Any document relating to the study will be discarded only with the prior consent of the sponsor.

The following materials and samples have to be stored according to the period of time specified in the GLP regulations:

A retained sample of the test item will be archived according to the GLP regulations, if possible, and will be discarded without the sponsor's prior consent.

Other materials and specimens have to be stored according to the GLP regulations and disposed of after the respective archiving period with the sponsor's prior consent.

Original raw data generated at AnaPath GmbH, paraffin blocks and tissue slides as well as all fixed tissues will be returned to the study director for archiving after finalisation of the study phase report. The original phase report generated at AnaPath GmbH will be sent to the study director for archiving after finalisation of the study phase report.

Copies of histotechnique raw data, pathology evaluation raw data and an electronic version of the phase report will be retained at AnaPath GmbH for at least 15 years.

As requested the remaining test item will be returned after the release of the last report of the project.

6. Statement of Compliance

Eurofins Munich / BSL Munich Study No.:	154307
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*
Study Director:	Dr. Philip Allingham

This study performed in the test facility BSL Munich was conducted in compliance with Good Laboratory Practice Regulations:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

"OECD Principles of Good Laboratory Practice (as revised in 1997)", Paris 1998 [3].

'OECD Series on principles of Good Laboratory Practice and compliance monitoring' Document No 13 ENV/JM/MONO (2002) 9 [4].

There were no circumstances that may have affected the quality or integrity of the study.

Study Director: Dr. Philip Allingham

(b) (6)

Date: 16 Sep 2016

7. Statement of the Quality Assurance Unit

Eurofins Munich / BSL Munich Study No.:	154307
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Title:	90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*
Study Director:	Dr. Philip Allingham

This report and the conduct of this study were inspected by the Quality Assurance Unit (Eurofins Munich) on the following dates:

Phases of QAU Inspections	Dates of QAU Inspections	Dates of Reports to the Study Director and Management
Audit Final Study Plan:	06 November 2015	06 November 2015
Audit Amendment to Final Study Plan:	11 March 2016	–
Audit 2nd Amendment to Final Study Plan:	30 March 2016	–
Audit 3rd Amendment to Final Study Plan:	10 May 2016	–
Audit Experimental Phase (study-based):	11 February 2016	11 February 2016
Audit Draft Report:	12 July 2016	12 July 2016
Audit Final Report:	16 SEP 2016	16 SEP 2016

This report reflects the raw data.

Member of the Quality Assurance Unit: (b) (6)

Print Name: Katrin Matscheko

Date: 16 Sep 2016

8. Summary

The aim of this study was to assess the possible health hazards which could arise from repeated exposure of Glucose oxidase produced with *Trichoderma reesei* via oral administration to rats over a period of 90 days.

The test item was administered daily in graduated doses to 3 groups of test animals, one dose level per group for a treatment period of 90 days. Animals of an additional control group were handled identically as the dose groups but received aqua ad injectionem (sterile water), the vehicle used in this study. The 4 groups comprised of 10 male and 10 female Wistar rats.

The following doses were evaluated:

Control:	0 mg/kg body weight
Low Dose:	100 mg/kg body weight
Medium Dose:	300 mg/kg body weight
High Dose:	1000 mg/kg body weight

The test item formulations were used not more than 10 days after preparation. The test item was dissolved in aqua ad injectionem and administered daily during a 90-day treatment period to male and female animals. Dose volumes were adjusted individually based on weekly body weight measurements.

During the period of administration, the animals were observed precisely each day for signs of toxicity. Animals no 54 and 71 that died was examined macroscopically and, surviving animals were sacrificed at the conclusion of the test and observed macroscopically.

Body weight and food consumption were measured weekly. At the conclusion of the treatment period, all animals were sacrificed and subjected to necropsy. The wet weight of a subset of tissues was taken and a set of organs/tissues was preserved.

A full histopathological evaluation of the tissues was performed on high dose and control animals. Any gross lesion macroscopically identified will be examined microscopically in all animals.

8.1. Summary Results

The acceptance criteria for concentration of test item in dose formulations were met and homogeneity was confirmed.

No test item related mortality and no clinical signs of toxicity were observed in this study. Treatment with Glucose oxidase produced with Trichoderma reesei had no influence on neurobehavioural parameters examined at the end of the treatment period. Body weight developed normally in all groups independent of treatment and Glucose oxidase produced with Trichoderma reesei did not affect food consumption.

At the end of the treatment period parameters of haematology, blood coagulation and clinical biochemistry were not affected by Glucose oxidase produced with Trichoderma reesei in a biologically relevant way. Urinary parameters were not affected by Glucose oxidase produced with Trichoderma reesei in this study. At necropsy of the animals macroscopic findings observed in Glucose oxidase produced with Trichoderma reesei treated animals were either incidental or also present in control animals. None of them was considered toxicologically relevant.

Differences in organ weight between Glucose oxidase produced with *Trichoderma reesei* treated animals were slight and either not statistically significant or only present in one gender, but in any case not associated with any histopathological findings. Moreover, Glucose oxidase produced with *Trichoderma reesei*, produced no histomorphologic evidence of toxicological properties in any organs and tissues examined.

8.2. Conclusion

On the basis of the present study, the 90-Day Repeated Dose Oral Toxicity study with Glucose oxidase produced with *Trichoderma reesei* in male and female Wistar rats, with dose levels of 100, 300, and 1000 mg/kg body weight day the following conclusions can be made:

There was no indicator for toxicity in any of the dose levels tested. Therefore, the NOEL may be established at 1000 mg/kg/day. Thus, the dose level of 1000 mg/kg/day also marks the NOAEL in this study.

9. Introduction

9.1. Justification for the Selection of the Test System

In the assessment and evaluation of the toxic characteristics of chemicals, the determination of toxicity using repeated doses by oral gavage is carried out after initial information on toxicity has been obtained by a dose range finding study.

The test is performed in the rat. The rat is a widely used rodent species in toxicological studies and acceptable to regular authorities.

This study provides information on the possible health hazards which could arise from repeated exposure over a certain period of time.

The test item is orally administered daily in graduated doses to several groups of test animals, one dose level per group, for a period of 90 days. During the period of administration, the animals are observed precisely each day for signs of toxicity. Animals which die or are euthanised for animal welfare reasons during the test are examined macroscopically and histopathologically. At the end of the test all surviving animals are euthanised and then examined macroscopically and histopathologically.

A battery of functional observation tests is performed to detect possible neurotoxic effects of the test item.

9.2. Justification for the Selection of the Test Method

No validated *in vitro* method is available for assessing systemic toxicity after repeated exposure.

10. Materials and Methods

10.1. Characterisation of the Test Item

The identity of the test item was inspected upon delivery at the test facility (e.g. test item name, batch no. and additional data were compared with the label) based on the following specifications provided by the sponsor.

Name:	Glucose oxidase produced with *Trichoderma reesei*
Chemical Name:	Glucose oxidase (food enzyme)
CAS No.:	9001-37-0
Batch No.:	P 140032 J
Expiry Date:	September 2016
Physical State:	powder
Colour:	brownish
Purity:	91.5 % TOS (Total Organic Substance) (Certificate of Analysis was attached in chapter 16)
Storage Conditions:	at room temperature, protected from light
Safety Precautions:	The routine hygienic procedures were sufficient to assure personnel health and safety.

10.2. Characterisation of the Vehicle

The vehicle used in this study was aqua ad injectionem (sterile water). The specifications provided by the supplier are listed as follows:

Name:	aqua ad injectionem
Manufacturer:	AlleMan Pharma
Batch No.:	503424
Physical State:	liquid
Storage Conditions:	at room temperature
Expiry Date:	one week after opening of respective vials; between 24 November 2015 and 14 February 2016
Safety Precautions:	The routine hygienic procedures were sufficient to assure personnel health and safety.

10.3. Preparation of the Test Item Formulations

The test item, as delivered, was weighed into a tarred plastic vial on a precision balance and the vehicle was added to give the appropriate final concentration of the test item. Homogeneity of the test item in the vehicle was maintained by stirring the prepared suspension thoroughly before and during every dose administration.

The vehicle was selected based on the test item's characteristics. The test item formulations were used not more than 10 days after preparation. Used formulation vials were discarded on the day of opening. The vehicle was also used as control item.

10.4. Dose Formulation Analysis

Stability of the dosing formulations was tested once before the start of the treatment period (analytical report was attached to final report (Annex 3)).

Once in weeks 1, 6 and 12 samples of at least 50 mL were taken from the top, middle and bottom from low and high dose groups and stored between -15 and -35 °C, for determination of the concentration and homogeneity of test item in dosing formulations, In total 16 samples. At the same time, additionally a sample was taken from control and medium dose groups.

Each sample was retained twice (sample A, sample B, each of at least 50 mL).

At the end of the treatment period all A samples of dosing formulations were shipped to IBACON GmbH and analysed in accordance with GLP under the reference number 106931100.

The B samples were retained at BSL Munich until the analysis has been performed, and will be discarded after completion of the final study report.

IBACON GmbH issued a phase plan that was amended to the study plan. The results were reported in the Annex 3 of the final report.

10.5. Test System

Species/strain:	healthy Wistar rats, Crl: WI(Han) (Full Barrier)
Source:	Charles River, 97633 Sulzfeld, Germany
Sex:	male and female; the female animals were non-pregnant and nulliparous.
Age at the start of the treatment period:	approx. 7-8 weeks old
Body weight at the allocation of the animals to the experimental groups:	males: 145 – 159 g (mean: 152.1 g, ± 20% = 121.7 – 182.6 g) females: 131 – 143 g (mean: 137.05 g, ± 20% = 109.64 – 164.46 g)

The animals were derived from a controlled full-barrier maintained breeding system (SPF). According to Art. 9.2, No. 7 of the German Act on Animal Welfare [9] the animals were bred for experimental purposes.

10.5.1. Housing and Feeding Conditions

- Full barrier in an air-conditioned room
- Temperature: 22 ± 3 °C
- Relative humidity: 55 ± 10%
- Artificial light, sequence being 12 hours light, 12 hours dark
- Air change: 10 x / hour
- Free access to Altromin 1324 maintenance diet for rats and mice

- Free access to tap water, sulphur acidified to a pH of approximately 2.8 (drinking water, municipal residue control, microbiological controls at regular intervals)
- The animals were kept in groups of 5 animals / sex / group / cage in IVC cages (type IV, polysulphone cages) on Altromin saw fibre bedding
- Certificates of food, water and bedding are filed for two years at BSL Munich and afterwards archived at Eurofins Munich
- Adequate acclimatisation period (at least 5 days)

10.6. Number and Sex of the Animals

80 animals (40 males and 40 females) were included in the study (10 male and 10 female animals per group).

10.7. Preparation of the Animals

Prior to the start of the treatment period a detailed clinical observation outside the home cage was made. Animals showed no pathological signs before the first administration. Before the first administration all animals used for the study were weighed and assigned to the experimental groups with achieving a most homogenous variation in body weight throughout the groups of males and females, respectively (randomisation was performed with IDBS Workbook 9.4.0 software).

10.8. Experimental Groups and Doses

According to the results of a previous dose range finding study (BSL Munich Study No. 154306) and in consultation with the sponsor the following doses (Table 1) were selected for the 3 dose groups (LD = low dose, MD = medium dose, HD = high dose). The animals were treated with the test item formulation or vehicle on 7 days per week for a period of 90 days. 10 animals per gender and group were subjected to necropsy one day after the last administration (end of treatment period).

Table 1: Group and Animal Identification

Group No.	Group Name	Dose [mg/kg bw]	Subjected to Necropsy at the End of the Treatment Period	
			Animal No.	
			Male	Female
1	**C**	0	1-10	41-50
2	**LD**	100	11-20	51-60
3	**MD**	300	21-30	61-70
4	**HD**	1000	31-40	71-80

C = control, LD = low dose, MD = medium dose, HD = high dose

The highest dose level was chosen with the aim of inducing toxic effects, but no death or severe suffering. Thereafter, a descending sequence of dose levels was selected with a view to demonstrate any dosage related response and NOAEL.

The animals in the control group were handled in an identical manner to the test group subjects and received the vehicle using the same volume as used for the high dose group.

10.9. Administration of Doses

The test item formulation or vehicle were administered at a single dose to the animals by oral gavage. The application volume for all groups was 5 mL/kg body weight (Table 2).

For each animal the individual dosing volume was calculated on the basis of the body weight most recently measured.

Table 2: Dose, Application Volume and Concentration

Group No.	Group Name	Dose [mg/kg bw]	Application volume [mL/kg bw]	Concentration [mg/mL]
1	**C**	0	5	0
2	**LD**	100	5	20
3	**MD**	300	5	60
4	**HD**	1000	5	200

C = control, LD = low dose, MD = medium dose, HD = high dose

10.10. Body Weight and Food Consumption

The body weight was recorded once before the assignment to the experimental groups, on the first day of administration and weekly during the treatment period.

Food consumption was measured weekly during the treatment period.

10.11. Clinical Observations

All animals were observed for clinical signs during the entire treatment period of 90 days.

General clinical observations were made once a day, preferably at the same time each day and considering the peak period of anticipated effects after dosing. The health condition of the animals was recorded. General clinical observations were not recorded on 19 November 2015, 01 December 2015 and 31 December 2015.

Detailed cage side observations considering spontaneous activity, lethargy, recumbent position, convulsions, tremors, apnoea, asphyxia, vocalisation, diarrhoea, changes in skin and fur, eyes and mucous membranes (salivation, discharge), piloerection and pupil size were made outside the home cage in a standard arena once before the first administration and at least once a week thereafter. Detailed cage side observations were not performed on animals no. 46-50, 56-60, 66-70 and 76-80 on week 7 and on animal no. 35 in week 9.

Ophthalmological examination, using an ophthalmoscope was made on all animals before the first administration and in the last week of the treatment period.

10.12. Functional Observations

Once before the first exposure and once in the last week of exposure multiple detailed behavioural observations were made outside the home cage using a functional observational battery of tests [11]. These tests were conducted in all animals.

10.13. Haematology

Haematological parameters were examined at the end of the treatment prior to or as part of the sacrifice of the animals (see 10.17).

After overnight fasting, blood from the abdominal aorta of the animals was collected in EDTA-coated tubes.

The following haematological parameters were examined (Table 3).

Table 3: Haematology

Parameter	Instrument	Units
haematocrit value (Hct)	ADVIA®120 (Siemens)	%
haemoglobin content (Hb)	ADVIA®120 (Siemens)	g/dL
red blood cell count (RBC)	ADVIA®120 (Siemens)	10^{12}/L
mean corpuscular volume (MCV)	ADVIA®120 (Siemens)	fL
mean corpuscular haemoglobin (MCH)	ADVIA®120 (Siemens)	pg/erythrocyte
mean corpuscular haemoglobin concentration (MCHC)	ADVIA®120 (Siemens)	g/dL
reticulocytes (Re)	ADVIA®120 (Siemens)	%
platelet count (PLT)	ADVIA®120 (Siemens)	10^9/L
white blood cells (WBC)	ADVIA®120 (Siemens)	10^9/L
neutrophils (Neu)	ADVIA®120 (Siemens)	%
lymphocytes (Lym)	ADVIA®120 (Siemens)	%
monocytes (Mono)	ADVIA®120 (Siemens)	%
eosinophils (Eos)	ADVIA®120 (Siemens)	%
basophils (Baso)	ADVIA®120 (Siemens)	%
large unstained cells (Luc)	ADVIA®120 (Siemens)	%

10.14. Blood Coagulation

Coagulation parameters were examined at the end of the treatment prior to or as part of the sacrifice of the animals (see 10.17).

After overnight fasting, blood from the abdominal aorta of the animals was collected in citrate tubes.

The following coagulation parameters were examined (Table 4):

Table 4: Coagulation Parameters

Parameter	Instrument	Units
prothrombin time (PT)	ACL 7000 (IL Instrumental) or Kugelkoagulometer (ADW)	sec
activated partial thromboplastin time (aPTT)	ACL 7000 (IL Instrumental) or Kugelkoagulometer (ADW)	sec

10.15. Clinical Biochemistry

Parameters of clinical biochemistry were examined at the end of the treatment prior to or as part of the sacrifice of the animals (see 10.17).

After overnight fasting, blood from the abdominal aorta of the animals was collected in serum separator tubes.

The following parameters of clinical biochemistry were examined (Table 5):

Table 5: Clinical Biochemistry

Parameter	Instrument	Units
alanine aminotransferase (ALAT)	Olympus AU 480 Beckman Coulter	U/L
aspartate-aminotransferase (ASAT)	Olympus AU 480 Beckman Coulter	U/L
alkaline phosphatase (AP)	Olympus AU 480 Beckman Coulter	U/L
gamma-glutamyl-transferase (GGT)	Olympus AU 480 Beckman Coulter	U/L
creatinine (Crea)	Olympus AU 480 Beckman Coulter	µmol/L
total protein (TP)	Olympus AU 480 Beckman Coulter	g/L
albumin (Alb)	Olympus AU 480 Beckman Coulter	g/L
urea	Olympus AU 480 Beckman Coulter	mmol/L
total bilirubin (TBIL)	Olympus AU 480 Beckman Coulter	µmol/L
total cholesterol (Chol)	Olympus AU 480 Beckman Coulter	mmol/L
glucose (Gluc)	Olympus AU 480 Beckman Coulter	mmol/L
sodium (Na)	Olympus AU 480 Beckman Coulter	mmol/L
potassium (K)	Olympus AU 480 Beckman Coulter	mmol/L
calcium (Ca)	Olympus AU 480 Beckman Coulter	mmol/L
phosphate (P)	Olympus AU 480 Beckman Coulter	mmol/L
chloride (Cl)	Olympus AU 480 Beckman Coulter	mmol/L

Additionally, at necropsy serum samples of all animals were retained at the end of the treatment period and stored at -20° C for an evaluation of test item-related effects on the pituitary-thyroid axis and thyroid hormones.

10.16. Urinalysis

A urinalysis was performed with samples collected from all animals prior to or as part of the sacrifice of the animals. Additionally, urine colour/appearance was recorded.

The following parameters (Table 6) were measured using qualitative indicators (Heiland Urine Stripes URI 10SL).

Table 6: Urinalysis

Parameter	Method/Device
specific gravity	URI 10SL
nitrite	URI 10SL
pH-value (pH)	URI 10SL
protein	URI 10SL
glucose	URI 10SL
ketone bodies (Ket)	URI 10SL
urobilinogen (UBG)	URI 10SL
bilirubin (BIL)	URI 10SL
erythroctes (Ery)	URI 10SL
leukocytes (Leu)	URI 10SL

10.17. Pathology

Gross necropsy

One day after the last administration (study day 91) all surviving animals of the treatment period were sacrificed using anesthesia (ketamine, xylazin) and were subjected to a detailed gross necropsy which included careful examination of the external surface of the body, all orifices and the cranial, thoracic and abdominal cavities and their contents.

10.18. Organ Weight

The wet weight of the organs (Table 7) was taken from sacrificed animals as soon as possible. Paired organs were weighed together. Organ weights of animal no 54 and 71 that were found dead were not recorded.

Table 7: Organs Weighed at Necropsy

Tissue/Organ	Tissue/Organ
liver	uterus with cervix
kidneys	thymus
adrenals	thyroid/ parathyroid glands
testes	spleen
epididymides	brain
prostate, seminal vesicles and coagulating glands	pituitary gland
ovaries	heart

The following tissues (Table 8) from all animals were preserved in 4% neutral-buffered formaldehyde except eyes, testes and epididymides which were fixed in Modified Davidson's fixative for approximately 24 hours before they were transferred to 70% ethanol.

Table 8: Preserved and Examined Tissues

Tissue/Organ	Preserved at Necropsy	Histopatho-logical Examination
adrenal glands	x	x
all gross lesions	x	x
aorta	x	x
brain (incl. medulla/pons, cerebellar and cerebral cortex)	x	x
caecum	x	x
colon	x	x
duodenum	x	x
epididymides	x	x
eyes with optic nerve and Harderian gland	x	x
femur with knee joint	x	--
heart	x	x
ileum (including Peyer´s patches)	x	x
jejunum	x	x
kidneys	x	x
liver	x	x
lungs	x	x
lymph nodes (mandibular)	x	--
lymph nodes (mesenteric and axillary)	x	x
mammary gland area (male and female)	x	x
oesophagus	x	x
ovaries	x	x
oviducts	x	--
pancreas	x	x
pituitary	x	x
prostate and seminal vesicles with coagulating glands as a whole	x	x
rectum	x	x
salivary glands (sublingual, submandibular)	x	x
sciatic nerve	x	x
skeletal muscle	x	x
skin	x	x
spinal cord (cervical, thoracic and lumbar segments)	x	x

Table 8: Preserved and Examined Tissues (Continued)

Tissue/Organ	Preserved at Necropsy	Histopatho-logical Examination
spleen	x	x
sternum (with bone marrow)	x	x
stomach	x	x
testes	x	x
thymus	x	x
thyroid gland including parathyroid glands	x	x
tongue	x	--
trachea	x	x
ureters	x	--
urinary bladder	x	x
uterus with cervix and vagina	x	x

All animals found dead and/or intercurrently euthanised for animal welfare reasons were subjected to a gross necropsy and the organs preserved for a histopathological examination.

10.19. Histopathology

The afore-listed organs (Table 8) were examined histopathologically after preparation of paraffin sections and haematoxylin-eosin staining for the animals of the groups 1 and 4 sacrificed at the end of the treatment period and any animal found dead or euthanised before the planned day of sacrifice.

Discoloration possibly due to the test item was evaluated in the organs of all dose groups.

Histological processing of tissues to microscope slides was performed at the GLP-certified contract laboratory AnaPath GmbH, AnaPath Services, Hammerstrasse 49, 4410 Liestal, Switzerland (test site for tissue processing). Histopathological evaluation was performed at the GLP-certified contract laboratory AnaPath GmbH, Buchsweg 56, 4625 Oberbuchsiten, Switzerland (test site for histopathology). The study phases from test site 1 and 2 was performed in compliance with the Swiss Ordinance relating to Good Laboratory Practice adopted 18 May 2005 [SR 813.112.1] (Status as of 01 December 2012) [10]. Blocking, embedding, cutting, H&E staining and scientific slide evaluation were performed according to the corresponding SOP's of the test sites.

The principal investigator for histopathological tissue processing sent all raw data (including blocks, slides, paper raw data, statement of compliance and quality assurance statement) to the study director.

The principal investigator for histopathological evaluation provided the histopathology results to the study director by e-mail and sent a pathology phase report to the study director upon the completion of the study (Annex 2).

10.20. Evaluation of Results and Statistical Analysis

The findings of this study were evaluated in terms of the observed effects.

Parameters like body weight gain and food consumption were calculated for each animal as the difference in weight measured from one week to the next. Mean body weights are also presented as figures.

The relative organ weights were calculated in relation to the brain weight and in relation to the body weight (measured at necropsy) and are presented as percentage.

All results are reported in a tabular form (summarised in mean or summary tables and/or listed in individual data tables).

Analytical results and histopathological findings are presented in separate phase-reports attached to this report (Annex 2 and Annex 3).

With few exceptions, toxicology and pathology data were captured, using the validated computerised system Ascentos® System (version 1.1., Pathology Data Systems Ltd.). If not possible raw data will be recorded on paper according to appropriate SOPs.

A statistical assessment of the results of the body weight, parameters of haematology, blood coagulation and clinical biochemistry and absolute and relative organ weights were performed for each gender by comparing values of dosed with control animals using a one-way ANOVA and a post-hoc Dunnett Test. These statistics were performed with GraphPad Prism V.6.01 software or Ascentos 1.1.3 software ($p<0.05$ is considered as statistically significant).

11. Deviations from the Study Plan

There were the following deviations from the study plan:

Concerning:

Archiving, study plan, p. 10

Before:

A copy of the final report, the study plan and a documentation of all raw data generated during the conduct of the study (documentation forms as well as any other notes of raw data, printouts of instruments and computers) and the correspondence with the sponsor concerning the study. Any document relating to the study will be discarded only with the prior consent of the sponsor.

New:

A copy of the final report, the study plan and documentation of all raw data generated during the conduct of the study (documentation forms as well as any other notes of raw data, printouts of instruments and computers) and the correspondence with the sponsor concerning the study. With exceptions, data were captured using the validated departmental computerised system Ascentos (Pathology Data Systems Ltd.) and these raw data will be archived electronically by E-WorkBook (version 9.4.0, ID Business Solutions Ltd.). For non electronic raw data archiving will be performed in paper form according to appropriate SOPs. Any document relating to the study will be discarded only with the prior consent of the sponsor.

Reason:

Adaption of archiving procedure due to usage of the computerised system Ascentos®

Concerning:

Clinical observations, study plan, p. 15

Before:

General clinical observations will be made at least once a day, preferably at the same time each day and considering the peak period of anticipated effects after dosing. The health condition of the animals will be recorded.

Detailed cage side observations considering spontaneous activity, lethargy, recumbent position, convulsions, tremors, apnoea, asphyxia, vocalisation, diarrhoea, changes in skin and fur, eyes and mucous membranes (salivation, discharge), piloerection and pupil size will be made outside the home cage in a standard arena once before the first administration and at least once a week thereafter.

New:

General clinical observations were made once a day, preferably at the same time each day and considering the peak period of anticipated effects after dosing. The health condition of the animals was recorded. General clinical observations were not recorded on 19 November 2015, 01 December 2015 and 31 December 2015.

Detailed cage side observations considering spontaneous activity, lethargy, recumbent position, convulsions, tremors, apnoea, asphyxia, vocalisation, diarrhoea, changes in skin and fur, eyes and mucous membranes (salivation, discharge), piloerection and pupil size were made outside the home cage in a standard arena once before the first administration and at least once a week thereafter. Detailed cage side observations were not performed on animals no. 46-50, 56-60, 66-70 and 76-80 on week 7 and on animal no. 35 in week 9.

Reason:

Inadvertently, clinical findings were not recorded on the above-mentioned days. Due to staggered start these dates refer to study days 1, 2 or 3, 12, 13, 14 or 15 and 42, 43, 44 or 45 of a subset of animals on the respective dates. Detailed cage side observations were inadvertently not performed.

These deviations did not influence the quality or integrity of the present study.

12. Results

12.1. Mortality

For a detailed description of the findings see Annex 1.

During the treatment period of the study 2/80 animals were found dead. Both mortalities were related to technical reasons and are not assumed to be a consequence of systemic toxicity of the test item.

Female animal no. 54 of the LD group was found dead on study day 27. Histopathological evaluation identified an accidentally caused tracheal tissue injury – most probably caused by oral misgavaging as reason for this mortality.

Female animal no. 71 of the HD group was found dead on study day 82. In this animal marked aspiration pneumonia caused by accidental influx of the dosing solution into the lung was observed.

12.2. Clinical Observations

For a detailed description of the findings see Annex 1.

No clinical signs of toxicity were observed during the course of the study.

Detailed weekly clinical observations in the arena showed a significantly higher score of sleeping in the cage and lower score of moving in the cage of female animals of the high dose group when compared to controls in treatment week 8. These represent an isolated finding they are not considered adverse. As they were not observed in subsequent weeks or in female animals of this group, they are not considered to be test item related.

12.3. Functional Observation Battery

For a detailed description of the findings see Annex 1.

Glucose oxidase produced with Trichoderma reesei had no effect on neurobehavioural parameters determined in a function observation battery at the end of the treatment period.

A slightly but statistically significantly lower number of supported rearings in male animals of the medium and high dose groups before the start of the treatment period is not assumed to be a sign of an impaired health condition and is not considered to affect the results of this study.

12.4. Body Weight Development

For a detailed description of the findings see Annex 1.

In all groups body weights developed normally and were in the normal range of variation for this strain. Throughout the treatment period there were no statistically significant or biologically relevant differences in weight gain of male and female animals between dose groups and the control group.

At the end of the treatment period there were no statistically significant or biologically relevant differences in body weight between dose groups and control group.

12.5. Food Consumption

For a detailed description of the findings see Annex 1.

Throughout the treatment period there were no statistically significant or biologically relevant differences in food consumption of male and female animals between dose groups and the control group.

12.6. Haematology and Blood Coagulation

For a detailed description of the findings see Annex 1.

At the end of the treatment period there were no statistically significant or biologically relevant differences in haematological parameters or blood coagulation parameters between dose groups and control group.

12.7. Clinical Biochemistry

For a detailed description of the findings see Annex 1.

At the end of the treatment period serum Total Bilirubin values of female animals of the medium dose group were statistically significantly higher than in controls and slightly above the range of historical control data. Due to the slightness of this increase and in the absence of a dose-dependency and of correlated histopathological findings, this is assumed to be an incidental finding and is not considered a test item related biologically relevant effect.

Besides, there were no statistically significant or biologically relevant differences in clinical biochemistry parameters between dose groups and control group.

12.8. Urinalysis

For a detailed description of the findings see Annex 1.

At the end of the treatment period there were no biologically relevant differences in urinary parameters between dose groups and control group.

12.9. Pathology

For a detailed description of the findings see Annex 1.

At the end of the treatment period no test item related macroscopic findings were identified.

Incidental macroscopic findings in single animals of the dose groups were: small testes in animal no. 23 of the medium dose group, a marbled and pale liver of animal no. 77 of the high dose group.

The uterus of animals no. 59 and 60 of the low dose group, 63 of the medium dose group and 73, 74 and 76 of the high dose group was fluid-filled. However, this was also seen in control animals no. 42, 43 and 44. This finding which is considered to dependent on the stage of the estrous cycle and is not assumed to be related to the test item.

Autolysis was seen in the brain and eyes of animal no. 54 of the medium dose group. The lung of this animal was abnormally dark and the stomach, small intestines and ovaries, oviducts and uterus cannibalized. All organs/tissues of animal no. 71 were autolytic.

12.10. Organ Weight

For a detailed description of the findings see Annex 1.

Thymus weight was slightly but statistically significantly and dose-dependently decreased in female animals at all dose levels, when compared to controls. The absolute weight was 17% (LD group), 18% (MD group) and 19% (HD groups) below

controls, respectively. This effect was reflected in relative weights, when compared to body weight (statistically significantly decreased in MD (-17%) and HD groups (-18%)). A tendency towards higher thymus weight was observed in male animals of the low and medium dose groups. This was not seen at the high dose level.

Prostate weight was slightly – but not statistically significantly higher in all dose groups (LD: 13%, MD: 10% and HD: 8%) than in controls. This slight increase is also reflected in relative organs weights. Due to the slightness of this increase and in the absence of a dose-dependency, this is not assumed to be a biologically relevant effect.

Ovary weight was slightly – but not statistically significantly higher in animals of the medium and high dose groups (approx 13% respectively), when compared to controls. In the absence of histopathological findings in the high dose group, this is not assumed to be biologically relevant.

A slight – but not statistically significant increase in the weight of the thyroid/parathyroid in male animals (20% above controls) and a slight – but not statistically significant decrease in the weight of the same organ in females of the medium dose group (13% below controls) are considered isolated findings. In the absence of histopathological findings in the high dose group, this is not assumed to be biologically relevant.

A slight – but not statistically significantly increased weight of adrenal glands of male animals of the HD group (12% above controls), in the absence of histopathological findings, is not assumed to be biologically relevant.

12.11. Histopathology

For a detailed description of the findings see Annex 2.

Under the conditions of this study, the test item, Glucose oxidase produced with *Trichoderma reesei*, produced no histomorphologic evidence of toxicological properties in any organs and tissues examined.

In this study two females died prematurely before the end of the treatment period. The cause of animals' death was considered an accidental influx of the dosing solution into the respiratory tract or an accidental tissue injury related to dosing procedure in the respiratory tract. Either were not test item-related deaths.

All findings recorded in survivors were within the range of normal background lesions which may be recorded in animals of this strain and age, or were incidental lesions that were not related to treatment with the test item.

12.12. Dose Formulation Analysis

For a detailed description of the individual findings see Annex 3.

Concentration analysis of formulation samples was determined in study weeks 1, 6 and 12 for all dose groups. The mean recoveries observed in the low dose (LD), medium dose (MD) and high dose (HD) groups were 98%, 96% and 95% of the nominal concentration, respectively. Nominal concentrations were confirmed for all dose groups, as measured mean concentration did not differ from nominal concentration by more than 20%.

There was no trace of test item in the control samples.

In the control sample taken in week 1 an elevated content of inorganic carbon was detected, which is not considered to be related to the test item. This was confirmed by measurement of the corresponding second replicate.

Homogeneity of formulation samples was determined in study weeks 1,6 and 12 for the LD, MD and HD dose groups. The mean recovery observed for the LD dose group was between 95% and 102% of the nominal value and between 88% and 101% of the

nominal value for the HD dose group. The relative standard deviation of the different sampling locations (top, middle, bottom) were between 1.2% and 3.1% in LD dose group and 0.6% and 2.1% in HD dose group. All samples were homogenous, as COV was below 20%.

13. Conclusion

On the basis of the present study, the 90-Day Repeated Dose Oral Toxicity study with Glucose oxidase produced with Trichoderma reesei in male and female Wistar rats, with dose levels of 100, 300, and 1000 mg/kg body weight day the following conclusions can be made:

There was no indicator for toxicity in any of the dose levels tested. Therefore, the NOEL may be established at 1000 mg/kg/day. Thus, the dose level of 1000 mg/kg/day also marks the NOAEL in this study.

14. Distribution of the Report

1 original (paper):	Sponsor
1 copy (paper):	Eurofins Munich
1 copy (electronic):	Sponsor

15. References

15.1. Internal Eurofins Munich and BSL Munich SOPs

Standard Operating Procedures (SOPs), No. 11-4-7

15.2. Literature and Guidelines

[1] Chemikaliengesetz (“Chemicals Act”) of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498)

[2] Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis (“Consensus Document of the National and Länder Working Party on Good Laboratory Practice“) on the archiving and storage of records and materials, 5 May 1998

[3] OECD Principles of Good Laboratory Practice (as revised in 1997); OECD Environmental Health and Safety Publications; Series on Principles of Good Laboratory Practice and Compliance Monitoring - Number 1. Environment Directorate, Organisation for Economic Co-operation and Development, Paris 1998

[4] ‘OECD Series on principles of Good Laboratory Practice and compliance monitoring’ Document No 13 ENV/JM/MONO (2002) 9

[5] OECD Guidelines for Testing of Chemicals, Section 4, No. 408, “Repeated Dose 90 day Oral Toxicity Study in Rodents” adopted 21 September 1998

[6] Commission Regulation (EC) No. 440/2008, L 142, Annex Part B, May 30, 2008

[7] Commission Directive 2001/59/EC of 6 August 2001, adapting to technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances

[8] Directive 2010/63/EU of the European parliament of the council of 22 September 2010 on the protection of animals used for scientific purposes

[9] German Animal Welfare Act, Art. 9.2, No. 7 (Deutsches Tierschutzgesetz, 24. Juli 1972 (BGBl. I S. 1277), Inkrafttreten der letzten Änderung: 13. Juli 2013, (Art. 1 ÄndG vom 04. Juli 2013)

[10] Swiss Ordinance relating to Good Laboratory Practice adopted 18 May 2005 [SR 813.112.1] (Status as of 01 December 2012)

[11] Moser, V.C., McDaniel, K.M., Philips, P.M. (1991). Rat Strain and Stock Comparisons Using a Functional Observational Battery: Baseline Values and Effects of Amitraz. Toxicol.Appl. Pharmacol., 108, 267-283, 1991

16. Appendix – Certificate of Analysis

NOVALAB OY

ANALYSIS REPORT

Order: 1404846 1(2)
Date: 28.11.2014

ROAL Oy
Vilma Ikonen
Tykkimäentie 15
PL 57, 05201 Rajamäki

FINAS
Finnish Accreditation Service
T071 (EN ISO/IEC 17025)

Order name:	**Enzyme sample,P140032J, nutritional analysis**
Sample:	14MU0883 Glukoosi-oksidaasi, P140032J
Sampling time:	10.11.2014
Sample arrived:	11.11.2014
Analysis started:	13.11.2014

Analysis		Result	Method
Dry matter	%	94.9	Novalab 010*
Ash	%	3.5	Novalab 009*
Moisture	%	5.1	Novalab 010*
Protein	%	68.3	Novalab 001.A, kjeldahl*
Carbohydrate, calculated	%	23.1	
Energy value, calculated	kJ/100 g	1554	
Fat	%	<0.1	Novalab 076*

* Accredited method. Statement is not accredited. Results apply only samples analyzed.

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Business ID 0733227-8
Location Karkkila
VAT reg.

NOVALAB OY

ANALYSIS REPORT

Order: 1404846 2(2)
Date: 28.11.2014

ROAL Oy
Vilma Ikonen
Tykkimäentie 15
PL 57, 05201 Rajamäki

FINAS
Finnish Accreditation Service
T071 (EN ISO/IEC 17025)

Novalab Oy
(b) (6)

Eeva Luoma
Head of Quality
The certificate has been signed electronically.

Add.details Methods:
Moisture: AOAC 2002 950.46 (39.1.02) modified
Protein: AOAC 2002 2001.11 (4.2.11) modified
Fat: NMKL 131:1989 modified
Ash: NMKL 173:2005 modified
Carbohydrate: By difference 100 % - (moisture+protein+fat+ash)%
Energy value: Calculated on the basis of contents of protein, fat and carbohydrate. Factors protein and carbohydrate 17 kJ/g, fat 37 kJ/g

Measurement uncertainty:
Moisture: ± 3 relative-%
Ash: ± 10 relative-%
Fat: under the limit of measurement
Protein: ± 5 relative-%
Carbonhydrates, calculated: ± 5 relative-%
Energy, calculated: ± 5 relative-%

Distribute vilma.ikonen@roal.fi

* Accredited method. Statement is not accredited. Results apply only samples analyzed.

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17. Annex

MEAN, SUMMARY AND INDIVIDUAL DATA TO STUDY:

90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*

Study Director:

Dr. Philip Allingham

Test Facility:

BSL BIOSERVICE
Scientific Laboratories Munich GmbH
Behringstr. 6/8
82152 Planegg
Germany

BSL Munich / Eurofins Munich Study No:

154307

Sponsor:

AB Enzymes GmbH
Feldbergstr. 78
64293 Darmstadt
Germany

Version:

Final

Date:

02 August 2016

Eurofins BioPharma Product Testing Munich GmbH
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Summary Mortality

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

			C / M	LD / M	MD / M	HD / M
day 1 -> 90	Animals examined	N	10	10	10	10
	Alive *Alive*	N	10	10	10	10

Summary Mortality

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

			C / F	LD / F	MD / F	HD / F
day 1 -> 90	Animals examined	N	10	10	10	10
	Animals with signs	N	0	1	0	1
	Dead *Found dead*	N	0	1	0	1
	Alive *Alive*	N	10	10	10	10

Summary Signs Report - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

			C / M	LD / M	MD / M	HD / M
day 1 -> 90	Animals examined	N	10	10	10	10
	Normal *Normal*	N	10	10	10	10

Summary Signs Report - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

			C / F	LD / F	MD / F	HD / F
day 1 -> 90	Animals examined	N	10	10	10	10
	Dead *Found Dead*	N	0	1	0	1
	Normal *Normal*	N	10	10	10	10

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Salivation	Mean	3.6 k	4.0	4.0	4.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week 1	N	10	10	10	10
Lacrimation	Mean	0.8 k	0.0	0.0	0.0
[Score]	S.d.	1.7	0.0	0.0	0.0
week 1	N	10	10	10	10
Changes in skin	Mean	0.4 k	0.0	0.0	0.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week 1	N	10	10	10	10
Cyanosis	Mean	0.4 k	0.0	0.0	0.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week 1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Exophthalmos	Mean	0.4 k	0.0	0.0	0.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week 1	N	10	10	10	10
Eyes opening	Mean	0.4 k	0.0	0.0	0.4
[Score]	S.d.	1.3	0.0	0.0	1.3
week 1	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Spontaneous activity	Mean	4.0 k	3.7	4.0	4.0
[Score]	S.d.	0.0	0.7	0.0	0.0
week 1	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Faeces consistency	Mean	3.6 k	4.0	4.0	4.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week 1	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Animal sleeps	Mean	0.5 k	0.4	0.5	0.5
[Score]	S.d.	0.5	0.5	0.5	0.5
week 2	N	10	10	10	10
Animal moving in cage	Mean	0.5 k	0.6	0.5	0.5
[Score]	S.d.	0.5	0.5	0.5	0.5
week 2	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Animal sleeps	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Animal moving in cage	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Animal sleeps	Mean	1.0 k	0.9	1.0	1.0
[Score]	S.d.	0.0	0.3	0.0	0.0
week 4	N	10	10	10	10
Animal moving in cage	Mean	0.0 k	0.1	0.0	0.0
[Score]	S.d.	0.0	0.3	0.0	0.0
week 4	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
response to handling	Mean	4.0 k	3.8	4.0	3.8
[Score]	S.d.	0.0	0.6	0.0	0.6
week 4	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Fear	Mean	4.0 k	4.0	3.8	3.8
[Score]	S.d.	0.0	0.0	0.6	0.6
week 4	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Finger approach	Mean	4.0 k	4.2	4.0	4.0
[Score]	S.d.	0.0	0.6	0.0	0.0
week 4	N	10	10	10	10
Head touch	Mean	3.8 k	3.6	3.8	3.8
[Score]	S.d.	0.6	0.8	0.6	0.6
week 4	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Spontaneous activity	Mean	4.0 k	3.8	3.9	3.9
[Score]	S.d.	0.0	0.4	0.3	0.3
week 4	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Finger approach	Mean	4.0 k	4.0	4.0	4.2
[Score]	S.d.	0.0	0.0	0.0	0.6
week 5	N	10	10	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Spontaneous activity	Mean	4.0 k	4.0	4.0	3.9
[Score]	S.d.	0.0	0.0	0.0	0.3
week 5	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	10	10	10
Animal sleeps	Mean	0.5 k	1.0	0.7	0.5
[Score]	S.d.	0.5	0.0	0.5	0.5
week 6	N	10	10	10	10
Animal moving in cage	Mean	0.5 k	0.0	0.3	0.5
[Score]	S.d.	0.5	0.0	0.5	0.5
week 6	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
response to handling	Mean	4.0 k	4.0	4.0	3.6
[Score]	S.d.	0.0	0.0	0.0	0.8
week 6	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Fear	Mean	4.0 k	3.8	4.0	3.8
[Score]	S.d.	0.0	0.6	0.0	0.6
week 6	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Head touch	Mean	4.0 k	3.8	4.0	3.8
[Score]	S.d.	0.0	0.6	0.0	0.6
week 6	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Spontaneous activity	Mean	4.0 k	3.9	4.0	3.9
[Score]	S.d.	0.0	0.3	0.0	0.3
week 6	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	10	10	10
Animal sleeps	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Animal moving in cage	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Faeces consistency	Mean	3.6 k	4.0	4.0	4.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week 7	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	10	10	10	10
Animal sleeps	Mean	0.5 k	0.6	0.5	0.6
[Score]	S.d.	0.5	0.5	0.5	0.5
week 8	N	10	10	10	10
Animal moving in cage	Mean	0.5 k	0.4	0.5	0.4
[Score]	S.d.	0.5	0.5	0.5	0.5
week 8	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Fear	Mean	3.8 k	4.0	3.8	3.8
[Score]	S.d.	0.6	0.0	0.6	0.6
week 8	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Head touch	Mean	3.8 k	3.8	3.8	3.8
[Score]	S.d.	0.6	0.6	0.6	0.6
week 8	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Spontaneous activity	Mean	3.5 k	3.7	3.7	3.7
[Score]	S.d.	0.5	0.5	0.5	0.5
week 8	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	10	10	10
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
response to handling	Mean	4.0 k	4.0	3.8	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 9	N	10	10	10	9
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Head touch	Mean	4.0 k	4.0	3.8	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 9	N	10	10	10	9
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Spontaneous activity	Mean	3.9 k	3.9	3.8	3.9
[Score]	S.d.	0.3	0.3	0.4	0.3
week 9	N	10	10	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	10	10	9

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
response to handling	Mean	4.0 k	4.0	3.6	3.8
[Score]	S.d.	0.0	0.0	0.8	0.6
week 10	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Fear	Mean	4.0 k	4.0	3.8	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 10	N	10	10	10	10
Finger approach	Mean	4.0 k	4.0	4.2	4.2
[Score]	S.d.	0.0	0.0	0.6	0.6
week 10	N	10	10	10	10
Head touch	Mean	4.0 k	4.0	3.8	3.8
[Score]	S.d.	0.0	0.0	0.6	0.6
week 10	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Spontaneous activity	Mean	4.0 k	3.9	3.7	3.8
[Score]	S.d.	0.0	0.3	0.5	0.4
week 10	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	10	10	10
Animal sleeps	Mean	1.0 k	1.0	1.0	0.9
[Score]	S.d.	0.0	0.0	0.0	0.3
week 11	N	10	10	10	10
Animal moving in cage	Mean	0.0 k	0.0	0.0	0.1
[Score]	S.d.	0.0	0.0	0.0	0.3
week 11	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
response to handling	Mean	3.6 k	4.0	4.0	3.8
[Score]	S.d.	0.8	0.0	0.0	0.6
week 11	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Fear	Mean	3.8 k	4.0	4.0	4.0
[Score]	S.d.	0.6	0.0	0.0	0.0
week 11	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Head touch	Mean	3.8 k	4.0	4.0	4.0
[Score]	S.d.	0.6	0.0	0.0	0.0
week 11	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Spontaneous activity	Mean	3.9 k	4.0	4.0	3.8
[Score]	S.d.	0.3	0.0	0.0	0.4
week 11	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	10	10	10
Animal sleeps	Mean	0.8 k	0.9	0.5	0.5
[Score]	S.d.	0.4	0.3	0.5	0.5
week 12	N	10	10	10	10
Animal moving in cage	Mean	0.2 k	0.1	0.5	0.5
[Score]	S.d.	0.4	0.3	0.5	0.5
week 12	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
response to handling	Mean	3.8 k	3.8	3.8	3.8
[Score]	S.d.	0.6	0.6	0.6	0.6
week 12	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Fear	Mean	4.0 k	3.8	4.0	4.0
[Score]	S.d.	0.0	0.6	0.0	0.0
week 12	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Head touch	Mean	4.0 k	3.8	3.8	4.0
[Score]	S.d.	0.0	0.6	0.6	0.0
week 12	N	10	10	10	10
Body position	Mean	4.0 k	3.6	4.0	4.0
[Score]	S.d.	0.0	1.3	0.0	0.0
week 12	N	10	10	10	10
Spontaneous activity	Mean	3.8 k	3.9	3.9	3.7
[Score]	S.d.	0.4	0.3	0.3	0.5
week 12	N	10	10	10	10
Ataxic gait	Mean	0.0 k	0.4	0.0	0.0
[Score]	S.d.	0.0	1.3	0.0	0.0
week 12	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 k	0.4	0.0	0.0
[Score]	S.d.	0.0	1.3	0.0	0.0
week 12	N	10	10	10	10
Aggressiveness	Mean	0.0 k	0.4	0.0	0.0
[Score]	S.d.	0.0	1.3	0.0	0.0
week 12	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Finger approach	Mean	4.2 k	4.2	4.0	4.0
[Score]	S.d.	0.6	0.6	0.0	0.0
week 1	N	10	10	10	10
Head touch	Mean	3.8 k	4.0	4.0	4.0
[Score]	S.d.	0.6	0.0	0.0	0.0
week 1	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Spontaneous activity	Mean	4.0 k	4.0	3.9	4.0
[Score]	S.d.	0.0	0.0	0.3	0.0
week 1	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 1	N	10	10	10	10
Animal sleeps	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Animal moving in cage	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 2	N	10	10	10	10
Animal sleeps	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Animal moving in cage	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 3	N	10	10	10	10
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
response to handling	Mean	4.0 k	4.0	3.8	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 4	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Finger approach	Mean	4.0 k	4.0	4.2	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 4	N	10	10	10	10
Head touch	Mean	4.0 k	4.0	3.8	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 4	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Spontaneous activity	Mean	4.0 k	3.9	4.0	4.0
[Score]	S.d.	0.0	0.3	0.0	0.0
week 4	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 4	N	10	10	10	10
Animal sleeps	Mean	1.0 k	1.0	1.0	0.8
[Score]	S.d.	0.0	0.0	0.0	0.4
week 5	N	10	9	10	10
Animal moving in cage	Mean	0.0 k	0.0	0.0	0.2
[Score]	S.d.	0.0	0.0	0.0	0.4
week 5	N	10	9	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
O Grooming	Mean	0.0 k	0.0	0.4	0.0
[Score]	S.d.	0.0	0.0	1.3	0.0
week 5	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Salivation	Mean	4.0 k	4.0	3.6	4.0
[Score]	S.d.	0.0	0.0	1.3	0.0
week 5	N	10	9	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Finger approach	Mean	4.0 k	4.0	4.2	4.4
[Score]	S.d.	0.0	0.0	0.6	0.8
week 5	N	10	9	10	10
Head touch	Mean	4.0 k	4.0	3.8	3.6
[Score]	S.d.	0.0	0.0	0.6	0.8
week 5	N	10	9	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Spontaneous activity	Mean	4.0 k	4.0	3.9	4.0
[Score]	S.d.	0.0	0.0	0.3	0.0
week 5	N	10	9	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 5	N	10	9	10	10
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 6	N	10	9	10	10
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
O Grooming	Mean	0.0 k	0.0	0.8	0.0
[Score]	S.d.	0.0	0.0	1.8	0.0
week 7	N	5	5	5	5
Salivation	Mean	4.0 k	4.0	3.2	4.0
[Score]	S.d.	0.0	0.0	1.8	0.0
week 7	N	5	5	5	5
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 7	N	5	5	5	5
Animal sleeps	Mean	0.0 u	0.0	0.0	0.5 **
[Score]	S.d.	0.0	0.0	0.0	0.5
week 8	N	10	9	10	10
Animal moving in cage	Mean	1.0 u	1.0	1.0	0.5 **
[Score]	S.d.	0.0	0.0	0.0	0.5
week 8	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; u=KRUSKALL-WALLIS-DUNN

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Ataxic gait	Mean	0.4 k	0.0	0.0	0.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week 8	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 8	N	10	9	10	10
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
response to handling	Mean	4.0 k	3.6	3.8	4.0
[Score]	S.d.	0.0	0.9	0.6	0.0
week 9	N	10	9	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Head touch	Mean	4.0 k	4.0	3.6	4.0
[Score]	S.d.	0.0	0.0	0.8	0.0
week 9	N	10	9	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Spontaneous activity	Mean	4.0 k	3.9	4.0	3.9
[Score]	S.d.	0.0	0.3	0.0	0.3
week 9	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 9	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Animal sleeps	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Animal moving in cage	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
response to handling	Mean	4.0 k	4.0	4.0	3.8
[Score]	S.d.	0.0	0.0	0.0	0.6
week 10	N	10	9	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Head touch	Mean	4.0 k	4.0	3.8	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 10	N	10	9	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Spontaneous activity	Mean	4.0 k	4.0	4.0	3.9
[Score]	S.d.	0.0	0.0	0.0	0.3
week 10	N	10	9	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 10	N	10	9	10	10
Animal sleeps	Mean	0.9 k	0.6	0.5	0.4
[Score]	S.d.	0.3	0.5	0.5	0.5
week 11	N	10	9	10	10
Animal moving in cage	Mean	0.1 k	0.4	0.5	0.6
[Score]	S.d.	0.3	0.5	0.5	0.5
week 11	N	10	9	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
response to handling	Mean	3.8 k	3.8	3.8	3.4
[Score]	S.d.	0.6	0.7	0.6	1.0
week 11	N	10	9	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Fear	Mean	4.0 k	4.0	3.8	4.0
[Score]	S.d.	0.0	0.0	0.6	0.0
week 11	N	10	9	10	10
Finger approach	Mean	4.0 k	4.0	4.2	4.2
[Score]	S.d.	0.0	0.0	0.6	0.6
week 11	N	10	9	10	10
Head touch	Mean	3.6 k	3.3	3.6	4.0
[Score]	S.d.	0.8	1.0	0.8	0.0
week 11	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
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Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Spontaneous activity	Mean	3.9 k	3.9	4.0	3.9
[Score]	S.d.	0.3	0.3	0.0	0.3
week 11	N	10	9	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 11	N	10	9	10	10
Animal sleeps	Mean	0.0 k	0.2	0.0	0.0
[Score]	S.d.	0.0	0.4	0.0	0.0
week 12	N	10	9	10	10
Animal moving in cage	Mean	1.0 k	0.8	1.0	1.0
[Score]	S.d.	0.0	0.4	0.0	0.0
week 12	N	10	9	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
O Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Resiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Faeces consistency	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 12	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Animal Sleeps	Mean	1.0 k	1.0	0.8	0.9
[Score]	S.d.	0.0	0.0	0.4	0.3
week -1	N	10	10	10	10
Animal moving in cage	Mean	0.0 k	0.0	0.2	0.1
[Score]	S.d.	0.0	0.0	0.4	0.3
week -1	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Respiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Spontaneous activity	Mean	4.0 k	3.9	3.9	4.0
[Score]	S.d.	0.0	0.3	0.3	0.0
week -1	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Unusual behavior	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Rearing supported	Mean	6.9 ad	6.7	4.1 *	4.1 *
[Score]	S.d.	1.6	2.2	2.3	2.1
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable; ad=ANOVA-DUNNETT

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Rearing not supported	Mean	0.0 k	0.1	0.3	0.0
[Score]	S.d.	0.0	0.3	0.7	0.0
week -1	N	10	10	10	10
Urination	Mean	0.0 k	0.0	0.0	0.1
[Score]	S.d.	0.0	0.0	0.0	0.3
week -1	N	10	10	10	10
Defecation	Mean	0.3 k	0.0	0.2	0.3
[Score]	S.d.	0.9	0.0	0.6	0.9
week -1	N	10	10	10	10
Feaces consistency	Mean	4.0 NA	4.0	4.0	4.0
	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Startle response	Mean	4.0 k	4.0	3.8	3.8
[Score]	S.d.	0.0	0.0	0.6	0.6
week -1	N	10	10	10	10
Equilibrium reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Positional passivity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Visual placing	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Grip strength	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Pinching the tail	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Toe pinch reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Limb tone	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Hind limb reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Righting reflex ground	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Air righting reflex	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Pupil response	Mean	3.6 k	4.0	4.0	4.0
[Score]	S.d.	1.3	0.0	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Body temperature	Mean	208.85 k	211.10	380.30	380.80
[°C]	S.d.	179.99	182.69	3.40	5.43
week -1	N	10	10	10	10
Anterior chamber of eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Fundus of the eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Animal Sleeps	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Animal moving in cage	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Respiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Spontaneous activity	Mean	3.7 k	3.7	3.8	3.8
[Score]	S.d.	0.5	0.5	0.4	0.4
week 13	N	10	10	10	10
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Unusual behavior	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Rearing supported	Mean	1.2 k	1.6	2.3	2.1
[Score]	S.d.	0.6	1.2	1.6	1.8
week 13	N	10	10	10	10
Rearing not supported	Mean	0.3 k	0.3	0.4	0.5
[Score]	S.d.	0.7	0.5	0.7	0.8
week 13	N	10	10	10	10
Urination	Mean	0.0 k	0.1	0.0	0.1
[Score]	S.d.	0.0	0.3	0.0	0.3
week 13	N	10	10	10	10
Defecation	Mean	0.3 k	0.6	0.3	0.1
[Score]	S.d.	0.5	0.7	0.5	0.3
week 13	N	10	10	10	10
Feaces consistency	Mean	4.0 NA	4.0	4.0	4.0
	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Startle response	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Equilibrium reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Positional passivity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Visual placing	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Grip strength	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Pinching the tail	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Toe pinch reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Limb tone	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Hind limb reflex	Mean	4.0 k	4.1	4.0	4.0
[Score]	S.d.	0.0	0.3	0.0	0.0
week 13	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
Righting reflex ground	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Air righting reflex	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Pupil response	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Body temperature	Mean	38.24 a	38.43	38.30	38.13
[°C]	S.d.	0.39	0.37	0.49	0.39
week 13	N	10	10	10	10
Anterior chamber of eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10
Fundus of the eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; a=ANOVA

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Animal Sleeps	Mean	1.0 k	1.0	1.0	0.8
[Score]	S.d.	0.0	0.0	0.0	0.4
week -1	N	10	10	10	10
Animal moving in cage	Mean	0.0 k	0.0	0.0	0.2
[Score]	S.d.	0.0	0.0	0.0	0.4
week -1	N	10	10	10	10
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Salivation	Mean	4.0 k	4.0	3.6	4.0
[Score]	S.d.	0.0	0.0	1.3	0.0
week -1	N	10	10	10	10
Lacrimation	Mean	0.0 k	0.0	0.4	0.0
[Score]	S.d.	0.0	0.0	1.3	0.0
week -1	N	10	10	10	10
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Respiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Finger approach	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Head touch	Mean	4.0 k	4.0	4.0	3.6
[Score]	S.d.	0.0	0.0	0.0	0.8
week -1	N	10	10	10	10
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Spontaneous activity	Mean	3.8 k	4.0	4.0	4.0
[Score]	S.d.	0.4	0.0	0.0	0.0
week -1	N	10	10	10	10
Ataxic gait	Mean	0.0 k	0.0	0.4	0.0
[Score]	S.d.	0.0	0.0	1.3	0.0
week -1	N	10	10	10	10
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Unusual behavior	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Rearing supported	Mean	7.9 k	8.3	7.5	8.1
[Score]	S.d.	2.1	1.5	1.5	2.3
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Rearing not supported	Mean	0.2 k	0.0	0.4	0.3
[Score]	S.d.	0.6	0.0	0.8	0.7
week -1	N	10	10	10	10
Urination	Mean	0.0 k	0.0	0.0	0.1
[Score]	S.d.	0.0	0.0	0.0	0.3
week -1	N	10	10	10	10
Defecation	Mean	0.5 k	0.0	0.6	0.2
[Score]	S.d.	1.1	0.0	1.4	0.6
week -1	N	10	10	10	10
Feaces consistency	Mean	4.0 NA	4.0	4.0	4.0
	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Startle response	Mean	4.0 k	3.8	4.0	3.8
[Score]	S.d.	0.0	0.6	0.0	0.6
week -1	N	10	10	10	10
Equilibrium reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Positional passivity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Visual placing	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Grip strength	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Pinching the tail	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Toe pinch reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Limb tone	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Hind limb reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Righting reflex ground	Mean	0.0 k	0.4	0.0	0.0
[Score]	S.d.	0.0	1.3	0.0	0.0
week -1	N	10	10	10	10
Air righting reflex	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Pupil response	Mean	4.0 k	3.6	4.0	4.0
[Score]	S.d.	0.0	1.3	0.0	0.0
week -1	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Body temperature	Mean	38.09 k	38.45	38.44	38.43
[°C]	S.d.	0.20	0.35	0.51	0.30
week -1	N	10	10	10	10
Anterior chamber of eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Fundus of the eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week -1	N	10	10	10	10
Animal Sleeps	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Animal moving in cage	Mean	1.0 NA	1.0	1.0	1.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Piloerection	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Vocalization	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Grooming	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Salivation	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Lacrimation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Changes in skin	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Cyanosis	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Exophthalmos	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Eyes opening	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Respiration	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Response to handling	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Arousal	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Fear	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9

Statistic Profile = DecisionTree, * = $p < 0.05$, ** = $p < 0.01$, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Finger approach	Mean	4.0 k	8.4	4.0	4.0
[Score]	S.d.	0.0	13.3	0.0	0.0
week 13	N	10	9	10	9
Head touch	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Body position	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Spontaneous activity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Ataxic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Hypotonic gait	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Twitches	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Tremors	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Seizures	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Unusual behavior	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Stereotypie	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Rearing supported	Mean	3.9 a	3.8	4.0	4.1
[Score]	S.d.	1.9	1.4	1.6	1.5
week 13	N	10	9	10	9
Rearing not supported	Mean	1.6 k	0.6	0.4	1.1
[Score]	S.d.	1.4	0.7	0.5	1.1
week 13	N	10	9	10	9
Urination	Mean	0.2 k	0.3	0.2	0.6
[Score]	S.d.	0.4	0.7	0.6	0.9
week 13	N	10	9	10	9
Defecation	Mean	0.9 k	0.7	1.0	0.9
[Score]	S.d.	1.1	1.1	1.2	1.3
week 13	N	10	9	10	9
Feaces consistency	Mean	4.0 NA	4.0	4.0	4.0
	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Abnormal vocalisation	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Aggressiveness	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; a=ANOVA; k=KRUSKALL-WALLIS

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Startle response	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Equilibrium reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Positional passivity	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Visual placing	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Grip strength	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Pinching the tail	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Toe pinch reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Limb tone	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Hind limb reflex	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable

Summary Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
Righting reflex ground	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Air righting reflex	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Pupil response	Mean	4.0 NA	4.0	4.0	4.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Body temperature	Mean	38.42 a	38.29	38.46	38.34
[°C]	S.d.	0.38	0.28	0.49	0.42
week 13	N	10	9	10	9
Anterior chamber of eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9
Fundus of the eye	Mean	0.0 NA	0.0	0.0	0.0
[Score]	S.d.	0.0	0.0	0.0	0.0
week 13	N	10	9	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
NA=No Test Applicable; a=ANOVA

Summary Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
day 1	Mean	204.20 a	208.90	207.20	208.20
	S.d.	7.30	10.56	10.34	9.27
	N	10	10	10	10
	Deviation Vs Control [%]		2.30	1.47	1.96
day 8	Mean	242.70 a	244.30	241.10	244.30
	S.d.	7.41	9.59	11.26	9.35
	N	10	10	10	10
	Deviation Vs Control [%]		0.66	-0.66	0.66
day 15	Mean	268.00 a	269.60	267.10	271.90
	S.d.	11.49	12.29	13.89	14.43
	N	10	10	10	10
	Deviation Vs Control [%]		0.60	-0.34	1.46
day 22	Mean	296.10 a	293.60	292.80	298.50
	S.d.	16.58	16.10	16.25	16.57
	N	10	10	10	10
	Deviation Vs Control [%]		-0.84	-1.11	0.81
day 29	Mean	312.70 a	310.20	309.50	314.30
	S.d.	18.09	17.51	20.07	17.59
	N	10	10	10	10
	Deviation Vs Control [%]		-0.80	-1.02	0.51
day 36	Mean	326.10 a	324.20	322.70	327.10
	S.d.	19.36	21.56	23.66	19.67
	N	10	10	10	10
	Deviation Vs Control [%]		-0.58	-1.04	0.31
day 43	Mean	343.40 a	338.50	337.10	341.00
	S.d.	21.54	21.17	26.02	20.50
	N	10	10	10	10
	Deviation Vs Control [%]		-1.43	-1.83	-0.70

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
a=ANOVA

Summary Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
day 50	Mean	349.30 a	343.90	346.60	346.10
	S.d.	21.36	22.97	27.54	22.23
	N	10	10	10	10
	Deviation Vs Control [%]		-1.55	-0.77	-0.92
day 57	Mean	360.40 a	353.40	354.40	357.80
	S.d.	20.87	23.20	28.37	24.14
	N	10	10	10	10
	Deviation Vs Control [%]		-1.94	-1.66	-0.72
day 64	Mean	366.80 a	356.90	362.40	362.90
	S.d.	23.66	20.89	29.71	23.68
	N	10	10	10	10
	Deviation Vs Control [%]		-2.70	-1.20	-1.06
day 71	Mean	376.40 a	367.30	371.90	371.60
	S.d.	23.59	26.06	29.19	25.89
	N	10	10	10	10
	Deviation Vs Control [%]		-2.42	-1.20	-1.28
day 78	Mean	387.20 a	380.60	383.10	381.70
	S.d.	25.24	26.53	28.72	26.00
	N	10	10	10	10
	Deviation Vs Control [%]		-1.70	-1.06	-1.42
day 85	Mean	391.00 a	381.40	384.80	385.00
	S.d.	25.41	25.95	28.69	29.26
	N	10	10	10	10
	Deviation Vs Control [%]		-2.46	-1.59	-1.53
day 90	Mean	396.53 a	379.87	383.33	387.53
	S.d.	24.05	23.69	31.55	26.28
	N	15	15	15	15
	Deviation Vs Control [%]		-4.20	-3.33	-2.27

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
a=ANOVA

Summary Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
day 1	Mean	165.50 a	161.40	159.10	161.90
	S.d.	7.49	7.92	5.93	10.17
	N	10	10	10	10
	Deviation Vs Control [%]		-2.48	-3.87	-2.18
day 8	Mean	179.00 a	175.90	173.70	175.90
	S.d.	7.10	8.54	6.22	12.67
	N	10	10	10	10
	Deviation Vs Control [%]		-1.73	-2.96	-1.73
day 15	Mean	191.60 a	189.40	188.10	187.50
	S.d.	9.22	8.17	6.10	11.27
	N	10	10	10	10
	Deviation Vs Control [%]		-1.15	-1.83	-2.14
day 22	Mean	199.70 a	199.00	199.30	196.60
	S.d.	10.91	10.40	7.78	10.98
	N	10	10	10	10
	Deviation Vs Control [%]		-0.35	-0.20	-1.55
day 29	Mean	212.10 a	204.89	206.00	205.10
	S.d.	8.79	8.54	8.11	11.94
	N	10	9	10	10
	Deviation Vs Control [%]		-3.40	-2.88	-3.30
day 36	Mean	214.10 a	211.44	210.60	212.60
	S.d.	7.67	12.26	5.50	12.51
	N	10	9	10	10
	Deviation Vs Control [%]		-1.24	-1.63	-0.70
day 43	Mean	217.90 a	215.89	215.60	215.30
	S.d.	10.15	10.52	6.72	13.01
	N	10	9	10	10
	Deviation Vs Control [%]		-0.92	-1.06	-1.19

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
a=ANOVA

Summary Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
day 50	Mean	220.30 a	219.78	219.70	218.60
	S.d.	11.28	9.24	8.73	10.30
	N	10	9	10	10
	Deviation Vs Control [%]		-0.24	-0.27	-0.77
day 57	Mean	223.20 a	220.78	222.40	222.60
	S.d.	9.98	10.38	10.48	13.48
	N	10	9	10	10
	Deviation Vs Control [%]		-1.09	-0.36	-0.27
day 64	Mean	229.10 a	226.22	226.60	227.70
	S.d.	8.70	12.03	7.18	13.84
	N	10	9	10	10
	Deviation Vs Control [%]		-1.26	-1.09	-0.61
day 71	Mean	228.90 a	228.11	227.10	230.10
	S.d.	9.40	10.58	3.76	11.72
	N	10	9	10	10
	Deviation Vs Control [%]		-0.34	-0.79	0.52
day 78	Mean	231.90 a	231.89	233.00	232.20
	S.d.	11.21	10.34	6.25	12.69
	N	10	9	10	10
	Deviation Vs Control [%]		0.00	0.47	0.13
day 85	Mean	234.90 a	232.22	233.60	233.11
	S.d.	10.14	12.15	10.93	15.74
	N	10	9	10	9
	Deviation Vs Control [%]		-1.14	-0.55	-0.76
day 90	Mean	233.30 a	236.33	234.60	231.33
	S.d.	12.45	12.18	8.17	13.21
	N	10	9	10	9
	Deviation Vs Control [%]		1.30	0.56	-0.84

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
a=ANOVA

Summary Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
d 1 -> 8	Mean	38.50 a	35.40	33.90	36.10
	S.d.	3.50	5.08	4.33	7.67
	N	10	10	10	10
d 8 -> 15	Mean	25.30 a	25.30	26.00	27.60
	S.d.	5.70	7.23	4.67	6.77
	N	10	10	10	10
d 15 -> 22	Mean	28.10 k	24.00	25.70	26.60
	S.d.	6.52	6.43	4.50	17.10
	N	10	10	10	10
d 22 -> 29	Mean	16.60 k	16.60	16.70	15.80
	S.d.	4.22	3.89	5.48	19.47
	N	10	10	10	10
d 29 -> 36	Mean	13.40 a	14.00	13.20	12.80
	S.d.	3.10	5.70	5.59	2.86
	N	10	10	10	10
d 36 -> 43	Mean	17.30 a	14.30	14.40	13.90
	S.d.	4.27	2.50	4.67	3.21
	N	10	10	10	10
d 43 -> 50	Mean	5.90 a	5.40	9.50	5.10
	S.d.	2.56	4.30	3.37	5.74
	N	10	10	10	10
d 50 -> 57	Mean	11.10 a	9.50	7.80	11.70
	S.d.	5.49	3.72	3.52	3.47
	N	10	10	10	10
d 57 -> 64	Mean	6.40 a	3.50	8.00	5.10
	S.d.	3.27	4.12	3.30	4.23
	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
d = day; a=ANOVA; k=KRUSKALL-WALLIS

Summary Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
d 64 -> 71	Mean	9.60 a	10.40	9.50	8.70
	S.d.	2.32	6.42	3.78	4.64
	N	10	10	10	10
d 71 -> 78	Mean	10.80 a	13.30	11.20	10.10
	S.d.	4.83	2.11	3.94	4.15
	N	10	10	10	10
d 78 -> 85	Mean	3.80 a	0.80	1.70	3.30
	S.d.	2.86	4.71	2.31	4.14
	N	10	10	10	10
d 85 -> 90	Mean	3.15 a	2.45	1.50	1.70
	S.d.	3.05	3.76	2.04	4.16
	N	10	10	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
a=ANOVA; d = day

Summary Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
d 1 -> 8	Mean	13.50 k	14.50	14.60	14.00
	S.d.	4.03	5.91	4.33	3.30
	N	10	10	10	10
d 8 -> 15	Mean	12.60 a	13.50	14.40	11.60
	S.d.	4.81	4.93	4.22	5.62
	N	10	10	10	10
d 15 -> 22	Mean	8.10 k	9.60	11.20	9.10
	S.d.	7.88	4.95	5.96	7.00
	N	10	10	10	10
d 22 -> 29	Mean	12.40 a	5.33	6.70	8.50
	S.d.	6.10	8.03	4.50	5.72
	N	10	9	10	10
d 29 -> 36	Mean	2.00 a	6.56	4.60	7.50
	S.d.	5.23	6.73	5.40	2.55
	N	10	9	10	10
d 36 -> 43	Mean	3.80 a	4.44	5.00	2.70
	S.d.	6.11	7.35	4.97	3.74
	N	10	9	10	10
d 43 -> 50	Mean	2.40 k	3.89	4.10	3.30
	S.d.	6.33	5.53	5.97	5.33
	N	10	9	10	10
d 50 -> 57	Mean	2.90 a	1.00	2.70	4.00
	S.d.	5.70	5.87	3.53	6.16
	N	10	9	10	10
d 57 -> 64	Mean	5.90 a	5.44	4.20	5.10
	S.d.	3.54	4.69	4.21	4.68
	N	10	9	10	10

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
d = day; k=KRUSKALL-WALLIS; a=ANOVA

Summary Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
d 64 -> 71	Mean	-0.20 k	1.89	0.50	2.40
	S.d.	3.29	3.59	5.21	5.02
	N	10	9	10	10
d 71 -> 78	Mean	3.00 a	3.78	5.90	2.10
	S.d.	4.11	3.73	3.93	3.21
	N	10	9	10	10
d 78 -> 85	Mean	3.00 a	0.33	0.60	1.56
	S.d.	3.50	4.21	6.67	5.25
	N	10	9	10	9
d 85 -> 90	Mean	-1.60 a	4.11	1.00	-1.78
	S.d.	5.52	6.31	4.71	4.38
	N	10	9	10	9

Statistic Profile = DecisionTree, * = p < 0.05, ** = p < 0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; d = day; a=ANOVA

Summary Food Consumption 1

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
d 1 -> 8	Mean [g]	97.50 NAX	97.25 X	96.89 X	97.03 X
	S.d.	0.07	2.60	0.88	0.82
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-0.26	-0.62	-0.48
d 8 -> 15	Mean [g]	91.86 NAX	90.90 X	93.57 X	93.82 X
	S.d.	0.83	0.50	4.96	0.20
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-1.05	1.86	2.13
d 15 -> 22	Mean [g]	84.07 NAX	81.61 X	83.17 X	82.95 X
	S.d.	1.11	1.10	4.13	0.35
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-2.93	-1.08	-1.33
d 22 -> 29	Mean [g]	80.04 NAX	77.22 X	78.89 X	78.83 X
	S.d.	3.57	0.46	0.21	2.23
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-3.53	-1.44	-1.51
d 29 -> 36	Mean [g]	74.69 NAX	71.92 X	73.37 X	74.70 X
	S.d.	0.71	0.02	1.73	0.07
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-3.70	-1.77	0.02
d 36 -> 43	Mean [g]	70.78 NAX	68.61 X	70.67 X	71.08 X
	S.d.	2.29	0.94	0.06	0.02
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-3.06	-0.16	0.42
d 43 -> 50	Mean [g]	68.22 NAX	67.17 X	69.36 X	70.86 X
	S.d.	0.12	1.64	0.87	0.81
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-1.54	1.67	3.87

d = day; X = Group excluded from statistics

Summary Food Consumption 2

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

		C / M	LD / M	MD / M	HD / M
d 50 -> 57	Mean [g]	65.18 NAX	64.45 X	66.02 X	67.63 X
	S.d.	0.25	0.09	0.75	2.00
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-1.11	1.29	3.76
d 57 -> 64	Mean [g]	64.45 NAX	63.28 X	65.18 X	67.60 X
	S.d.	1.31	1.68	2.03	2.83
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-1.81	1.14	4.89
d 64 -> 71	Mean [g]	62.58 NAX	61.86 X	62.94 X	63.96 X
	S.d.	0.54	0.10	1.42	1.46
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-1.15	0.57	2.20
d 71 -> 78	Mean [g]	59.23 NAX	59.30 X	60.36 X	62.33 X
	S.d.	0.34	0.33	0.02	2.73
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	0.12	1.91	5.24
d 78 -> 85	Mean [g]	58.22 NAX	59.62 X	60.19 X	60.63 X
	S.d.	0.87	1.53	1.87	0.50
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	2.40	3.39	4.15
d 85 -> 90	Mean [g]	57.88 NAX	57.58 X	58.51 X	59.75 X
	S.d.	2.05	2.42	2.22	0.45
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	-0.51	1.09	3.22
Total	Total [g]	934.70	920.77	939.12	951.17
	Mean [g]	71.9	70.83	72.24	73.17

X = Group excluded from statistics; d = day

Summary Food Consumption 3

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
d 1 -> 8	Mean [g]	93.14 NAX	98.81 X	98.39 X	97.37 X
	S.d.	0.03	1.88	0.53	0.90
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	6.09	5.64	4.54
d 8 -> 15	Mean [g]	93.60 NAX	95.96 X	100.14 X	95.22 X
	S.d.	0.69	2.73	1.16	0.41
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	2.52	6.99	1.73
d 15 -> 22	Mean [g]	87.59 NAX	88.90 X	94.77 X	96.57 X
	S.d.	3.16	1.72	0.80	6.50
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	1.49	8.20	10.25
d 22 -> 29	Mean [g]	86.74 NAX	86.92 X	90.16 X	87.34 X
	S.d.	0.97	0.70	1.60	0.89
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	0.20	3.94	0.68
d 29 -> 36	Mean [g]	80.85 NAX	84.74 X	86.07 X	84.26 X
	S.d.	0.17	2.70	1.18	1.19
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	4.81	6.46	4.22
d 36 -> 43	Mean [g]	79.49 NAX	80.23 X	85.28 X	81.92 X
	S.d.	1.17	2.30	1.40	1.20
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	0.93	7.28	3.05
d 43 -> 50	Mean [g]	79.27 NAX	79.64 X	84.86 X	82.05 X
	S.d.	1.53	3.94	2.28	0.38
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	0.47	7.06	3.51

d = day; X = Group excluded from statistics

Summary Food Consumption 4

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

		C / F	LD / F	MD / F	HD / F
d 50 -> 57	Mean [g]	76.08 NAX	78.29 X	81.55 X	79.64 X
	S.d.	0.12	1.22	1.46	2.77
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	2.90	7.19	4.68
d 57 -> 64	Mean [g]	77.94 NAX	80.66 X	86.22 X	82.74 X
	S.d.	1.36	2.80	0.56	0.31
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	3.50	10.63	6.16
d 64 -> 71	Mean [g]	73.93 NAX	75.75 X	79.54 X	78.25 X
	S.d.	0.62		0.45	0.78
	N	2	1	2	2
	Deviation Vs Control [%]	0.00	2.46	7.58	5.85
d 71 -> 78	Mean [g]	74.29 NAX	75.41 X	78.99 X	76.60 X
	S.d.	0.89		0.63	3.24
	N	2	1	2	2
	Deviation Vs Control [%]	0.00	1.50	6.32	3.11
d 78 -> 85	Mean [g]	70.05 NAX	72.40 X	75.08 X	70.34 X
	S.d.	2.34	2.65	1.81	3.77
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	3.35	7.18	0.41
d 85 -> 90	Mean [g]	73.40 NAX	74.76 X	76.81 X	74.39 X
	S.d.	0.67	0.18	0.06	2.69
	N	2	2	2	2
	Deviation Vs Control [%]	0.00	1.86	4.64	1.36
Total	Total [g]	1,046.37	1,072.47	1,117.86	1,086.69
	Mean [g]	80.49	82.5	85.99	83.59

X = Group excluded from statistics; d = day

Mean Haematology- Males

Group		RBC	Hb	Hct	MCV	MCH	MCHC	PLT	WBC	Neu	Lym	Mono	Eos	Baso	Luc	RE
	Units	10^{12}/L	g/dL	%	fL	pg/Ery	g/dL	10^{9}/L	10^{9}/L	%	%	%	%	%	%	%
C	Mean	9.02	15.83	47.06	52.23	17.58	33.65	766.00	4.41	24.28	72.21	2.67	0.58	0.05	0.21	1.62
	SD	0.31	0.52	1.47	1.56	0.74	0.70	58.53	1.00	7.20	7.69	0.75	0.22	0.05	0.10	0.20
	N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
LD	Mean	8.98	15.89	46.30	51.58	17.70	34.30	800.50	3.94	27.90	68.60	2.77	0.49	0.06	0.20	1.51
	SD	0.28	0.51	1.36	0.81	0.67	1.04	61.80	0.99	6.73	7.13	1.05	0.26	0.05	0.12	0.17
	N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
MD	Mean	9.02	15.94	47.06	52.21	17.70	33.91	765.80	3.80	28.59	67.63	3.00	0.55	0.06	0.20	1.43
	SD	0.28	0.41	0.99	0.90	0.44	0.81	56.64	0.67	6.93	7.32	1.03	0.30	0.05	0.16	0.23
	N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
HD	Mean	9.24	16.24	48.10	52.11	17.57	33.75	728.30	4.51	24.16	72.06	3.02	0.43	0.10	0.22	1.53
	SD	0.35	0.59	1.58	1.76	0.51	0.68	122.25	1.10	6.23	6.58	1.10	0.17	0.05	0.14	0.30
	N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Mean Haematology - Females

Group		RBC	Hb	Hct	MCV	MCH	MCHC	PLT	WBC	Neu	Lym	Mono	Eos	Baso	Luc	RE
	Units	10^{12}/L	g/dL	%	fL	pg/Ery	g/dL	10^{9}/L	10^{9}/L	%	%	%	%	%	%	%
C	Mean	8.27	15.42	45.23	54.73	18.67	34.10	768.70	2.32	20.12	76.80	2.39	0.49	0.05	0.13	1.98
	SD	0.33	0.53	1.28	1.30	0.53	0.54	114.60	0.76	5.21	5.57	0.83	0.26	0.07	0.05	0.28
	N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
LD	Mean	8.37	15.63	45.08	53.86	18.69	34.71	784.89	2.86	17.34	79.24	2.77	0.38	0.11	0.17	1.74
	SD	0.27	0.43	1.11	1.02	0.57	0.73	70.90	0.90	4.75	4.61	0.80	0.14	0.06	0.07	0.25
	N	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
MD	Mean	8.39	15.53	45.03	53.72	18.53	34.49	749.40	2.90	17.37	78.92	3.06	0.41	0.07	0.22	1.81
	SD	0.51	0.67	2.03	1.08	0.57	0.73	94.71	0.87	2.97	3.51	1.34	0.38	0.05	0.15	0.46
	N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
HD	Mean	8.43	15.46	45.24	53.73	18.37	34.19	748.44	2.56	23.11	73.90	2.44	0.32	0.07	0.17	1.90
	SD	0.34	0.71	1.52	1.36	0.63	0.55	146.82	1.08	14.03	14.42	0.65	0.15	0.07	0.09	0.24
	N	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9

Mean Coagulation - Males

Group		PT	aPTT
	Units	sec	sec
C	Mean	23.47	15.26
	SD	1.87	1.53
	N	10	10
LD	Mean	23.88	15.93
	SD	1.62	2.59
	N	10	10
MD	Mean	24.50	16.12
	SD	1.33	1.71
	N	10	10
HD	Mean	23.43	17.30
	SD	1.02	6.72
	N	10	10

Mean Coagulation - Females

Group		PT	aPTT
	Units	sec	sec
C	Mean	25.58	15.03
	SD	0.84	1.59
	N	10	10
LD	Mean	26.27	15.33
	SD	1.14	1.63
	N	9	9
MD	Mean	25.89	14.29
	SD	1.72	2.86
	N	10	10
HD	Mean	25.42	15.48
	SD	1.14	2.24
	N	9	9

Mean Clinical Biochemistry - Males

Group		ASAT	ALAT	AP	GGT	Crea	TP	Alb	Urea	TBIL	Chol	Gluc	Na	K	Ca	P	Cl
	Units	U/L	U/L	U/L	U/L	µmol/L	g/L	g/L	mmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
C	Mean	68.23	32.42	95.53	0.32	17.67	53.10	30.60	6.15	2.36	1.65	7.78	114.78	3.24	2.15	1.64	90.75
	SD	22.76	13.84	45.76	0.29	4.21	9.72	5.59	0.74	0.42	0.35	2.12	33.12	0.86	0.22	0.13	20.11
	N	9	9	9	7	9	9	8	9	9	9	9	9	9	9	9	8
LD	Mean	62.04	33.16	106.41	0.27	18.10	52.01	28.72	6.24	2.49	1.38	7.46	113.80	3.17	2.23	1.70	86.10
	SD	15.29	9.52	38.57	0.23	7.32	9.35	6.93	0.77	0.58	0.35	2.97	30.52	0.78	0.17	0.33	23.19
	N	10	10	10	7	10	10	10	10	10	10	10	10	10	10	10	10
MD	Mean	68.51	38.52	109.48	0.32	19.70	54.24	30.50	6.22	2.49	1.51	7.59	122.60	3.49	2.21	1.76	96.89
	SD	17.14	9.59	35.46	0.20	5.52	9.64	7.16	0.97	0.64	0.49	2.12	29.69	0.75	0.23	0.33	17.23
	N	10	10	10	7	10	10	10	10	10	10	10	10	10	10	10	9
HD	Mean	71.17	38.36	142.33	0.38	20.40	56.22	31.10	7.03	2.52	1.74	8.25	126.00	3.60	2.26	1.82	94.60
	SD	15.55	11.45	36.37	0.14	4.67	7.78	5.53	1.16	0.40	0.33	2.37	23.71	0.66	0.20	0.23	18.40
	N	10	10	10	5	10	10	10	10	10	10	10	10	10	10	10	10

Mean Clinical Biochemistry – Females

Group		ASAT	ALAT	AP	GGT	Crea	TP	Alb	Urea	TBIL	Chol	Gluc	Na	K	Ca	P	Cl
	Units	U/L	U/L	U/L	U/L	µmol/L	g/L	g/L	mmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
C	Mean	78.80	28.16	55.14	0.40	19.80	55.95	37.43	6.81	3.40	1.25	7.67	134.80	3.54	2.37	1.69	101.50
	SD	11.64	7.18	14.37	0.15	3.71	18.51	1.59	0.74	0.64	0.21	1.00	1.23	0.14	0.06	0.33	1.18
	N	10	10	10	8	10	10	10	10	10	10	10	10	10	10	10	10
LD	Mean	78.41	41.12	63.33	0.36	18.22	61.43	37.17	6.88	3.56	1.19	7.08	135.11	3.41	2.41	1.71	102.00
	SD	13.43	21.97	21.33	0.27	4.92	3.07	1.94	0.59	0.65	0.27	1.05	0.78	0.13	0.06	0.21	1.32
	N	9	9	9	4	9	9	9	9	9	9	9	9	9	9	9	9
MD	Mean	73.48	31.05	60.85	0.35	20.40	61.06	36.80	7.31	4.26*	1.15	6.67	134.60	3.70	2.44	1.89	101.60
	SD	13.17	10.15	23.71	0.29	8.19	3.59	2.12	1.07	0.72	0.31	1.88	1.35	0.28	0.06	0.18	1.07
	N	10	10	10	9	10	10	10	10	10	10	10	10	10	10	10	10
HD	Mean	73.26	30.51	52.04	0.71	18.11	61.67	36.63	6.64	3.47	1.35	6.80	135.33	3.40	2.38	1.68	101.67
	SD	7.44	6.84	13.36	0.40	5.86	2.60	2.07	1.10	0.91	0.27	1.32	1.50	0.18	0.04	0.29	1.22
	N	9	9	9	8	9	9	9	9	9	9	9	9	9	9	9	9

Asterisks indicate statistically significant differences to control group C, with* $p<0.05$, ** $p<0.01$ and *** $p<0.001$.

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	M	M	M	M
		Groups	C / M	LD / M	MD / M	HD / M
		No. Animals	10	10	10	10
BRAIN	BRAIN					
		NO. EXAM.	10	10	10	10
		NAD	10	10	8	10
	Autolytic		0	0	0	0
SPINAL CORD	SPINAL CORD					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
SCIATIC NERVES	SCIATIC NERVES					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
HEART	HEART					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
AORTA	AORTA					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
TRACHEA	TRACHEA					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
LUNG	LUNG					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Abnormal color		0	0	0	0
	Abnormal surface		0	0	0	0
	dark		0	0	0	0
	Autolytic		0	0	0	0
TONGUE	TONGUE					
		NO. EXAM.	10	10	10	10

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	M	M	M	M
		Groups	C / M	LD / M	MD / M	HD / M
		No. Animals	10	10	10	10
TONGUE		NAD	10	10	10	10
	Autolytic		0	0	0	0
ESOPHAGUS	ESOPHAGUS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
STOMACH	STOMACH					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
	Cannibalized		0	0	0	0
DUODENUM	DUODENUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
	Cannibalized		0	0	0	0
JEJUNUM	JEJUNUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
	Cannibalized		0	0	0	0
ILEUM	ILEUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
	Cannibalized		0	0	0	0
CECUM	CECUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
COLON	COLON					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	M	M	M	M
		Groups	C / M	LD / M	MD / M	HD / M
		No. Animals	10	10	10	10
COL	Autolytic		0	0	0	0
RECTUM	RECTUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
LIVER	LIVER					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Abnormal surface		0	0	0	0
	marbled		0	0	0	0
	pale		0	0	0	0
	Autolytic		0	0	0	0
PANCREAS	PANCREAS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
KIDNEYS	KIDNEYS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
URETERS	URETERS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
URINARY BLADDER	URINARY BLADDER					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
TESTES	TESTES					
		NO. EXAM.	10	10	10	10
		NAD	10	9	9	10
	Small		0	0	1	0
	right		0	0	1	0

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

	Sex	M	M	M	M
	Groups	C / M	LD / M	MD / M	HD / M
	No. Animals	10	10	10	10
TEST	Technician/Location	0	1	0	0
EPIDIDYMIDES	EPIDIDYMIDES				
	NO. EXAM.	10	10	10	10
	NAD	9	10	9	10
	Abnormal color	1	0	0	0
	yellow	1	0	0	0
	Abnormal position	1	0	0	0
	right	1	0	0	0
PITUITARY GLAND	PITUITARY GLAND				
	NO. EXAM.	10	10	10	10
	NAD	10	9	9	10
	Autolytic	0	0	0	0
THYROID GLAND	THYROID GLAND				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
THYROID/PARATHYROID	THYROID/PARATHYROID				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
PARATHYROID GLANDS	PARATHYROID GLANDS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
ADRENAL GLANDS	ADRENAL GLANDS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Enlarged	0	0	0	0
	both sides	0	0	0	0
	Autolytic	0	0	0	0
SPLEEN	SPLEEN				
	NO. EXAM.	10	10	10	10

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

	Sex	M	M	M	M
	Groups	C / M	LD / M	MD / M	HD / M
	No. Animals	10	10	10	10
SPLEEN	NAD	10	10	10	10
	Autolytic	0	0	0	0
THYMUS	THYMUS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Abnormal color	0	0	0	0
	red	0	0	0	0
	Autolytic	0	0	0	0
MESENT. LYMPH NODE	MESENT. LYMPH NODE				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
MANDIB.LYMPH	MANDIB.LYMPH NODES				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
SALIVARY GLANDS	SALIVARY GLANDS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
HARDERIAN GLANDS	HARDERIAN GLANDS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
MAMMARY GLAND	MAMMARY GLAND				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
SKIN/SUBCUTIS	SKIN/SUBCUTIS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	10
	Autolytic	0	0	0	0
SKEL	SKELETAL MUSCLE				

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	M	M	M	M
		Groups	C / M	LD / M	MD / M	HD / M
SKELETAL		No. Animals	10	10	10	10
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
EYES	EYES					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
FEMURS	FEMURS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0
STERNUM	STERNUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	10
	Autolytic		0	0	0	0

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	F	F	F	F
		Groups	C / F	LD / F	MD / F	HD / F
		No. Animals	10	10	10	10
BRAIN	BRAIN					
		NO. EXAM.	10	10	10	10
		NAD	6	6	8	9
	Autolytic		0	1	0	1
SPINAL CORD	SPINAL CORD					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
SCIATIC NERVES	SCIATIC NERVES					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
HEART	HEART					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
AORTA	AORTA					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
TRACHEA	TRACHEA					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
LUNG	LUNG					
		NO. EXAM.	10	10	10	10
		NAD	9	9	10	9
	Abnormal color		0	0	0	1
	Abnormal surface		0	1	0	0
	dark		0	1	0	0
	Autolytic		0	0	0	1
TONGUE	TONGUE					
		NO. EXAM.	10	10	10	10

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	F	F	F	F
		Groups	C / F	LD / F	MD / F	HD / F
		No. Animals	10	10	10	10
TONGUE		NAD	9	10	10	7
	Autolytic		0	0	0	1
ESOPHAGUS	ESOPHAGUS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
STOMACH	STOMACH					
		NO. EXAM.	10	10	10	10
		NAD	10	9	10	9
	Autolytic		0	0	0	1
	Cannibalized		0	1	0	0
DUODENUM	DUODENUM					
		NO. EXAM.	10	10	10	10
		NAD	10	9	10	9
	Autolytic		0	0	0	1
	Cannibalized		0	1	0	0
JEJUNUM	JEJUNUM					
		NO. EXAM.	10	10	10	10
		NAD	10	9	10	9
	Autolytic		0	0	0	1
	Cannibalized		0	1	0	0
ILEUM	ILEUM					
		NO. EXAM.	10	10	10	10
		NAD	10	9	10	9
	Autolytic		0	0	0	1
	Cannibalized		0	1	0	0
CECUM	CECUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
COLON	COLON					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	F	F	F	F
		Groups	C / F	LD / F	MD / F	HD / F
		No. Animals	10	10	10	10
COL	Autolytic		0	0	0	1
RECTUM	RECTUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
LIVER	LIVER					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	8
	Abnormal surface		0	0	0	1
	marbled		0	0	0	1
	pale		0	0	0	1
	Autolytic		0	0	0	1
PANCREAS	PANCREAS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
KIDNEYS	KIDNEYS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
URETERS	URETERS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
URINARY BLADDER	URINARY BLADDER					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
OVARIES	OVARIES					
		NO. EXAM.	10	10	10	10
		NAD	10	9	10	9
	Autolytic		0	0	0	1
	Cannibalized		0	1	0	0

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	F	F	F	F
		Groups	C / F	LD / F	MD / F	HD / F
		No. Animals	10	10	10	10
OVIDUCTS	OVIDUCTS					
		NO. EXAM.	10	10	10	10
		NAD	10	9	10	9
	Autolytic		0	0	0	1
	Cannibalized		0	1	0	0
UTERUS	UTERUS					
		NO. EXAM.	10	10	10	10
		NAD	7	7	9	6
	Autolytic		0	0	0	1
	Cannibalized		0	1	0	0
	fluid filled		3	2	1	3
CERVIX	CERVIX					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
VAGINA	VAGINA					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
PITUITARY GLAND	PITUITARY GLAND					
		NO. EXAM.	10	10	10	10
		NAD	10	8	10	8
	Autolytic		0	0	0	1
THYROID GLAND	THYROID GLAND					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
THYROID/PARATHYROID	THYROID/PARATHYROID					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
PAR	PARATHYROID GLANDS					

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

	Sex	F	F	F	F
	Groups	C / F	LD / F	MD / F	HD / F
	No. Animals	10	10	10	10
PARATHYROID	NO. EXAM.	10	10	10	10
	NAD	10	10	10	9
	Autolytic	0	0	0	1
ADRENAL GLANDS	ADRENAL GLANDS				
	NO. EXAM.	10	10	10	10
	NAD	9	10	10	9
	Enlarged	0	0	0	1
	both sides	0	0	0	1
	Autolytic	0	0	0	1
SPLEEN	SPLEEN				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	9
	Autolytic	0	0	0	1
THYMUS	THYMUS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	9	9
	Abnormal color	0	0	0	1
	red	0	0	0	1
	Autolytic	0	0	0	1
MESENT. LYMPH NODE	MESENT. LYMPH NODE				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	9
	Autolytic	0	0	0	1
MANDIB.LYMPH	MANDIB.LYMPH NODES				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	9
	Autolytic	0	0	0	1
SALIVARY GLANDS	SALIVARY GLANDS				
	NO. EXAM.	10	10	10	10
	NAD	10	10	10	9
	Autolytic	0	0	0	1
HARDERIAN	HARDERIAN GLANDS				
	NO. EXAM.	10	10	10	10

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Number of Animals with Necropsy Findings by Organ/Group/Sex
Status at Necropsy: K0, incl. Decedents

		Sex	F	F	F	F
		Groups	C / F	LD / F	MD / F	HD / F
		No. Animals	10	10	10	10
HARDERIAN		NAD	10	10	10	9
	Autolytic		0	0	0	1
MAMMARY GLAND	MAMMARY GLAND					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
SKIN/SUBCUTIS	SKIN/SUBCUTIS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
SKELETAL MUSCLE	SKELETAL MUSCLE					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
EYES	EYES					
		NO. EXAM.	10	10	10	10
		NAD	10	9	10	9
	Autolytic		0	1	0	1
FEMURS	FEMURS					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1
STERNUM	STERNUM					
		NO. EXAM.	10	10	10	10
		NAD	10	10	10	9
	Autolytic		0	0	0	1

NO.EXAM. = Number of animals examined
NAD = Nothing Abnormal Discovered

Codes and Symbols

Abbreviation	Description
-	No value(s) recorded / value not calculated
K0	Final Necropsy

Dose Groups

Dose Group	Description
C / M	Control, males:
C / F	Control, females:
LD / M	Treated, males:
LD / F	Treated, females:
MD / M	Treated, males:
MD / F	Treated, females:
HD / M	Treated, males:
HD / F	Treated, females:

Summary Table of Body and Organ Weights and Statistics
Status at Necropsy: K0

Sex		M	M	M	M
Groups		C / M	LD / M	MD / M	HD / M
No. Animals		10	10	10	10
FINAL BODY WEIGHT	FINAL BODY WEIGHT				
	NO. WGTS	10	10	10	10
	Mean weight [g]	378a	374	377	377
	SD [g]	24	22	27	29
BRAIN	BRAIN				
	NO. WGTS	10	10	10	10
	Mean weight [g]	2.24k	2.21	2.19	2.23
	SD [g]	0.17	0.11	0.12	0.09
	Mean Organ/Body [%]	0.59a	0.59	0.59	0.60
	SD [%]	0.05	0.04	0.05	0.06
SPLEEN	SPLEEN				
	NO. WGTS	10	10	10	10
	Mean weight [g]	0.75a	0.76	0.76	0.75
	SD [g]	0.10	0.08	0.08	0.10
	Mean Organ/Body [%]	0.20a	0.20	0.20	0.20
	SD [%]	0.03	0.02	0.02	0.02
	Mean Organ/Brain [%]	33.57a	34.52	34.82	33.54
	SD [%]	4.54	3.94	5.09	5.02
THYMUS	THYMUS				
	NO. WGTS	10	10	10	10
	Mean weight [g]	0.32a	0.36	0.34	0.33
	SD [g]	0.05	0.07	0.07	0.05
	Mean Organ/Body [%]	0.09a	0.10	0.09	0.09
	SD [%]	0.02	0.02	0.02	0.01
	Mean Organ/Brain [%]	14.49a	16.24	15.70	14.82
	SD [%]	2.55	3.64	3.15	2.27
TESTES	TESTES				
	NO. WGTS	10	10	10	10
	Mean weight [g]	3.82k	3.78	3.76	3.87
	SD [g]	0.42	0.31	0.33	0.30
	Mean Organ/Body [%]	1.01a	1.01	1.00	1.03

NO. WGTS = Number of weights recorded
SD = Standard Deviation
Statistic Profile = DecisionTree
a = ANOVA; k = KRUSKALL-WALLIS;

Summary Table of Body and Organ Weights and Statistics
Status at Necropsy: K0

Sex		M	M	M	M
Groups		C / M	LD / M	MD / M	HD / M
No. Animals		10	10	10	10
TESTES	SD [%]	0.10	0.08	0.11	0.11
	Mean Organ/Brain [%]	171.03k	171.12	171.83	173.58
	SD [%]	17.78	15.78	20.14	16.25
KIDNEYS	KIDNEYS				
	NO. WGTS	10	10	10	10
	Mean weight [g]	2.41a	2.32	2.39	2.43
	SD [g]	0.21	0.15	0.13	0.18
	Mean Organ/Body [%]	0.64k	0.62	0.64	0.65
	SD [%]	0.06	0.03	0.04	0.05
	Mean Organ/Brain [%]	107.82a	104.96	109.10	108.91
	SD [%]	6.26	5.76	9.64	10.21
PROSTATE WHOLE	PROSTATE WHOLE				
	NO. WGTS	10	10	10	10
	Mean weight [g]	2.50a	2.82	2.75	2.70
	SD [g]	0.68	0.32	0.39	0.43
	Mean Organ/Body [%]	0.66a	0.75	0.73	0.72
	SD [%]	0.17	0.08	0.10	0.12
	Mean Organ/Brain [%]	111.34a	127.67	125.15	121.55
	SD [%]	27.03	16.50	16.10	22.86
PITUITARY GLAND	PITUITARY GLAND				
	NO. WGTS	10	10	10	10
	Mean weight [g]	0.011a	0.012	0.010	0.011
	SD [g]	0.003	0.002	0.003	0.002
	Mean Organ/Body [%]	0.003a	0.003	0.003	0.003
	SD [%]	0.001	0.001	0.001	0.001
	Mean Organ/Brain [%]	0.469a	0.530	0.462	0.491
	SD [%]	0.121	0.095	0.127	0.091
THYROID/PARATHYROID	THYROID/PARATHYROID				
	NO. WGTS	10	10	10	10
	Mean weight [g]	0.03a	0.03	0.04	0.03

NO. WGTS = Number of weights recorded
SD = Standard Deviation
Statistic Profile = DecisionTree
a = ANOVA; k = KRUSKALL-WALLIS;

Summary Table of Body and Organ Weights and Statistics
Status at Necropsy: K0

Sex		M	M	M	M
Groups		C / M	LD / M	MD / M	HD / M
No. Animals		10	10	10	10
THYROID/PARATHYROID	SD [g]	0.01	0.01	0.01	0.01
	Mean Organ/Body [%]	0.01a	0.01	0.01	0.01
	SD [%]	0.00	0.00	0.00	0.00
	Mean Organ/Brain [%]	1.42a	1.47	1.72	1.54
	SD [%]	0.58	0.24	0.33	0.44
ADRENAL GLANDS	ADRENAL GLANDS				
	NO. WGTS	10	10	10	10
	Mean weight [g]	0.057a	0.055	0.061	0.064
	SD [g]	0.006	0.012	0.007	0.008
	Mean Organ/Body [%]	0.015a	0.015	0.016	0.017
	SD [%]	0.001	0.003	0.001	0.002
	Mean Organ/Brain [%]	2.565k	2.512	2.773	2.872
	SD [%]	0.295	0.586	0.369	0.385
HEART	HEART				
	NO. WGTS	10	10	10	10
	Mean weight [g]	0.98a	0.96	0.99	1.01
	SD [g]	0.12	0.10	0.14	0.11
	Mean Organ/Body [%]	0.26a	0.26	0.26	0.27
	SD [%]	0.03	0.02	0.03	0.03
	Mean Organ/Brain [%]	43.89a	43.66	45.26	45.40
	SD [%]	4.59	5.01	6.77	6.17
EPIDIDYMIDES	EPIDIDYMIDES				
	NO. WGTS	10	10	10	10
	Mean weight [g]	1.49a	1.49	1.41	1.54
	SD [g]	0.23	0.16	0.13	0.21
	Mean Organ/Body [%]	0.40a	0.40	0.38	0.41
	SD [%]	0.06	0.04	0.04	0.06
	Mean Organ/Brain [%]	66.88a	67.45	64.47	69.14
	SD [%]	8.96	8.94	6.85	10.77
LIVER	LIVER				
	NO. WGTS	10	10	10	10

NO. WGTS = Number of weights recorded
SD = Standard Deviation
Statistic Profile = DecisionTree
a = ANOVA; k = KRUSKALL-WALLIS;

Summary Table of Body and Organ Weights and Statistics
Status at Necropsy: K0

Sex		M	M	M	M
Groups		C / M	LD / M	MD / M	HD / M
No. Animals		10	10	10	10
LIVER	Mean weight [g]	9.08k	8.72	8.79	9.30
	SD [g]	0.89	0.75	0.94	1.44
	Mean Organ/Body [%]	2.40a	2.33	2.33	2.46
	SD [%]	0.16	0.17	0.17	0.29
	Mean Organ/Brain [%]	407.09a	393.99	401.54	417.64
	SD [%]	40.80	28.38	47.73	70.63

NO. WGTS = Number of weights recorded
SD = Standard Deviation
Statistic Profile = DecisionTree
a = ANOVA; k = KRUSKALL-WALLIS;

Summary Table of Body and Organ Weights and Statistics
Status at Necropsy: K0

Sex		F	F	F	F
Groups		C / F	LD / F	MD / F	HD / F
No. Animals		10	10	10	10
FINAL BODY WEIGHT	FINAL BODY WEIGHT				
	NO. WGTS	10	10	10	10
	Mean weight [g]	221a	218	218	221
	SD [g]	9	14	6	16
BRAIN	BRAIN				
	NO. WGTS	10	9	10	9
	Mean weight [g]	1.98a	2.01	1.96	1.97
	SD [g]	0.07	0.11	0.04	0.05
	Mean Organ/Body [%]	0.90a	0.91	0.90	0.90
	SD [%]	0.03	0.05	0.03	0.07
SPLEEN	SPLEEN				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.57a	0.57	0.53	0.55
	SD [g]	0.11	0.06	0.11	0.08
	Mean Organ/Body [%]	0.26a	0.26	0.24	0.25
	SD [%]	0.04	0.02	0.04	0.03
	Mean Organ/Brain [%]	28.62a	28.50	27.14	28.17
	SD [%]	5.13	3.34	5.32	4.00
THYMUS	THYMUS				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.37ad	0.31*	0.31*	0.30*
	SD [g]	0.06	0.05	0.06	0.05
	Mean Organ/Body [%]	0.17ad	0.14	0.14*	0.14*
	SD [%]	0.03	0.03	0.03	0.02
	Mean Organ/Brain [%]	18.84ad	15.41	15.59	15.37
	SD [%]	3.38	2.45	3.12	2.32
KIDNEYS	KIDNEYS				
	NO. WGTS	10	9	10	9
	Mean weight [g]	1.59a	1.58	1.57	1.55
	SD [g]	0.13	0.14	0.18	0.17
	Mean Organ/Body [%]	0.72a	0.72	0.72	0.71

NO. WGTS = Number of weights recorded
SD = Standard Deviation
Statistic Profile = DecisionTree
* = $p < 0.05$; a = ANOVA; ad = ANOVA-DUNNETT;

Summary Table of Body and Organ Weights and Statistics
Status at Necropsy: K0

Sex		F	F	F	F
Groups		C / F	LD / F	MD / F	HD / F
No. Animals		10	10	10	10
KIDNEYS	SD [%]	0.04	0.05	0.09	0.04
	Mean Organ/Brain [%]	80.14a	78.73	80.38	79.01
	SD [%]	4.81	5.46	9.47	8.77
PITUITARY GLAND	PITUITARY GLAND				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.014k	0.012	0.014	0.014
	SD [g]	0.002	0.003	0.003	0.002
	Mean Organ/Body [%]	0.006k	0.006	0.006	0.006
	SD [%]	0.001	0.002	0.001	0.001
	Mean Organ/Brain [%]	0.707k	0.618	0.711	0.716
	SD [%]	0.083	0.185	0.132	0.132
THYROID/PARATHYROID	THYROID/PARATHYROID				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.03a	0.03	0.02	0.03
	SD [g]	0.01	0.00	0.01	0.00
	Mean Organ/Body [%]	0.01a	0.01	0.01	0.01
	SD [%]	0.00	0.00	0.00	0.00
	Mean Organ/Brain [%]	1.38a	1.36	1.21	1.25
	SD [%]	0.34	0.21	0.24	0.16
ADRENAL GLANDS	ADRENAL GLANDS				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.081a	0.082	0.079	0.078
	SD [g]	0.009	0.008	0.009	0.007
	Mean Organ/Body [%]	0.037a	0.037	0.036	0.036
	SD [%]	0.004	0.004	0.004	0.004
	Mean Organ/Brain [%]	4.102a	4.113	4.041	3.974
	SD [%]	0.385	0.518	0.482	0.253
HEART	HEART				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.66a	0.66	0.66	0.68

NO. WGTS = Number of weights recorded
SD = Standard Deviation
Statistic Profile = DecisionTree
a = ANOVA; k = KRUSKALL-WALLIS;

Summary Table of Body and Organ Weights and Statistics
Status at Necropsy: K0

Sex		F	F	F	F
Groups		C / F	LD / F	MD / F	HD / F
No. Animals		10	10	10	10
HEART	SD [g]	0.04	0.04	0.04	0.05
	Mean Organ/Body [%]	0.30a	0.30	0.30	0.31
	SD [%]	0.02	0.02	0.03	0.02
	Mean Organ/Brain [%]	33.49a	32.76	33.56	34.62
	SD [%]	2.08	2.88	2.20	2.50
LIVER	LIVER				
	NO. WGTS	10	9	10	9
	Mean weight [g]	6.07a	5.89	5.80	6.09
	SD [g]	0.60	0.74	0.46	0.48
	Mean Organ/Body [%]	2.74a	2.67	2.66	2.78
	SD [%]	0.20	0.24	0.21	0.12
	Mean Organ/Brain [%]	305.86a	293.91	296.19	310.27
	SD [%]	25.75	33.51	24.01	27.18
OVARIES	OVARIES				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.13a	0.14	0.15	0.15
	SD [g]	0.02	0.02	0.02	0.02
	Mean Organ/Body [%]	0.06a	0.07	0.07	0.07
	SD [%]	0.01	0.01	0.01	0.01
	Mean Organ/Brain [%]	6.78a	7.07	7.72	7.74
	SD [%]	1.28	1.12	1.08	1.20
UTERUS	UTERUS				
	NO. WGTS	10	9	10	9
	Mean weight [g]	0.89k	0.88	0.82	0.95
	SD [g]	0.39	0.39	0.39	0.66
	Mean Organ/Body [%]	0.40a	0.40	0.37	0.44
	SD [%]	0.17	0.19	0.17	0.31
	Mean Organ/Brain [%]	44.79k	44.53	42.03	48.07
	SD [%]	19.35	21.46	20.52	32.54

NO. WGTS = Number of weights recorded
SD = Standard Deviation
Statistic Profile = DecisionTree
a = ANOVA; k = KRUSKALL-WALLIS;

Summary Table of Body and Organ Weights and Statistics

Animal Number	Dose Group	Sex	Necropsy Status	Organ	Comment
054	LD / F	F	K0 / K0	SPLEEN	EXCLUDED
				THYROID/PARATHYROID	EXCLUDED
				THYMUS	EXCLUDED
				PITUITARY GLAND	EXCLUDED
				LIVER	EXCLUDED
				BRAIN	EXCLUDED
				KIDNEYS	EXCLUDED
				OVARIES	EXCLUDED
				ADRENAL GLANDS	EXCLUDED
				UTERUS	EXCLUDED
				HEART	EXCLUDED

Dose Groups

Dose Group	Description
C / M	Control, males:
C / F	Control, females:
LD / M	Treated, males:
LD / F	Treated, females:
MD / M	Treated, males:
MD / F	Treated, females:
HD / M	Treated, males:
HD / F	Treated, females:

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
C / M	001	Alive	Alive		1	90	90
	002	Alive	Alive		1	90	90
	003	Alive	Alive		1	90	90
	004	Alive	Alive		1	90	90
	005	Alive	Alive		1	90	90
	006	Alive	Alive		1	90	90
	007	Alive	Alive		1	90	90
	008	Alive	Alive		1	90	90
	009	Alive	Alive		1	90	90
	010	Alive	Alive		1	90	90

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
LD / M	011	Alive	Alive		1	90	90
	012	Alive	Alive		1	90	90
	013	Alive	Alive		1	90	90
	014	Alive	Alive		1	90	90
	015	Alive	Alive		1	90	90
	016	Alive	Alive		1	90	90
	017	Alive	Alive		1	90	90
	018	Alive	Alive		1	90	90
	019	Alive	Alive		1	90	90
	020	Alive	Alive		1	90	90

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
MD / M	021	Alive	Alive		1	90	90
	022	Alive	Alive		1	90	90
	023	Alive	Alive		1	90	90
	024	Alive	Alive		1	90	90
	025	Alive	Alive		1	90	90
	026	Alive	Alive		1	90	90
	027	Alive	Alive		1	90	90
	028	Alive	Alive		1	90	90
	029	Alive	Alive		1	90	90
	030	Alive	Alive		1	90	90

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
HD / M	031	Alive	Alive		1	90	90
	032	Alive	Alive		1	90	90
	033	Alive	Alive		1	90	90
	034	Alive	Alive		1	90	90
	035	Alive	Alive		1	90	90
	036	Alive	Alive		1	90	90
	037	Alive	Alive		1	90	90
	038	Alive	Alive		1	90	90
	039	Alive	Alive		1	90	90
	040	Alive	Alive		1	90	90

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
C / F	041	Alive	Alive		1	90	90
	042	Alive	Alive		1	90	90
	043	Alive	Alive		1	90	90
	044	Alive	Alive		1	90	90
	045	Alive	Alive		1	90	90
	046	Alive	Alive		1	90	90
	047	Alive	Alive		1	90	90
	048	Alive	Alive		1	90	90
	049	Alive	Alive		1	90	90
	050	Alive	Alive		1	90	90

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
	051	Alive	Alive		1	90	90
	052	Alive	Alive		1	90	90
	053	Alive	Alive		1	90	90
	054	Alive	Alive		1	26	26
		Dead	Found dead		27	27	1
LD / F	055	Alive	Alive		1	90	90
	056	Alive	Alive		1	90	90
	057	Alive	Alive		1	90	90
	058	Alive	Alive		1	90	90
	059	Alive	Alive		1	90	90
	060	Alive	Alive		1	90	90

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
MD / F	061	Alive	Alive		1	90	90
	062	Alive	Alive		1	90	90
	063	Alive	Alive		1	90	90
	064	Alive	Alive		1	90	90
	065	Alive	Alive		1	90	90
	066	Alive	Alive		1	90	90
	067	Alive	Alive		1	90	90
	068	Alive	Alive		1	90	90
	069	Alive	Alive		1	90	90
	070	Alive	Alive		1	90	90

Individual Signs - Mortality Check

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	First Day	Last Day	Duration [Days]
HD / F	071	Alive	Alive		1	81	81
		Dead	Found dead		82	82	1
	072	Alive	Alive		1	90	90
	073	Alive	Alive		1	90	90
	074	Alive	Alive		1	90	90
	075	Alive	Alive		1	90	90
	076	Alive	Alive		1	90	90
	077	Alive	Alive		1	90	90
	078	Alive	Alive		1	90	90
	079	Alive	Alive		1	90	90
	080	Alive	Alive		1	90	90

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
C / M	001	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	002	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	003	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	004	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	005	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	006	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	007	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	008	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
C / M	009	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	010	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
LD / M	011	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	012	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	013	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	014	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	015	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	016	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	017	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	018	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
LD / M	019	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	020	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
MD / M	021	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	022	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	023	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	024	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	025	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	026	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	027	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	028	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
MD / M	029	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	030	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
HD / M	031	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	032	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	033	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	034	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	035	Normal	Normal	1	2	2
		Normal	Normal	4	14	11
		Normal	Normal	16	44	29
		Normal	Normal	46	90	45
	036	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	037	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	038	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
HD / M	039	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46
	040	Normal	Normal	1	1	1
		Normal	Normal	3	13	11
		Normal	Normal	15	43	29
		Normal	Normal	45	90	46

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
C / F	041	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	042	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	043	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	044	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	045	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	046	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	047	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	048	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	049	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	050	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
LD / F	051...	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	052	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	053	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	054	Normal	Normal	2	12	11
		Normal	Normal	14	26	13
		Dead	Found Dead	27	27	1
	055	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	056	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	057	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	058	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	059	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	060	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
MD / F	061...	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	062	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	063	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	064	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	065	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	066	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	067	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	068	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	069	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	070	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48

Individual Signs - Clinical Sign - BSL

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	First Day	Last Day	Duration [Days]
HD / F	071...	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	82	39
		Dead	Found Dead	82	82	1
	072	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	073	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	074	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	075	Normal	Normal	2	12	11
		Normal	Normal	14	42	29
		Normal	Normal	44	90	47
	076	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	077	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	078	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	079	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48
	080	Normal	Normal	1	11	11
		Normal	Normal	13	41	29
		Normal	Normal	43	90	48

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 1	Animal moving in cage [Score] week 1	Piloerection [Score] week 1	Vocalization [Score] week 1	O Grooming [Score] week 1	Salivation [Score] week 1	Lacrimation [Score] week 1	Changes in skin [Score] week 1	Cyanosis [Score] week 1	Exophthalmos [Score] week 1	Eyes opening [Score] week 1	Resiration [Score] week 1	response to handling [Score] week 1	Arousal [Score] week 1	Fear [Score] week 1	Finger approach [Score] week 1
LD / M	011	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	012	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	013	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	014	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	015	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	016	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	017	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	018	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	019	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	020	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 1	Body position [Score] week 1	Spontaneous activity [Score] week 1	Ataxic gait [Score] week 1	Hypotonic gait [Score] week 1	Twitches [Score] week 1	Tremors [Score] week 1	Seizures [Score] week 1	Stereotypie [Score] week 1	Faeces consistency [Score] week 1	Abnormal vocalisation [Score] week 1	Aggressiveness [Score] week 1	Animal sleeps [Score] week 2	Animal moving in cage [Score] week 2	Piloerection [Score] week 2	Vocalization [Score] week 2
LD / M	011	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	012	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	013	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	014	4	4	2	0	0	0	0	0	0	4	0	0	1	0	0	0
	015	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	016	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	017	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	018	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	019	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	020	4	4	3	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 2	Salivation [Score] week 2	Lacrimation [Score] week 2	Changes in skin [Score] week 2	Cyanosis [Score] week 2	Exophthalmos [Score] week 2	Eyes opening [Score] week 2	Resiration [Score] week 2	response to handling [Score] week 2	Arousal [Score] week 2	Fear [Score] week 2	Finger approach [Score] week 2	Head touch [Score] week 2	Body position [Score] week 2	Spontaneous activity [Score] week 2	Ataxic gait [Score] week 2
LD / M	011	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	012	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	013	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	014	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	015	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	016	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	017	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	018	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	019	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	020	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 2	Twitches [Score] week 2	Tremors [Score] week 2	Seizures [Score] week 2	Stereotypie [Score] week 2	Faeces consistency [Score] week 2	Abnormal vocalisation [Score] week 2	Aggressiveness [Score] week 2	Animal sleeps [Score] week 3	Animal moving in cage [Score] week 3	Piloerection [Score] week 3	Vocalization [Score] week 3	O Grooming [Score] week 3	Salivation [Score] week 3	Lacrimation [Score] week 3	Changes in skin [Score] week 3
LD / M	011	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	012	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	013	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	014	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	015	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	016	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	017	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	018	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	019	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	020	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 3	Exophthalmos [Score] week 3	Eyes opening [Score] week 3	Resiration [Score] week 3	response to handling [Score] week 3	Arousal [Score] week 3	Fear [Score] week 3	Finger approach [Score] week 3	Head touch [Score] week 3	Body position [Score] week 3	Spontaneous activity [Score] week 3	Ataxic gait [Score] week 3	Hypotonic gait [Score] week 3	Twitches [Score] week 3	Tremors [Score] week 3	Seizures [Score] week 3
LD / M	011	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	012	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	013	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	014	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	015	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	016	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	017	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	018	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	019	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	020	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 3	Faeces consistency [Score] week 3	Abnormal vocalisation [Score] week 3	Aggressiveness [Score] week 3	Animal sleeps [Score] week 4	Animal moving in cage [Score] week 4	Piloerection [Score] week 4	Vocalization [Score] week 4	O Grooming [Score] week 4	Salivation [Score] week 4	Lacrimation [Score] week 4	Changes in skin [Score] week 4	Cyanosis [Score] week 4	Exophthalmos [Score] week 4	Eyes opening [Score] week 4	Resiration [Score] week 4
LD / M	011	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	012	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	013	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	014	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	015	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	016	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	017	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	018	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	019	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	020	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 4	Arousal [Score] week 4	Fear [Score] week 4	Finger approach [Score] week 4	Head touch [Score] week 4	Body position [Score] week 4	Spontaneous activity [Score] week 4	Ataxic gait [Score] week 4	Hypotonic gait [Score] week 4	Twitches [Score] week 4	Tremors [Score] week 4	Seizures [Score] week 4	Stereotypie [Score] week 4	Faeces consistency [Score] week 4	Abnormal vocalisation [Score] week 4	Aggressiveness [Score] week 4
LD / M	011	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	012	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	013	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	014	4	4	4	4	2	4	4	0	0	0	0	0	0	4	0	0
	015	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	016	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	017	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	018	2	4	4	6	2	4	4	0	0	0	0	0	0	4	0	0
	019	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	020	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 5	Animal moving in cage [Score] week 5	Piloerection [Score] week 5	Vocalization [Score] week 5	O Grooming [Score] week 5	Salivation [Score] week 5	Lacrimation [Score] week 5	Changes in skin [Score] week 5	Cyanosis [Score] week 5	Exophthalmos [Score] week 5	Eyes opening [Score] week 5	Resiration [Score] week 5	response to handling [Score] week 5	Arousal [Score] week 5	Fear [Score] week 5	Finger approach [Score] week 5
LD / M	011	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	012	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	013	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	014	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	015	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	016	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	017	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	018	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	019	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	020	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 5	Body position [Score] week 5	Spontaneous activity [Score] week 5	Ataxic gait [Score] week 5	Hypotonic gait [Score] week 5	Twitches [Score] week 5	Tremors [Score] week 5	Seizures [Score] week 5	Stereotypie [Score] week 5	Faeces consistency [Score] week 5	Abnormal vocalisation [Score] week 5	Aggressiveness [Score] week 5	Animal sleeps [Score] week 6	Animal moving in cage [Score] week 6	Piloerection [Score] week 6	Vocalization [Score] week 6
LD / M	011	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	012	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	013	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	014	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	015	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	016	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	017	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	018	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	019	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	020	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 6	Salivation [Score] week 6	Lacrimation [Score] week 6	Changes in skin [Score] week 6	Cyanosis [Score] week 6	Exophthalmos [Score] week 6	Eyes opening [Score] week 6	Resiration [Score] week 6	response to handling [Score] week 6	Arousal [Score] week 6	Fear [Score] week 6	Finger approach [Score] week 6	Head touch [Score] week 6	Body position [Score] week 6	Spontaneous activity [Score] week 6	Ataxic gait [Score] week 6
LD / M	011	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	012	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	013	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	014	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	015	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	016	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	017	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	018	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	019	0	4	0	0	0	0	0	4	4	4	2	4	2	4	4	0
	020	0	4	0	0	0	0	0	4	4	4	4	4	4	4	3	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 6	Twitches [Score] week 6	Tremors [Score] week 6	Seizures [Score] week 6	Stereotypie [Score] week 6	Faeces consistency [Score] week 6	Abnormal vocalisation [Score] week 6	Aggressiveness [Score] week 6	Animal sleeps [Score] week 7	Animal moving in cage [Score] week 7	Piloerection [Score] week 7	Vocalization [Score] week 7	O Grooming [Score] week 7	Salivation [Score] week 7	Lacrimation [Score] week 7	Changes in skin [Score] week 7
LD / M	011	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	012	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	013	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	014	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	015	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	016	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	017	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	018	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	019	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	020	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 7	Exophthalmos [Score] week 7	Eyes opening [Score] week 7	Resiration [Score] week 7	response to handling [Score] week 7	Arousal [Score] week 7	Fear [Score] week 7	Finger approach [Score] week 7	Head touch [Score] week 7	Body position [Score] week 7	Spontaneous activity [Score] week 7	Ataxic gait [Score] week 7	Hypotonic gait [Score] week 7	Twitches [Score] week 7	Tremors [Score] week 7	Seizures [Score] week 7
LD / M	011	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	012	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	013	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	014	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	015	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	016	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	017	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	018	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	019	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	020	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 7	Faeces consistency [Score] week 7	Abnormal vocalisation [Score] week 7	Aggressiveness [Score] week 7	Animal sleeps [Score] week 8	Animal moving in cage [Score] week 8	Piloerection [Score] week 8	Vocalization [Score] week 8	O Grooming [Score] week 8	Salivation [Score] week 8	Lacrimation [Score] week 8	Changes in skin [Score] week 8	Cyanosis [Score] week 8	Exophthalmos [Score] week 8	Eyes opening [Score] week 8	Resiration [Score] week 8
LD / M	011	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	012	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	013	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	014	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	015	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	016	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	017	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	018	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	019	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	020	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 8	Arousal [Score] week 8	Fear [Score] week 8	Finger approach [Score] week 8	Head touch [Score] week 8	Body position [Score] week 8	Spontaneous activity [Score] week 8	Ataxic gait [Score] week 8	Hypotonic gait [Score] week 8	Twitches [Score] week 8	Tremors [Score] week 8	Seizures [Score] week 8	Stereotypie [Score] week 8	Faeces consistency [Score] week 8	Abnormal vocalisation [Score] week 8	Aggressiveness [Score] week 8
LD / M	011	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	012	4	4	4	4	2	4	3	0	0	0	0	0	0	4	0	0
	013	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	014	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	015	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	016	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	017	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	018	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	019	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	020	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 9	Animal moving in cage [Score] week 9	Piloerection [Score] week 9	Vocalization [Score] week 9	O Grooming [Score] week 9	Salivation [Score] week 9	Lacrimation [Score] week 9	Changes in skin [Score] week 9	Cyanosis [Score] week 9	Exophthalmos [Score] week 9	Eyes opening [Score] week 9	Resiration [Score] week 9	response to handling [Score] week 9	Arousal [Score] week 9	Fear [Score] week 9	Finger approach [Score] week 9
LD / M	011	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	012	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	013	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	014	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	015	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	016	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	017	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	018	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	019	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	020	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 9	Body position [Score] week 9	Spontaneous activity [Score] week 9	Ataxic gait [Score] week 9	Hypotonic gait [Score] week 9	Twitches [Score] week 9	Tremors [Score] week 9	Seizures [Score] week 9	Stereotypie [Score] week 9	Faeces consistency [Score] week 9	Abnormal vocalisation [Score] week 9	Aggressiveness [Score] week 9	Animal sleeps [Score] week 10	Animal moving in cage [Score] week 10	Piloerection [Score] week 10	Vocalization [Score] week 10
LD / M	011	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	012	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	013	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	014	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	015	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	016	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	017	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	018	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	019	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	020	4	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 10	Salivation [Score] week 10	Lacrimation [Score] week 10	Changes in skin [Score] week 10	Cyanosis [Score] week 10	Exophthalmos [Score] week 10	Eyes opening [Score] week 10	Resiration [Score] week 10	response to handling [Score] week 10	Arousal [Score] week 10	Fear [Score] week 10	Finger approach [Score] week 10	Head touch [Score] week 10	Body position [Score] week 10	Spontaneous activity [Score] week 10	Ataxic gait [Score] week 10
LD / M	011	0	4	0	0	0	0	0	4	4	4	4	4	4	4	3	0
	012	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	013	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	014	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	015	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	016	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	017	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	018	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	019	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	020	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 10	Twitches [Score] week 10	Tremors [Score] week 10	Seizures [Score] week 10	Stereotypie [Score] week 10	Faeces consistency [Score] week 10	Abnormal vocalisation [Score] week 10	Aggressiveness [Score] week 10	Animal sleeps [Score] week 11	Animal moving in cage [Score] week 11	Piloerection [Score] week 11	Vocalization [Score] week 11	O Grooming [Score] week 11	Salivation [Score] week 11	Lacrimation [Score] week 11	Changes in skin [Score] week 11
LD / M	011	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	012	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	013	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	014	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	015	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	016	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	017	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	018	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	019	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	020	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 11	Exophthalmos [Score] week 11	Eyes opening [Score] week 11	Resiration [Score] week 11	response to handling [Score] week 11	Arousal [Score] week 11	Fear [Score] week 11	Finger approach [Score] week 11	Head touch [Score] week 11	Body position [Score] week 11	Spontaneous activity [Score] week 11	Ataxic gait [Score] week 11	Hypotonic gait [Score] week 11	Twitches [Score] week 11	Tremors [Score] week 11	Seizures [Score] week 11
LD / M	011	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	012	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	013	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	014	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	015	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	016	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	017	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	018	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	019	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	020	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 11	Faeces consistency [Score] week 11	Abnormal vocalisation [Score] week 11	Aggressiveness [Score] week 11	Animal sleeps [Score] week 12	Animal moving in cage [Score] week 12	Piloerection [Score] week 12	Vocalization [Score] week 12	O Grooming [Score] week 12	Salivation [Score] week 12	Lacrimation [Score] week 12	Changes in skin [Score] week 12	Cyanosis [Score] week 12	Exophthalmos [Score] week 12	Eyes opening [Score] week 12	Resiration [Score] week 12
LD / M	011	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	012	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	013	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	014	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	015	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	016	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	017	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	018	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	019	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	020	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 12	Arousal [Score] week 12	Fear [Score] week 12	Finger approach [Score] week 12	Head touch [Score] week 12	Body position [Score] week 12	Spontaneous activity [Score] week 12	Ataxic gait [Score] week 12	Hypotonic gait [Score] week 12	Twitches [Score] week 12	Tremors [Score] week 12	Seizures [Score] week 12	Stereotypie [Score] week 12	Faeces consistency [Score] week 12	Abnormal vocalisation [Score] week 12	Aggressiveness [Score] week 12
LD / M	011	4	4	4	4	4	4	4	0	0	0	0	0	0	4	4	4
	012	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	013	2	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	014	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	015	4	4	2	4	2	4	4	0	0	0	0	0	0	4	0	0
	016	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	017	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	018	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	019	4	4	4	4	4	0	4	4	0	0	0	0	0	4	0	0
	020	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 1	Animal moving in cage [Score] week 1	Piloerection [Score] week 1	Vocalization [Score] week 1	O Grooming [Score] week 1	Salivation [Score] week 1	Lacrimation [Score] week 1	Changes in skin [Score] week 1	Cyanosis [Score] week 1	Exophthalmos [Score] week 1	Eyes opening [Score] week 1	Resiration [Score] week 1	response to handling [Score] week 1	Arousal [Score] week 1	Fear [Score] week 1	Finger approach [Score] week 1
LD / F	051	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	6
	052	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	053	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	054	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	055	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	056	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	057	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	058	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	059	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	060	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 1	Body position [Score] week 1	Spontaneous activity [Score] week 1	Ataxic gait [Score] week 1	Hypotonic gait [Score] week 1	Twitches [Score] week 1	Tremors [Score] week 1	Seizures [Score] week 1	Stereotypie [Score] week 1	Faeces consistency [Score] week 1	Abnormal vocalisation [Score] week 1	Aggressiveness [Score] week 1	Animal sleeps [Score] week 2	Animal moving in cage [Score] week 2	Piloerection [Score] week 2	Vocalization [Score] week 2
LD / F	051	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	052	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	053	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	054	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	055	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	056	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	057	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	058	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	059	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	060	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 2	Salivation [Score] week 2	Lacrimation [Score] week 2	Changes in skin [Score] week 2	Cyanosis [Score] week 2	Exophthalmos [Score] week 2	Eyes opening [Score] week 2	Resiration [Score] week 2	response to handling [Score] week 2	Arousal [Score] week 2	Fear [Score] week 2	Finger approach [Score] week 2	Head touch [Score] week 2	Body position [Score] week 2	Spontaneous activity [Score] week 2	Ataxic gait [Score] week 2
LD / F	051	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	052	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	053	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	054	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	055	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	056	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	057	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	058	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	059	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	060	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 2	Twitches [Score] week 2	Tremors [Score] week 2	Seizures [Score] week 2	Stereotypie [Score] week 2	Faeces consistency [Score] week 2	Abnormal vocalisation [Score] week 2	Aggressiveness [Score] week 2	Animal sleeps [Score] week 3	Animal moving in cage [Score] week 3	Piloerection [Score] week 3	Vocalization [Score] week 3	O Grooming [Score] week 3	Salivation [Score] week 3	Lacrimation [Score] week 3	Changes in skin [Score] week 3
LD / F	051	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	052	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	053	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	054	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	055	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	056	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	057	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	058	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	059	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	060	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 3	Exophthalmos [Score] week 3	Eyes opening [Score] week 3	Resiration [Score] week 3	response to handling [Score] week 3	Arousal [Score] week 3	Fear [Score] week 3	Finger approach [Score] week 3	Head touch [Score] week 3	Body position [Score] week 3	Spontaneous activity [Score] week 3	Ataxic gait [Score] week 3	Hypotonic gait [Score] week 3	Twitches [Score] week 3	Tremors [Score] week 3	Seizures [Score] week 3
LD / F	051	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	052	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	053	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	054	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	055	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	056	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	057	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	058	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	059	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	060	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 3	Faeces consistency [Score] week 3	Abnormal vocalisation [Score] week 3	Aggressiveness [Score] week 3	Animal sleeps [Score] week 4	Animal moving in cage [Score] week 4	Piloerection [Score] week 4	Vocalization [Score] week 4	O Grooming [Score] week 4	Salivation [Score] week 4	Lacrimation [Score] week 4	Changes in skin [Score] week 4	Cyanosis [Score] week 4	Exophthalmos [Score] week 4	Eyes opening [Score] week 4	Resiration [Score] week 4
LD / F	051	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	052	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	053	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	054	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	055	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	056	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	057	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	058	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	059	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	060	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 4	Arousal [Score] week 4	Fear [Score] week 4	Finger approach [Score] week 4	Head touch [Score] week 4	Body position [Score] week 4	Spontaneous activity [Score] week 4	Ataxic gait [Score] week 4	Hypotonic gait [Score] week 4	Twitches [Score] week 4	Tremors [Score] week 4	Seizures [Score] week 4	Stereotypie [Score] week 4	Faeces consistency [Score] week 4	Abnormal vocalisation [Score] week 4	Aggressiveness [Score] week 4
LD / F	051	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	052	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	053	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	054	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	055	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	056	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	057	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	058	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	059	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	060	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 5	Animal moving in cage [Score] week 5	Piloerection [Score] week 5	Vocalization [Score] week 5	O Grooming [Score] week 5	Salivation [Score] week 5	Lacrimation [Score] week 5	Changes in skin [Score] week 5	Cyanosis [Score] week 5	Exophthalmos [Score] week 5	Eyes opening [Score] week 5	Resiration [Score] week 5	response to handling [Score] week 5	Arousal [Score] week 5	Fear [Score] week 5	Finger approach [Score] week 5
LD / F	051	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	052	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	053	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	056	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	057	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	058	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	059	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	060	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 5	Body position [Score] week 5	Spontaneous activity [Score] week 5	Ataxic gait [Score] week 5	Hypotonic gait [Score] week 5	Twitches [Score] week 5	Tremors [Score] week 5	Seizures [Score] week 5	Stereotypie [Score] week 5	Faeces consistency [Score] week 5	Abnormal vocalisation [Score] week 5	Aggressiveness [Score] week 5	Animal sleeps [Score] week 6	Animal moving in cage [Score] week 6	Piloerection [Score] week 6	Vocalization [Score] week 6
LD / F	051	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	052	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	053	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	056	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	057	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	058	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	059	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	060	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 6	Salivation [Score] week 6	Lacrimation [Score] week 6	Changes in skin [Score] week 6	Cyanosis [Score] week 6	Exophthalmos [Score] week 6	Eyes opening [Score] week 6	Resiration [Score] week 6	response to handling [Score] week 6	Arousal [Score] week 6	Fear [Score] week 6	Finger approach [Score] week 6	Head touch [Score] week 6	Body position [Score] week 6	Spontaneous activity [Score] week 6	Ataxic gait [Score] week 6
LD / F	051	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	052	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	053	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	056	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	057	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	058	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	059	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	060	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 6	Twitches [Score] week 6	Tremors [Score] week 6	Seizures [Score] week 6	Stereotypie [Score] week 6	Faeces consistency [Score] week 6	Abnormal vocalisation [Score] week 6	Aggressiveness [Score] week 6	Animal sleeps [Score] week 7	Animal moving in cage [Score] week 7	Piloerection [Score] week 7	Vocalization [Score] week 7	O Grooming [Score] week 7	Salivation [Score] week 7	Lacrimation [Score] week 7	Changes in skin [Score] week 7
LD / F	051	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	052	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	053	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	056	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	057	0	0	0	0	0	4	0	0								
	058	0	0	0	0	0	4	0	0								
	059	0	0	0	0	0	4	0	0								
	060	0	0	0	0	0	4	0	0								

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 7	Exophthalmos [Score] week 7	Eyes opening [Score] week 7	Resiration [Score] week 7	response to handling [Score] week 7	Arousal [Score] week 7	Fear [Score] week 7	Finger approach [Score] week 7	Head touch [Score] week 7	Body position [Score] week 7	Spontaneous activity [Score] week 7	Ataxic gait [Score] week 7	Hypotonic gait [Score] week 7	Twitches [Score] week 7	Tremors [Score] week 7	Seizures [Score] week 7
LD / F	051	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	052	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	053	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	056	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	057																
	058																
	059																
	060																

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 7	Faeces consistency [Score] week 7	Abnormal vocalisation [Score] week 7	Aggressiveness [Score] week 7	Animal sleeps [Score] week 8	Animal moving in cage [Score] week 8	Piloerection [Score] week 8	Vocalization [Score] week 8	O Grooming [Score] week 8	Salivation [Score] week 8	Lacrimation [Score] week 8	Changes in skin [Score] week 8	Cyanosis [Score] week 8	Exophthalmos [Score] week 8	Eyes opening [Score] week 8	Resiration [Score] week 8
LD / F	051	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	052	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	053	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	056	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	057					0	1	0	0	0	4	0	0	0	0	0	4
	058					0	1	0	0	0	4	0	0	0	0	0	4
	059					0	1	0	0	0	4	0	0	0	0	0	4
	060					0	1	0	0	0	4	0	0	0	0	0	4

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 8	Arousal [Score] week 8	Fear [Score] week 8	Finger approach [Score] week 8	Head touch [Score] week 8	Body position [Score] week 8	Spontaneous activity [Score] week 8	Ataxic gait [Score] week 8	Hypotonic gait [Score] week 8	Twitches [Score] week 8	Tremors [Score] week 8	Seizures [Score] week 8	Stereotypie [Score] week 8	Faeces consistency [Score] week 8	Abnormal vocalisation [Score] week 8	Aggressiveness [Score] week 8
LD / F	051	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	052	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	053	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	056	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	057	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	058	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	059	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	060	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 9	Animal moving in cage [Score] week 9	Piloerection [Score] week 9	Vocalization [Score] week 9	O Grooming [Score] week 9	Salivation [Score] week 9	Lacrimation [Score] week 9	Changes in skin [Score] week 9	Cyanosis [Score] week 9	Exophthalmos [Score] week 9	Eyes opening [Score] week 9	Resiration [Score] week 9	response to handling [Score] week 9	Arousal [Score] week 9	Fear [Score] week 9	Finger approach [Score] week 9
LD / F	051	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	052	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	053	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	1	0	0	0	0	4	0	0	0	0	0	4	2	4	4	4
	056	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	057	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	058	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	059	1	0	0	0	0	4	0	0	0	0	0	4	2	4	4	4
	060	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 9	Body position [Score] week 9	Spontaneous activity [Score] week 9	Ataxic gait [Score] week 9	Hypotonic gait [Score] week 9	Twitches [Score] week 9	Tremors [Score] week 9	Seizures [Score] week 9	Stereotypie [Score] week 9	Faeces consistency [Score] week 9	Abnormal vocalisation [Score] week 9	Aggressiveness [Score] week 9	Animal sleeps [Score] week 10	Animal moving in cage [Score] week 10	Piloerection [Score] week 10	Vocalization [Score] week 10
LD / F	051	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	052	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	053	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	056	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	057	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	058	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	059	4	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0
	060	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 10	Salivation [Score] week 10	Lacrimation [Score] week 10	Changes in skin [Score] week 10	Cyanosis [Score] week 10	Exophthalmos [Score] week 10	Eyes opening [Score] week 10	Resiration [Score] week 10	response to handling [Score] week 10	Arousal [Score] week 10	Fear [Score] week 10	Finger approach [Score] week 10	Head touch [Score] week 10	Body position [Score] week 10	Spontaneous activity [Score] week 10	Ataxic gait [Score] week 10
LD / F	051	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	052	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	053	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	056	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	057	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	058	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	059	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	060	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 10	Twitches [Score] week 10	Tremors [Score] week 10	Seizures [Score] week 10	Stereotypie [Score] week 10	Faeces consistency [Score] week 10	Abnormal vocalisation [Score] week 10	Aggressiveness [Score] week 10	Animal sleeps [Score] week 11	Animal moving in cage [Score] week 11	Piloerection [Score] week 11	Vocalization [Score] week 11	O Grooming [Score] week 11	Salivation [Score] week 11	Lacrimation [Score] week 11	Changes in skin [Score] week 11
LD / F	051	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	052	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	053	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	056	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	057	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	058	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	059	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	060	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 11	Exophthalmos [Score] week 11	Eyes opening [Score] week 11	Resiration [Score] week 11	response to handling [Score] week 11	Arousal [Score] week 11	Fear [Score] week 11	Finger approach [Score] week 11	Head touch [Score] week 11	Body position [Score] week 11	Spontaneous activity [Score] week 11	Ataxic gait [Score] week 11	Hypotonic gait [Score] week 11	Twitches [Score] week 11	Tremors [Score] week 11	Seizures [Score] week 11
LD / F	051	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	052	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	053	0	0	0	4	4	4	4	4	2	4	4	0	0	0	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	056	0	0	0	4	4	4	4	4	2	4	4	0	0	0	0	0
	057	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	058	0	0	0	4	4	4	4	4	2	4	3	0	0	0	0	0
	059	0	0	0	4	2	4	4	4	4	4	4	0	0	0	0	0
	060	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 11	Faeces consistency [Score] week 11	Abnormal vocalisation [Score] week 11	Aggressiveness [Score] week 11	Animal sleeps [Score] week 12	Animal moving in cage [Score] week 12	Piloerection [Score] week 12	Vocalization [Score] week 12	O Grooming [Score] week 12	Salivation [Score] week 12	Lacrimation [Score] week 12	Changes in skin [Score] week 12	Cyanosis [Score] week 12	Exophthalmos [Score] week 12	Eyes opening [Score] week 12	Resiration [Score] week 12
LD / F	051	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	052	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	053	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	056	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	057	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	058	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	059	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	060	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 12	Arousal [Score] week 12	Fear [Score] week 12	Finger approach [Score] week 12	Head touch [Score] week 12	Body position [Score] week 12	Spontaneous activity [Score] week 12	Ataxic gait [Score] week 12	Hypotonic gait [Score] week 12	Twitches [Score] week 12	Tremors [Score] week 12	Seizures [Score] week 12	Stereotypie [Score] week 12	Faeces consistency [Score] week 12	Abnormal vocalisation [Score] week 12	Aggressiveness [Score] week 12
LD / F	051	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	052	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	053	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	056	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	057	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	058	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	059	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	060	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

NS = No More Scheduled

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 1	Animal moving in cage [Score] week 1	Piloerection [Score] week 1	Vocalization [Score] week 1	O Grooming [Score] week 1	Salivation [Score] week 1	Lacrimation [Score] week 1	Changes in skin [Score] week 1	Cyanosis [Score] week 1	Exophthalmos [Score] week 1	Eyes opening [Score] week 1	Resiration [Score] week 1	response to handling [Score] week 1	Arousal [Score] week 1	Fear [Score] week 1	Finger approach [Score] week 1
MD / M	021	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	022	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	023	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	024	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	025	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	026	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	027	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	028	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	029	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	030	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 1	Body position [Score] week 1	Spontaneous activity [Score] week 1	Ataxic gait [Score] week 1	Hypotonic gait [Score] week 1	Twitches [Score] week 1	Tremors [Score] week 1	Seizures [Score] week 1	Stereotypie [Score] week 1	Faeces consistency [Score] week 1	Abnormal vocalisation [Score] week 1	Animal Aggressiveness [Score] week 1	Animal sleeps [Score] week 2	moving in cage [Score] week 2	Piloerection [Score] week 2	Vocalization [Score] week 2
MD / M	021	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	022	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	023	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	024	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	025	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	026	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	027	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	028	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	029	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	030	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 2	Salivation [Score] week 2	Lacrimation [Score] week 2	Changes in skin [Score] week 2	Cyanosis [Score] week 2	Exophthalmos [Score] week 2	Eyes opening [Score] week 2	Resiration [Score] week 2	response to handling [Score] week 2	Arousal [Score] week 2	Fear [Score] week 2	Finger approach [Score] week 2	Head touch [Score] week 2	Body position [Score] week 2	Spontaneous activity [Score] week 2	Ataxic gait [Score] week 2
MD / M	021	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	022	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	023	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	024	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	025	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	026	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	027	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	028	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	029	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	030	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 2	Twitches [Score] week 2	Tremors [Score] week 2	Seizures [Score] week 2	Stereotypie [Score] week 2	Faeces consistency [Score] week 2	Abnormal vocalisation [Score] week 2	Aggressiveness [Score] week 2	Animal sleeps [Score] week 3	Animal moving in cage [Score] week 3	Piloerection [Score] week 3	Vocalization [Score] week 3	O Grooming [Score] week 3	Salivation [Score] week 3	Lacrimation [Score] week 3	Changes in skin [Score] week 3
MD / M	021	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	022	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	023	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	024	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	025	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	026	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	027	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	028	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	029	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	030	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 3	Exophthalmos [Score] week 3	Eyes opening [Score] week 3	Resiration [Score] week 3	response to handling [Score] week 3	Arousal [Score] week 3	Fear [Score] week 3	Finger approach [Score] week 3	Head touch [Score] week 3	Body position [Score] week 3	Spontaneous activity [Score] week 3	Ataxic gait [Score] week 3	Hypotonic gait [Score] week 3	Twitches [Score] week 3	Tremors [Score] week 3	Seizures [Score] week 3
MD / M	021	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	022	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	023	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	024	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	025	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	026	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	027	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	028	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	029	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	030	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 3	Faeces consistency [Score] week 3	Abnormal vocalisation [Score] week 3	Aggressiveness [Score] week 3	Animal sleeps [Score] week 4	Animal moving in cage [Score] week 4	Piloerection [Score] week 4	Vocalization [Score] week 4	O Grooming [Score] week 4	Salivation [Score] week 4	Lacrimation [Score] week 4	Changes in skin [Score] week 4	Cyanosis [Score] week 4	Exophthalmos [Score] week 4	Eyes opening [Score] week 4	Resiration [Score] week 4
MD / M	021	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	022	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	023	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	024	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	025	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	026	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	027	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	028	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	029	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	030	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 4	Arousal [Score] week 4	Fear [Score] week 4	Finger approach [Score] week 4	Head touch [Score] week 4	Body position [Score] week 4	Spontaneous activity [Score] week 4	Ataxic gait [Score] week 4	Hypotonic gait [Score] week 4	Twitches [Score] week 4	Tremors [Score] week 4	Seizures [Score] week 4	Stereotypie [Score] week 4	Faeces consistency [Score] week 4	Abnormal vocalisation [Score] week 4	Aggressiveness [Score] week 4
MD / M	021	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	022	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	023	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	024	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	025	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	026	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	027	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	028	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	029	4	4	2	4	2	4	4	0	0	0	0	0	0	4	0	0
	030	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 5	Animal moving in cage [Score] week 5	Piloerection [Score] week 5	Vocalization [Score] week 5	O Grooming [Score] week 5	Salivation [Score] week 5	Lacrimation [Score] week 5	Changes in skin [Score] week 5	Cyanosis [Score] week 5	Exophthalmos [Score] week 5	Eyes opening [Score] week 5	Resiration [Score] week 5	response to handling [Score] week 5	Arousal [Score] week 5	Fear [Score] week 5	Finger approach [Score] week 5
MD / M	021	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	022	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	023	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	024	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	025	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	026	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	027	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	028	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	029	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	030	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 5	Body position [Score] week 5	Spontaneous activity [Score] week 5	Ataxic gait [Score] week 5	Hypotonic gait [Score] week 5	Twitches [Score] week 5	Tremors [Score] week 5	Seizures [Score] week 5	Stereotypie [Score] week 5	Faeces consistency [Score] week 5	Abnormal vocalisation [Score] week 5	Animal Aggressiveness [Score] week 5	Animal sleeps [Score] week 6	moving in cage [Score] week 6	Piloerection [Score] week 6	Vocalization [Score] week 6
MD / M	021	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	022	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	023	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	024	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	025	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	026	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	027	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	028	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	029	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	030	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 6	Salivation [Score] week 6	Lacrimation [Score] week 6	Changes in skin [Score] week 6	Cyanosis [Score] week 6	Exophthalmos [Score] week 6	Eyes opening [Score] week 6	Resiration [Score] week 6	response to handling [Score] week 6	Arousal [Score] week 6	Fear [Score] week 6	Finger approach [Score] week 6	Head touch [Score] week 6	Body position [Score] week 6	Spontaneous activity [Score] week 6	Ataxic gait [Score] week 6
MD / M	021	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	022	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	023	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	024	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	025	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	026	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	027	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	028	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	029	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	030	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 6	Twitches [Score] week 6	Tremors [Score] week 6	Seizures [Score] week 6	Stereotypie [Score] week 6	Faeces consistency [Score] week 6	Abnormal vocalisation [Score] week 6	Aggressiveness [Score] week 6	Animal sleeps [Score] week 7	Animal moving in cage [Score] week 7	Piloerection [Score] week 7	Vocalization [Score] week 7	O Grooming [Score] week 7	Salivation [Score] week 7	Lacrimation [Score] week 7	Changes in skin [Score] week 7
MD / M	021	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	022	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	023	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	024	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	025	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	026	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	027	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	028	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	029	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	030	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 7	Exophthalmos [Score] week 7	Eyes opening [Score] week 7	Resiration [Score] week 7	response to handling [Score] week 7	Arousal [Score] week 7	Fear [Score] week 7	Finger approach [Score] week 7	Head touch [Score] week 7	Body position [Score] week 7	Spontaneous activity [Score] week 7	Ataxic gait [Score] week 7	Hypotonic gait [Score] week 7	Twitches [Score] week 7	Tremors [Score] week 7	Seizures [Score] week 7
MD / M	021	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	022	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	023	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	024	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	025	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	026	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	027	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	028	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	029	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	030	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 7	Faeces consistency [Score] week 7	Abnormal vocalisation [Score] week 7	Aggressiveness [Score] week 7	Animal sleeps [Score] week 8	Animal moving in cage [Score] week 8	Piloerection [Score] week 8	Vocalization [Score] week 8	O Grooming [Score] week 8	Salivation [Score] week 8	Lacrimation [Score] week 8	Changes in skin [Score] week 8	Cyanosis [Score] week 8	Exophthalmos [Score] week 8	Eyes opening [Score] week 8	Resiration [Score] week 8
MD / M	021	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	022	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	023	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	024	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	025	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	026	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	027	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	028	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	029	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	030	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 8	Arousal [Score] week 8	Fear [Score] week 8	Finger approach [Score] week 8	Head touch [Score] week 8	Body position [Score] week 8	Spontaneous activity [Score] week 8	Ataxic gait [Score] week 8	Hypotonic gait [Score] week 8	Twitches [Score] week 8	Tremors [Score] week 8	Seizures [Score] week 8	Stereotypie [Score] week 8	Faeces consistency [Score] week 8	Abnormal vocalisation [Score] week 8	Aggressiveness [Score] week 8
MD / M	021	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	022	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	023	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	024	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	025	4	4	2	4	2	4	3	0	0	0	0	0	0	4	0	0
	026	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	027	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	028	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	029	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	030	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 9	Animal moving in cage [Score] week 9	Piloerection [Score] week 9	Vocalization [Score] week 9	O Grooming [Score] week 9	Salivation [Score] week 9	Lacrimation [Score] week 9	Changes in skin [Score] week 9	Cyanosis [Score] week 9	Exophthalmos [Score] week 9	Eyes opening [Score] week 9	Resiration [Score] week 9	response to handling [Score] week 9	Arousal [Score] week 9	Fear [Score] week 9	Finger approach [Score] week 9
MD / M	021	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	022	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	023	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	024	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	025	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	026	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	027	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	028	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	029	1	0	0	0	0	4	0	0	0	0	0	4	2	4	4	4
	030	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 9	Body position [Score] week 9	Spontaneous activity [Score] week 9	Ataxic gait [Score] week 9	Hypotonic gait [Score] week 9	Twitches [Score] week 9	Tremors [Score] week 9	Seizures [Score] week 9	Stereotypie [Score] week 9	Faeces consistency [Score] week 9	Abnormal vocalisation [Score] week 9	Aggressiveness [Score] week 9	Animal sleeps [Score] week 10	Animal moving in cage [Score] week 10	Piloerection [Score] week 10	Vocalization [Score] week 10
MD / M	021	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	022	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	023	2	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0
	024	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	025	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	026	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	027	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	028	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	029	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	030	4	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 10	Salivation [Score] week 10	Lacrimation [Score] week 10	Changes in skin [Score] week 10	Cyanosis [Score] week 10	Exophthalmos [Score] week 10	Eyes opening [Score] week 10	Resiration [Score] week 10	response to handling [Score] week 10	Arousal [Score] week 10	Fear [Score] week 10	Finger approach [Score] week 10	Head touch [Score] week 10	Body position [Score] week 10	Spontaneous activity [Score] week 10	Ataxic gait [Score] week 10
MD / M	021	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	022	0	4	0	0	0	0	0	4	2	4	2	6	2	4	3	0
	023	0	4	0	0	0	0	0	4	2	4	4	4	4	4	3	0
	024	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	025	0	4	0	0	0	0	0	4	4	4	4	4	4	4	3	0
	026	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	027	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	028	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	029	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	030	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 10	Twitches [Score] week 10	Tremors [Score] week 10	Seizures [Score] week 10	Stereotypie [Score] week 10	Faeces consistency [Score] week 10	Abnormal vocalisation [Score] week 10	Aggressiveness [Score] week 10	Animal sleeps [Score] week 11	Animal moving in cage [Score] week 11	Piloerection [Score] week 11	Vocalization [Score] week 11	O Grooming [Score] week 11	Salivation [Score] week 11	Lacrimation [Score] week 11	Changes in skin [Score] week 11
MD / M	021	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	022	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	023	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	024	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	025	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	026	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	027	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	028	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	029	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	030	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 11	Exophthalmos [Score] week 11	Eyes opening [Score] week 11	Resiration [Score] week 11	response to handling [Score] week 11	Arousal [Score] week 11	Fear [Score] week 11	Finger approach [Score] week 11	Head touch [Score] week 11	Body position [Score] week 11	Spontaneous activity [Score] week 11	Ataxic gait [Score] week 11	Hypotonic gait [Score] week 11	Twitches [Score] week 11	Tremors [Score] week 11	Seizures [Score] week 11
MD / M	021	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	022	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	023	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	024	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	025	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	026	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	027	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	028	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	029	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	030	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 11	Faeces consistency [Score] week 11	Abnormal vocalisation [Score] week 11	Aggressiveness [Score] week 11	Animal sleeps [Score] week 12	Animal moving in cage [Score] week 12	Piloerection [Score] week 12	Vocalization [Score] week 12	Grooming [Score] week 12	Salivation [Score] week 12	Lacrimation [Score] week 12	Changes in skin [Score] week 12	Cyanosis [Score] week 12	Exophthalmos [Score] week 12	Eyes opening [Score] week 12	Resiration [Score] week 12
MD / M	021	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	022	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	023	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	024	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	025	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	026	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	027	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	028	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	029	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	030	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 12	Arousal [Score] week 12	Fear [Score] week 12	Finger approach [Score] week 12	Head touch [Score] week 12	Body position [Score] week 12	Spontaneous activity [Score] week 12	Ataxic gait [Score] week 12	Hypotonic gait [Score] week 12	Twitches [Score] week 12	Tremors [Score] week 12	Seizures [Score] week 12	Stereotypie [Score] week 12	Faeces consistency [Score] week 12	Abnormal vocalisation [Score] week 12	Aggressiveness [Score] week 12
MD / M	021	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	022	4	4	4	4	2	4	4	0	0	0	0	0	0	4	0	0
	023	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	024	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	025	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	026	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	027	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	028	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	029	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	030	2	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 1	Animal moving in cage [Score] week 1	Piloerection [Score] week 1	Vocalization [Score] week 1	O Grooming [Score] week 1	Salivation [Score] week 1	Lacrimation [Score] week 1	Changes in skin [Score] week 1	Cyanosis [Score] week 1	Exophthalmos [Score] week 1	Eyes opening [Score] week 1	Resiration [Score] week 1	response to handling [Score] week 1	Arousal [Score] week 1	Fear [Score] week 1	Finger approach [Score] week 1
MD / F	061	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	062	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	063	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	064	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	065	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	066	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	067	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	068	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	069	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	070	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 1	Body position [Score] week 1	Spontaneous activity [Score] week 1	Ataxic gait [Score] week 1	Hypotonic gait [Score] week 1	Twitches [Score] week 1	Tremors [Score] week 1	Seizures [Score] week 1	Stereotypie [Score] week 1	Faeces consistency [Score] week 1	Abnormal vocalisation [Score] week 1	Animal Aggressiveness [Score] week 1	Animal sleeps [Score] week 2	moving in cage [Score] week 2	Piloerection [Score] week 2	Vocalization [Score] week 2
MD / F	061	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	062	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	063	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	064	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	065	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	066	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	067	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	068	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	069	4	4	3	0	0	0	0	0	0	4	0	0	0	1	0	0
	070	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 2	Salivation [Score] week 2	Lacrimation [Score] week 2	Changes in skin [Score] week 2	Cyanosis [Score] week 2	Exophthalmos [Score] week 2	Eyes opening [Score] week 2	Resiration [Score] week 2	response to handling [Score] week 2	Arousal [Score] week 2	Fear [Score] week 2	Finger approach [Score] week 2	Head touch [Score] week 2	Body position [Score] week 2	Spontaneous activity [Score] week 2	Ataxic gait [Score] week 2
MD / F	061	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	062	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	063	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	064	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	065	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	066	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	067	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	068	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	069	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	070	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 2	Twitches [Score] week 2	Tremors [Score] week 2	Seizures [Score] week 2	Stereotypie [Score] week 2	Faeces consistency [Score] week 2	Abnormal vocalisation [Score] week 2	Aggressiveness [Score] week 2	Animal sleeps [Score] week 3	Animal moving in cage [Score] week 3	Piloerection [Score] week 3	Vocalization [Score] week 3	O Grooming [Score] week 3	Salivation [Score] week 3	Lacrimation [Score] week 3	Changes in skin [Score] week 3
MD / F	061	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	062	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	063	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	064	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	065	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	066	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	067	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	068	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	069	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	070	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 3	Exophthalmos [Score] week 3	Eyes opening [Score] week 3	Resiration [Score] week 3	response to handling [Score] week 3	Arousal [Score] week 3	Fear [Score] week 3	Finger approach [Score] week 3	Head touch [Score] week 3	Body position [Score] week 3	Spontaneous activity [Score] week 3	Ataxic gait [Score] week 3	Hypotonic gait [Score] week 3	Twitches [Score] week 3	Tremors [Score] week 3	Seizures [Score] week 3
MD / F	061	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	062	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	063	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	064	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	065	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	066	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	067	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	068	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	069	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	070	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 3	Faeces consistency [Score] week 3	Abnormal vocalisation [Score] week 3	Aggressiveness [Score] week 3	Animal sleeps [Score] week 4	Animal moving in cage [Score] week 4	Piloerection [Score] week 4	Vocalization [Score] week 4	O Grooming [Score] week 4	Salivation [Score] week 4	Lacrimation [Score] week 4	Changes in skin [Score] week 4	Cyanosis [Score] week 4	Exophthalmos [Score] week 4	Eyes opening [Score] week 4	Resiration [Score] week 4
MD / F	061	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	062	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	063	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	064	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	065	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	066	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	067	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	068	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	069	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	070	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 4	Arousal [Score] week 4	Fear [Score] week 4	Finger approach [Score] week 4	Head touch [Score] week 4	Body position [Score] week 4	Spontaneous activity [Score] week 4	Ataxic gait [Score] week 4	Hypotonic gait [Score] week 4	Twitches [Score] week 4	Tremors [Score] week 4	Seizures [Score] week 4	Stereotypie [Score] week 4	Faeces consistency [Score] week 4	Abnormal vocalisation [Score] week 4	Aggressiveness [Score] week 4
MD / F	061	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	062	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	063	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	064	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	065	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	066	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	067	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	068	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	069	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	070	2	4	4	6	2	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 5	Animal moving in cage [Score] week 5	Piloerection [Score] week 5	Vocalization [Score] week 5	O Grooming [Score] week 5	Salivation [Score] week 5	Lacrimation [Score] week 5	Changes in skin [Score] week 5	Cyanosis [Score] week 5	Exophthalmos [Score] week 5	Eyes opening [Score] week 5	Resiration [Score] week 5	response to handling [Score] week 5	Arousal [Score] week 5	Fear [Score] week 5	Finger approach [Score] week 5
MD / F	061	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	062	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	063	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	064	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	065	1	0	0	0	4	0	0	0	0	0	0	4	4	4	4	4
	066	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	067	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	068	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	069	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	6
	070	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 5	Body position [Score] week 5	Spontaneous activity [Score] week 5	Ataxic gait [Score] week 5	Hypotonic gait [Score] week 5	Twitches [Score] week 5	Tremors [Score] week 5	Seizures [Score] week 5	Stereotypie [Score] week 5	Faeces consistency [Score] week 5	Abnormal vocalisation [Score] week 5	Animal Aggressiveness [Score] week 5	Animal sleeps [Score] week 6	moving in cage [Score] week 6	Piloerection [Score] week 6	Vocalization [Score] week 6
MD / F	061	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	062	4	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0
	063	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	064	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	065	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	066	2	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	067	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	068	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	069	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	070	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 6	Salivation [Score] week 6	Lacrimation [Score] week 6	Changes in skin [Score] week 6	Cyanosis [Score] week 6	Exophthalmos [Score] week 6	Eyes opening [Score] week 6	Resiration [Score] week 6	response to handling [Score] week 6	Arousal [Score] week 6	Fear [Score] week 6	Finger approach [Score] week 6	Head touch [Score] week 6	Body position [Score] week 6	Spontaneous activity [Score] week 6	Ataxic gait [Score] week 6
MD / F	061	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	062	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	063	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	064	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	065	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	066	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	067	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	068	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	069	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	070	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 6	Twitches [Score] week 6	Tremors [Score] week 6	Seizures [Score] week 6	Stereotypie [Score] week 6	Faeces consistency [Score] week 6	Abnormal vocalisation [Score] week 6	Aggressiveness [Score] week 6	Animal sleeps [Score] week 7	Animal moving in cage [Score] week 7	Piloerection [Score] week 7	Vocalization [Score] week 7	O Grooming [Score] week 7	Salivation [Score] week 7	Lacrimation [Score] week 7	Changes in skin [Score] week 7
MD / F	061	0	0	0	0	0	4	0	0	1	0	0	0	4	0	0	0
	062	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	063	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	064	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	065	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	066	0	0	0	0	0	4	0	0								
	067	0	0	0	0	0	4	0	0								
	068	0	0	0	0	0	4	0	0								
	069	0	0	0	0	0	4	0	0								
	070	0	0	0	0	0	4	0	0								

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 7	Exophthalmos [Score] week 7	Eyes opening [Score] week 7	Resiration [Score] week 7	response to handling [Score] week 7	Arousal [Score] week 7	Fear [Score] week 7	Finger approach [Score] week 7	Head touch [Score] week 7	Body position [Score] week 7	Spontaneous activity [Score] week 7	Ataxic gait [Score] week 7	Hypotonic gait [Score] week 7	Twitches [Score] week 7	Tremors [Score] week 7	Seizures [Score] week 7
MD / F	061	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	062	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	063	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	064	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	065	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	066																
	067																
	068																
	069																
	070																

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 7	Faeces consistency [Score] week 7	Abnormal vocalisation [Score] week 7	Aggressiveness [Score] week 7	Animal sleeps [Score] week 8	Animal moving in cage [Score] week 8	Piloerection [Score] week 8	Vocalization [Score] week 8	O Grooming [Score] week 8	Salivation [Score] week 8	Lacrimation [Score] week 8	Changes in skin [Score] week 8	Cyanosis [Score] week 8	Exophthalmos [Score] week 8	Eyes opening [Score] week 8	Resiration [Score] week 8
MD / F	061	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	062	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	063	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	064	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	065	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	066					0	1	0	0	0	4	0	0	0	0	0	4
	067					0	1	0	0	0	4	0	0	0	0	0	4
	068					0	1	0	0	0	4	0	0	0	0	0	4
	069					0	1	0	0	0	4	0	0	0	0	0	4
	070					0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 8	Arousal [Score] week 8	Fear [Score] week 8	Finger approach [Score] week 8	Head touch [Score] week 8	Body position [Score] week 8	Spontaneous activity [Score] week 8	Ataxic gait [Score] week 8	Hypotonic gait [Score] week 8	Twitches [Score] week 8	Tremors [Score] week 8	Seizures [Score] week 8	Stereotypie [Score] week 8	Faeces consistency [Score] week 8	Abnormal vocalisation [Score] week 8	Aggressiveness [Score] week 8
MD / F	061	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	062	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	063	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	064	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	065	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	066	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	067	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	068	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	069	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	070	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 9	Animal moving in cage [Score] week 9	Piloerection [Score] week 9	Vocalization [Score] week 9	O Grooming [Score] week 9	Salivation [Score] week 9	Lacrimation [Score] week 9	Changes in skin [Score] week 9	Cyanosis [Score] week 9	Exophthalmos [Score] week 9	Eyes opening [Score] week 9	Resiration [Score] week 9	response to handling [Score] week 9	Arousal [Score] week 9	Fear [Score] week 9	Finger approach [Score] week 9
MD / F	061	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	062	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	063	1	0	0	0	0	4	0	0	0	0	0	4	2	4	4	4
	064	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	065	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	066	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	067	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	068	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	069	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	070	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 9	Body position [Score] week 9	Spontaneous activity [Score] week 9	Ataxic gait [Score] week 9	Hypotonic gait [Score] week 9	Twitches [Score] week 9	Tremors [Score] week 9	Seizures [Score] week 9	Stereotypie [Score] week 9	Faeces consistency [Score] week 9	Abnormal vocalisation [Score] week 9	Aggressiveness [Score] week 9	Animal sleeps [Score] week 10	Animal moving in cage [Score] week 10	Piloerection [Score] week 10	Vocalization [Score] week 10
MD / F	061	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	062	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	063	2	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	064	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	065	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	066	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	067	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	068	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	069	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	070	2	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 10	Salivation [Score] week 10	Lacrimation [Score] week 10	Changes in skin [Score] week 10	Cyanosis [Score] week 10	Exophthalmos [Score] week 10	Eyes opening [Score] week 10	Resiration [Score] week 10	response to handling [Score] week 10	Arousal [Score] week 10	Fear [Score] week 10	Finger approach [Score] week 10	Head touch [Score] week 10	Body position [Score] week 10	Spontaneous activity [Score] week 10	Ataxic gait [Score] week 10
MD / F	061	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	062	0	4	0	0	0	0	0	4	4	4	4	4	2	4	4	0
	063	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	064	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	065	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	066	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	067	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	068	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	069	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	070	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 10	Twitches [Score] week 10	Tremors [Score] week 10	Seizures [Score] week 10	Stereotypie [Score] week 10	Faeces consistency [Score] week 10	Abnormal vocalisation [Score] week 10	Aggressiveness [Score] week 10	Animal sleeps [Score] week 11	Animal moving in cage [Score] week 11	Piloerection [Score] week 11	Vocalization [Score] week 11	O Grooming [Score] week 11	Salivation [Score] week 11	Lacrimation [Score] week 11	Changes in skin [Score] week 11
MD / F	061	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	062	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	063	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	064	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	065	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	066	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	067	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	068	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	069	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	070	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 11	Exophthalmos [Score] week 11	Eyes opening [Score] week 11	Resiration [Score] week 11	response to handling [Score] week 11	Arousal [Score] week 11	Fear [Score] week 11	Finger approach [Score] week 11	Head touch [Score] week 11	Body position [Score] week 11	Spontaneous activity [Score] week 11	Ataxic gait [Score] week 11	Hypotonic gait [Score] week 11	Twitches [Score] week 11	Tremors [Score] week 11	Seizures [Score] week 11
MD / F	061	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	062	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	063	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	064	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	065	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	066	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	067	0	0	0	4	4	4	4	4	2	4	4	0	0	0	0	0
	068	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	069	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	070	0	0	0	4	2	4	2	6	2	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 11	Faeces consistency [Score] week 11	Abnormal vocalisation [Score] week 11	Aggressiveness [Score] week 11	Animal sleeps [Score] week 12	Animal moving in cage [Score] week 12	Piloerection [Score] week 12	Vocalization [Score] week 12	O Grooming [Score] week 12	Salivation [Score] week 12	Lacrimation [Score] week 12	Changes in skin [Score] week 12	Cyanosis [Score] week 12	Exophthalmos [Score] week 12	Eyes opening [Score] week 12	Resiration [Score] week 12
MD / F	061	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	062	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	063	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	064	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	065	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	066	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	067	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	068	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	069	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	070	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 12	Arousal [Score] week 12	Fear [Score] week 12	Finger approach [Score] week 12	Head touch [Score] week 12	Body position [Score] week 12	Spontaneous activity [Score] week 12	Ataxic gait [Score] week 12	Hypotonic gait [Score] week 12	Twitches [Score] week 12	Tremors [Score] week 12	Seizures [Score] week 12	Stereotypie [Score] week 12	Faeces consistency [Score] week 12	Abnormal vocalisation [Score] week 12	Aggressiveness [Score] week 12
MD / F	061	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	062	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	063	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	064	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	065	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	066	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	067	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	068	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	069	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	070	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 1	Animal moving in cage [Score] week 1	Piloerection [Score] week 1	Vocalization [Score] week 1	O Grooming [Score] week 1	Salivation [Score] week 1	Lacrimation [Score] week 1	Changes in skin [Score] week 1	Cyanosis [Score] week 1	Exophthalmos [Score] week 1	Eyes opening [Score] week 1	Resiration [Score] week 1	response to handling [Score] week 1	Arousal [Score] week 1	Fear [Score] week 1	Finger approach [Score] week 1
HD / M	031	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	032	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	033	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	034	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	035	1	0	0	0	0	4	0	0	0	0	4	4	4	4	4	4
	036	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	037	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	038	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	039	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	040	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 1	Body position [Score] week 1	Spontaneous activity [Score] week 1	Ataxic gait [Score] week 1	Hypotonic gait [Score] week 1	Twitches [Score] week 1	Tremors [Score] week 1	Seizures [Score] week 1	Stereotypie [Score] week 1	Faeces consistency [Score] week 1	Abnormal vocalisation [Score] week 1	Animal Aggressiveness [Score] week 1	Animal sleeps [Score] week 2	moving in cage [Score] week 2	Piloerection [Score] week 2	Vocalization [Score] week 2
HD / M	031	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	032	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	033	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	034	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	035	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	036	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	037	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	038	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	039	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	040	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 2	Salivation [Score] week 2	Lacrimation [Score] week 2	Changes in skin [Score] week 2	Cyanosis [Score] week 2	Exophthalmos [Score] week 2	Eyes opening [Score] week 2	Resiration [Score] week 2	response to handling [Score] week 2	Arousal [Score] week 2	Fear [Score] week 2	Finger approach [Score] week 2	Head touch [Score] week 2	Body position [Score] week 2	Spontaneous activity [Score] week 2	Ataxic gait [Score] week 2
HD / M	031	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	032	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	033	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	034	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	035	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	036	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	037	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	038	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	039	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	040	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 2	Twitches [Score] week 2	Tremors [Score] week 2	Seizures [Score] week 2	Stereotypie [Score] week 2	Faeces consistency [Score] week 2	Abnormal vocalisation [Score] week 2	Aggressiveness [Score] week 2	Animal sleeps [Score] week 3	Animal moving in cage [Score] week 3	Piloerection [Score] week 3	Vocalization [Score] week 3	O Grooming [Score] week 3	Salivation [Score] week 3	Lacrimation [Score] week 3	Changes in skin [Score] week 3
HD / M	031	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	032	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	033	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	034	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	035	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	036	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	037	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	038	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	039	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	040	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 3	Exophthalmos [Score] week 3	Eyes opening [Score] week 3	Resiration [Score] week 3	response to handling [Score] week 3	Arousal [Score] week 3	Fear [Score] week 3	Finger approach [Score] week 3	Head touch [Score] week 3	Body position [Score] week 3	Spontaneous activity [Score] week 3	Ataxic gait [Score] week 3	Hypotonic gait [Score] week 3	Twitches [Score] week 3	Tremors [Score] week 3	Seizures [Score] week 3
HD / M	031	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	032	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	033	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	034	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	035	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	036	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	037	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	038	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	039	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	040	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 3	Faeces consistency [Score] week 3	Abnormal vocalisation [Score] week 3	Aggressiveness [Score] week 3	Animal sleeps [Score] week 4	Animal moving in cage [Score] week 4	Piloerection [Score] week 4	Vocalization [Score] week 4	O Grooming [Score] week 4	Salivation [Score] week 4	Lacrimation [Score] week 4	Changes in skin [Score] week 4	Cyanosis [Score] week 4	Exophthalmos [Score] week 4	Eyes opening [Score] week 4	Resiration [Score] week 4
HD / M	031	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	032	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	033	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	034	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	035	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	036	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	037	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	038	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	039	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	040	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 4	Arousal [Score] week 4	Fear [Score] week 4	Finger approach [Score] week 4	Head touch [Score] week 4	Body position [Score] week 4	Spontaneous activity [Score] week 4	Ataxic gait [Score] week 4	Hypotonic gait [Score] week 4	Twitches [Score] week 4	Tremors [Score] week 4	Seizures [Score] week 4	Stereotypie [Score] week 4	Faeces consistency [Score] week 4	Abnormal vocalisation [Score] week 4	Aggressiveness [Score] week 4
HD / M	031	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	032	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	033	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	034	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	035	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	036	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	037	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	038	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	039	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	040	2	4	2	4	2	4	3	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 5	Animal moving in cage [Score] week 5	Piloerection [Score] week 5	Vocalization [Score] week 5	O Grooming [Score] week 5	Salivation [Score] week 5	Lacrimation [Score] week 5	Changes in skin [Score] week 5	Cyanosis [Score] week 5	Exophthalmos [Score] week 5	Eyes opening [Score] week 5	Resiration [Score] week 5	response to handling [Score] week 5	Arousal [Score] week 5	Fear [Score] week 5	Finger approach [Score] week 5
HD / M	031	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	032	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	033	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	6
	034	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	035	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	036	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	037	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	038	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	039	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	040	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 5	Body position [Score] week 5	Spontaneous activity [Score] week 5	Ataxic gait [Score] week 5	Hypotonic gait [Score] week 5	Twitches [Score] week 5	Tremors [Score] week 5	Seizures [Score] week 5	Stereotypie [Score] week 5	Faeces consistency [Score] week 5	Abnormal vocalisation [Score] week 5	Animal Aggressiveness [Score] week 5	Animal sleeps [Score] week 6	moving in cage [Score] week 6	Piloerection [Score] week 6	Vocalization [Score] week 6
HD / M	031	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	032	4	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0
	033	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	034	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	035	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	036	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	037	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	038	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	039	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	040	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 6	Salivation [Score] week 6	Lacrimation [Score] week 6	Changes in skin [Score] week 6	Cyanosis [Score] week 6	Exophthalmos [Score] week 6	Eyes opening [Score] week 6	Resiration [Score] week 6	response to handling [Score] week 6	Arousal [Score] week 6	Fear [Score] week 6	Finger approach [Score] week 6	Head touch [Score] week 6	Body position [Score] week 6	Spontaneous activity [Score] week 6	Ataxic gait [Score] week 6
HD / M	031	0	4	0	0	0	0	0	4	2	4	2	4	2	4	4	0
	032	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	033	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	034	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	035	0	4	0	0	0	0	0	4	2	4	4	4	4	4	3	0
	036	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	037	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	038	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	039	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	040	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 6	Twitches [Score] week 6	Tremors [Score] week 6	Seizures [Score] week 6	Stereotypie [Score] week 6	Faeces consistency [Score] week 6	Abnormal vocalisation [Score] week 6	Aggressiveness [Score] week 6	Animal sleeps [Score] week 7	Animal moving in cage [Score] week 7	Piloerection [Score] week 7	Vocalization [Score] week 7	O Grooming [Score] week 7	Salivation [Score] week 7	Lacrimation [Score] week 7	Changes in skin [Score] week 7
HD / M	031	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	032	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	033	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	034	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	035	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	036	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	037	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	038	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	039	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	040	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 7	Exophthalmos [Score] week 7	Eyes opening [Score] week 7	Resiration [Score] week 7	response to handling [Score] week 7	Arousal [Score] week 7	Fear [Score] week 7	Finger approach [Score] week 7	Head touch [Score] week 7	Body position [Score] week 7	Spontaneous activity [Score] week 7	Ataxic gait [Score] week 7	Hypotonic gait [Score] week 7	Twitches [Score] week 7	Tremors [Score] week 7	Seizures [Score] week 7
HD / M	031	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	032	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	033	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	034	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	035	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	036	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	037	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	038	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	039	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	040	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 7	Faeces consistency [Score] week 7	Abnormal vocalisation [Score] week 7	Aggressiveness [Score] week 7	Animal sleeps [Score] week 8	Animal moving in cage [Score] week 8	Piloerection [Score] week 8	Vocalization [Score] week 8	O Grooming [Score] week 8	Salivation [Score] week 8	Lacrimation [Score] week 8	Changes in skin [Score] week 8	Cyanosis [Score] week 8	Exophthalmos [Score] week 8	Eyes opening [Score] week 8	Resiration [Score] week 8
HD / M	031	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	032	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	033	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	034	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	035	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	036	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	037	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	038	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	039	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	040	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 8	Arousal [Score] week 8	Fear [Score] week 8	Finger approach [Score] week 8	Head touch [Score] week 8	Body position [Score] week 8	Spontaneous activity [Score] week 8	Ataxic gait [Score] week 8	Hypotonic gait [Score] week 8	Twitches [Score] week 8	Tremors [Score] week 8	Seizures [Score] week 8	Stereotypie [Score] week 8	Faeces consistency [Score] week 8	Abnormal vocalisation [Score] week 8	Aggressiveness [Score] week 8
HD / M	031	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	032	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	033	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	034	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	035	4	4	2	4	2	4	4	0	0	0	0	0	0	4	0	0
	036	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	037	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	038	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	039	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	040	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 9	Animal moving in cage [Score] week 9	Piloerection [Score] week 9	Vocalization [Score] week 9	O Grooming [Score] week 9	Salivation [Score] week 9	Lacrimation [Score] week 9	Changes in skin [Score] week 9	Cyanosis [Score] week 9	Exophthalmos [Score] week 9	Eyes opening [Score] week 9	Resiration [Score] week 9	response to handling [Score] week 9	Arousal [Score] week 9	Fear [Score] week 9	Finger approach [Score] week 9
HD / M	031	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	032	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	033	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	034	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	035																
	036	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	037	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	038	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	039	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	040	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 9	Body position [Score] week 9	Spontaneous activity [Score] week 9	Ataxic gait [Score] week 9	Hypotonic gait [Score] week 9	Twitches [Score] week 9	Tremors [Score] week 9	Seizures [Score] week 9	Stereotypie [Score] week 9	Faeces consistency [Score] week 9	Abnormal vocalisation [Score] week 9	Aggressiveness [Score] week 9	Animal sleeps [Score] week 10	Animal moving in cage [Score] week 10	Piloerection [Score] week 10	Vocalization [Score] week 10
HD / M	031	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	032	4	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0
	033	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	034	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	035													1	0	0	0
	036	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	037	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	038	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	039	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	040	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 10	Salivation [Score] week 10	Lacrimation [Score] week 10	Changes in skin [Score] week 10	Cyanosis [Score] week 10	Exophthalmos [Score] week 10	Eyes opening [Score] week 10	Resiration [Score] week 10	response to handling [Score] week 10	Arousal [Score] week 10	Fear [Score] week 10	Finger approach [Score] week 10	Head touch [Score] week 10	Body position [Score] week 10	Spontaneous activity [Score] week 10	Ataxic gait [Score] week 10
HD / M	031	0	4	0	0	0	0	0	4	4	4	4	4	4	4	3	0
	032	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	033	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	034	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	035	0	4	0	0	0	0	0	4	2	4	4	6	2	4	3	0
	036	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	037	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	038	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	039	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	040	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 10	Twitches [Score] week 10	Tremors [Score] week 10	Seizures [Score] week 10	Stereotypie [Score] week 10	Faeces consistency [Score] week 10	Abnormal vocalisation [Score] week 10	Aggressiveness [Score] week 10	Animal sleeps [Score] week 11	Animal moving in cage [Score] week 11	Piloerection [Score] week 11	Vocalization [Score] week 11	O Grooming [Score] week 11	Salivation [Score] week 11	Lacrimation [Score] week 11	Changes in skin [Score] week 11
HD / M	031	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	032	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	033	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	034	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	035	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	036	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	037	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	038	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	039	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	040	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 11	Exophthalmos [Score] week 11	Eyes opening [Score] week 11	Resiration [Score] week 11	response to handling [Score] week 11	Arousal [Score] week 11	Fear [Score] week 11	Finger approach [Score] week 11	Head touch [Score] week 11	Body position [Score] week 11	Spontaneous activity [Score] week 11	Ataxic gait [Score] week 11	Hypotonic gait [Score] week 11	Twitches [Score] week 11	Tremors [Score] week 11	Seizures [Score] week 11
HD / M	031	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	032	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	033	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	034	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	035	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	036	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	037	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	038	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	039	0	0	0	4	4	4	4	4	4	4	3	0	0	0	0	0
	040	0	0	0	4	2	4	4	4	4	4	3	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 11	Faeces consistency [Score] week 11	Abnormal vocalisation [Score] week 11	Aggressiveness [Score] week 11	Animal sleeps [Score] week 12	Animal moving in cage [Score] week 12	Piloerection [Score] week 12	Vocalization [Score] week 12	Grooming [Score] week 12	Salivation [Score] week 12	Lacrimation [Score] week 12	Changes in skin [Score] week 12	Cyanosis [Score] week 12	Exophthalmos [Score] week 12	Eyes opening [Score] week 12	Resiration [Score] week 12
HD / M	031	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	032	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	033	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	034	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	035	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	036	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	037	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	038	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	039	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	040	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 12	Arousal [Score] week 12	Fear [Score] week 12	Finger approach [Score] week 12	Head touch [Score] week 12	Body position [Score] week 12	Spontaneous activity [Score] week 12	Ataxic gait [Score] week 12	Hypotonic gait [Score] week 12	Twitches [Score] week 12	Tremors [Score] week 12	Seizures [Score] week 12	Stereotypie [Score] week 12	Faeces consistency [Score] week 12	Abnormal vocalisation [Score] week 12	Aggressiveness [Score] week 12
HD / M	031	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	032	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	033	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	034	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	035	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	036	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	037	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	038	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	039	4	4	4	4	4	4	3	0	0	0	0	0	0	4	0	0
	040	2	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 1	Animal moving in cage [Score] week 1	Piloerection [Score] week 1	Vocalization [Score] week 1	O Grooming [Score] week 1	Salivation [Score] week 1	Lacrimation [Score] week 1	Changes in skin [Score] week 1	Cyanosis [Score] week 1	Exophthalmos [Score] week 1	Eyes opening [Score] week 1	Resiration [Score] week 1	response to handling [Score] week 1	Arousal [Score] week 1	Fear [Score] week 1	Finger approach [Score] week 1
HD / F	071	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	072	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	073	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	074	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	075	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	076	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	077	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	078	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	079	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	080	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 1	Body position [Score] week 1	Spontaneous activity [Score] week 1	Ataxic gait [Score] week 1	Hypotonic gait [Score] week 1	Twitches [Score] week 1	Tremors [Score] week 1	Seizures [Score] week 1	Stereotypie [Score] week 1	Faeces consistency [Score] week 1	Abnormal vocalisation [Score] week 1	Animal Aggressiveness [Score] week 1	Animal sleeps [Score] week 2	moving in cage [Score] week 2	Piloerection [Score] week 2	Vocalization [Score] week 2
HD / F	071	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	072	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	073	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	074	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	075	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	076	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	077	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	078	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	079	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0
	080	4	4	4	0	0	0	0	0	0	4	0	0	0	1	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 2	Salivation [Score] week 2	Lacrimation [Score] week 2	Changes in skin [Score] week 2	Cyanosis [Score] week 2	Exophthalmos [Score] week 2	Eyes opening [Score] week 2	Resiration [Score] week 2	response to handling [Score] week 2	Arousal [Score] week 2	Fear [Score] week 2	Finger approach [Score] week 2	Head touch [Score] week 2	Body position [Score] week 2	Spontaneous activity [Score] week 2	Ataxic gait [Score] week 2
HD / F	071	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	072	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	073	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	074	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	075	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	076	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	077	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	078	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	079	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	080	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 2	Twitches [Score] week 2	Tremors [Score] week 2	Seizures [Score] week 2	Stereotypie [Score] week 2	Faeces consistency [Score] week 2	Abnormal vocalisation [Score] week 2	Aggressiveness [Score] week 2	Animal sleeps [Score] week 3	Animal moving in cage [Score] week 3	Piloerection [Score] week 3	Vocalization [Score] week 3	O Grooming [Score] week 3	Salivation [Score] week 3	Lacrimation [Score] week 3	Changes in skin [Score] week 3
HD / F	071	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	072	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	073	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	074	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	075	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	076	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	077	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	078	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	079	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	080	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 3	Exophthalmos [Score] week 3	Eyes opening [Score] week 3	Resiration [Score] week 3	response to handling [Score] week 3	Arousal [Score] week 3	Fear [Score] week 3	Finger approach [Score] week 3	Head touch [Score] week 3	Body position [Score] week 3	Spontaneous activity [Score] week 3	Ataxic gait [Score] week 3	Hypotonic gait [Score] week 3	Twitches [Score] week 3	Tremors [Score] week 3	Seizures [Score] week 3
HD / F	071	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	072	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	073	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	074	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	075	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	076	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	077	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	078	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	079	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	080	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 3	Faeces consistency [Score] week 3	Abnormal vocalisation [Score] week 3	Aggressiveness [Score] week 3	Animal sleeps [Score] week 4	Animal moving in cage [Score] week 4	Piloerection [Score] week 4	Vocalization [Score] week 4	O Grooming [Score] week 4	Salivation [Score] week 4	Lacrimation [Score] week 4	Changes in skin [Score] week 4	Cyanosis [Score] week 4	Exophthalmos [Score] week 4	Eyes opening [Score] week 4	Resiration [Score] week 4
HD / F	071	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	072	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	073	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	074	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	075	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	076	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	077	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	078	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	079	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	080	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 4	Arousal [Score] week 4	Fear [Score] week 4	Finger approach [Score] week 4	Head touch [Score] week 4	Body position [Score] week 4	Spontaneous activity [Score] week 4	Ataxic gait [Score] week 4	Hypotonic gait [Score] week 4	Twitches [Score] week 4	Tremors [Score] week 4	Seizures [Score] week 4	Stereotypie [Score] week 4	Faeces consistency [Score] week 4	Abnormal vocalisation [Score] week 4	Aggressiveness [Score] week 4
HD / F	071	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	072	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	073	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	074	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	075	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	076	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	077	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	078	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	079	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	080	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 5	Animal moving in cage [Score] week 5	Piloerection [Score] week 5	Vocalization [Score] week 5	O Grooming [Score] week 5	Salivation [Score] week 5	Lacrimation [Score] week 5	Changes in skin [Score] week 5	Cyanosis [Score] week 5	Exophthalmos [Score] week 5	Eyes opening [Score] week 5	Resiration [Score] week 5	response to handling [Score] week 5	Arousal [Score] week 5	Fear [Score] week 5	Finger approach [Score] week 5
HD / F	071	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	072	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	6
	073	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	074	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	075	0	1	0	0	0	4	0	0	0	0	0	4	4	4	4	6
	076	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	077	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	078	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	079	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	080	0	1	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 5	Body position [Score] week 5	Spontaneous activity [Score] week 5	Ataxic gait [Score] week 5	Hypotonic gait [Score] week 5	Twitches [Score] week 5	Tremors [Score] week 5	Seizures [Score] week 5	Stereotypie [Score] week 5	Faeces consistency [Score] week 5	Abnormal vocalisation [Score] week 5	Animal Aggressiveness [Score] week 5	Animal sleeps [Score] week 6	moving in cage [Score] week 6	Piloerection [Score] week 6	Vocalization [Score] week 6
HD / F	071	2	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	072	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	073	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	074	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	075	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	076	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	077	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	078	2	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	079	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	080	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 6	Salivation [Score] week 6	Lacrimation [Score] week 6	Changes in skin [Score] week 6	Cyanosis [Score] week 6	Exophthalmos [Score] week 6	Eyes opening [Score] week 6	Resiration [Score] week 6	response to handling [Score] week 6	Arousal [Score] week 6	Fear [Score] week 6	Finger approach [Score] week 6	Head touch [Score] week 6	Body position [Score] week 6	Spontaneous activity [Score] week 6	Ataxic gait [Score] week 6
HD / F	071	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	072	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	073	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	074	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	075	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	076	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	077	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	078	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	079	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	080	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 6	Twitches [Score] week 6	Tremors [Score] week 6	Seizures [Score] week 6	Stereotypie [Score] week 6	Faeces consistency [Score] week 6	Abnormal vocalisation [Score] week 6	Aggressiveness [Score] week 6	Animal sleeps [Score] week 7	Animal moving in cage [Score] week 7	Piloerection [Score] week 7	Vocalization [Score] week 7	O Grooming [Score] week 7	Salivation [Score] week 7	Lacrimation [Score] week 7	Changes in skin [Score] week 7
HD / F	071	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	072	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	073	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	074	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	075	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	076	0	0	0	0	0	4	0	0								
	077	0	0	0	0	0	4	0	0								
	078	0	0	0	0	0	4	0	0								
	079	0	0	0	0	0	4	0	0								
	080	0	0	0	0	0	4	0	0								

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 7	Exophthalmos [Score] week 7	Eyes opening [Score] week 7	Resiration [Score] week 7	response to handling [Score] week 7	Arousal [Score] week 7	Fear [Score] week 7	Finger approach [Score] week 7	Head touch [Score] week 7	Body position [Score] week 7	Spontaneous activity [Score] week 7	Ataxic gait [Score] week 7	Hypotonic gait [Score] week 7	Twitches [Score] week 7	Tremors [Score] week 7	Seizures [Score] week 7
HD / F	071	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	072	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	073	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	074	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	075	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	076																
	077																
	078																
	079																
	080																

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 7	Faeces consistency [Score] week 7	Abnormal vocalisation [Score] week 7	Aggressiveness [Score] week 7	Animal sleeps [Score] week 8	Animal moving in cage [Score] week 8	Piloerection [Score] week 8	Vocalization [Score] week 8	O Grooming [Score] week 8	Salivation [Score] week 8	Lacrimation [Score] week 8	Changes in skin [Score] week 8	Cyanosis [Score] week 8	Exophthalmos [Score] week 8	Eyes opening [Score] week 8	Resiration [Score] week 8
HD / F	071	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	072	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	073	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	074	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	075	0	4	0	0	1	0	0	0	0	4	0	0	0	0	0	4
	076					0	1	0	0	0	4	0	0	0	0	0	4
	077					0	1	0	0	0	4	0	0	0	0	0	4
	078					0	1	0	0	0	4	0	0	0	0	0	4
	079					0	1	0	0	0	4	0	0	0	0	0	4
	080					0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 8	Arousal [Score] week 8	Fear [Score] week 8	Finger approach [Score] week 8	Head touch [Score] week 8	Body position [Score] week 8	Spontaneous activity [Score] week 8	Ataxic gait [Score] week 8	Hypotonic gait [Score] week 8	Twitches [Score] week 8	Tremors [Score] week 8	Seizures [Score] week 8	Stereotypie [Score] week 8	Faeces consistency [Score] week 8	Abnormal vocalisation [Score] week 8	Aggressiveness [Score] week 8
HD / F	071	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	072	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	073	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	074	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	075	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	076	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	077	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	078	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	079	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	080	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal sleeps [Score] week 9	Animal moving in cage [Score] week 9	Piloerection [Score] week 9	Vocalization [Score] week 9	O Grooming [Score] week 9	Salivation [Score] week 9	Lacrimation [Score] week 9	Changes in skin [Score] week 9	Cyanosis [Score] week 9	Exophthalmos [Score] week 9	Eyes opening [Score] week 9	Resiration [Score] week 9	response to handling [Score] week 9	Arousal [Score] week 9	Fear [Score] week 9	Finger approach [Score] week 9
HD / F	071	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	072	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	073	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	074	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	075	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	076	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	077	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	078	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	079	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4
	080	1	0	0	0	0	4	0	0	0	0	0	4	4	4	4	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Head touch [Score] week 9	Body position [Score] week 9	Spontaneous activity [Score] week 9	Ataxic gait [Score] week 9	Hypotonic gait [Score] week 9	Twitches [Score] week 9	Tremors [Score] week 9	Seizures [Score] week 9	Stereotypie [Score] week 9	Faeces consistency [Score] week 9	Abnormal vocalisation [Score] week 9	Aggressiveness [Score] week 9	Animal sleeps [Score] week 10	Animal moving in cage [Score] week 10	Piloerection [Score] week 10	Vocalization [Score] week 10
HD / F	071	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	072	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	073	4	4	3	0	0	0	0	0	0	4	0	0	1	0	0	0
	074	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	075	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	076	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	077	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	078	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	079	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0
	080	4	4	4	0	0	0	0	0	0	4	0	0	1	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	O Grooming [Score] week 10	Salivation [Score] week 10	Lacrimation [Score] week 10	Changes in skin [Score] week 10	Cyanosis [Score] week 10	Exophthalmos [Score] week 10	Eyes opening [Score] week 10	Resiration [Score] week 10	response to handling [Score] week 10	Arousal [Score] week 10	Fear [Score] week 10	Finger approach [Score] week 10	Head touch [Score] week 10	Body position [Score] week 10	Spontaneous activity [Score] week 10	Ataxic gait [Score] week 10
HD / F	071	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	072	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	073	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	074	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	075	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	076	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	077	0	4	0	0	0	0	0	4	2	4	4	4	4	4	3	0
	078	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	079	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0
	080	0	4	0	0	0	0	0	4	4	4	4	4	4	4	4	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Hypotonic gait [Score] week 10	Twitches [Score] week 10	Tremors [Score] week 10	Seizures [Score] week 10	Stereotypie [Score] week 10	Faeces consistency [Score] week 10	Abnormal vocalisation [Score] week 10	Aggressiveness [Score] week 10	Animal sleeps [Score] week 11	Animal moving in cage [Score] week 11	Piloerection [Score] week 11	Vocalization [Score] week 11	O Grooming [Score] week 11	Salivation [Score] week 11	Lacrimation [Score] week 11	Changes in skin [Score] week 11
HD / F	071	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	072	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	073	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	074	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	075	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	076	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	077	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	078	0	0	0	0	0	4	0	0	1	0	0	0	0	4	0	0
	079	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0
	080	0	0	0	0	0	4	0	0	0	1	0	0	0	4	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Cyanosis [Score] week 11	Exophthalmos [Score] week 11	Eyes opening [Score] week 11	Resiration [Score] week 11	response to handling [Score] week 11	Arousal [Score] week 11	Fear [Score] week 11	Finger approach [Score] week 11	Head touch [Score] week 11	Body position [Score] week 11	Spontaneous activity [Score] week 11	Ataxic gait [Score] week 11	Hypotonic gait [Score] week 11	Twitches [Score] week 11	Tremors [Score] week 11	Seizures [Score] week 11
HD / F	071	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	072	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	073	0	0	0	4	2	4	4	4	4	4	3	0	0	0	0	0
	074	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	075	0	0	0	4	2	4	4	4	4	4	4	0	0	0	0	0
	076	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	077	0	0	0	4	4	4	4	6	4	4	4	0	0	0	0	0
	078	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0
	079	0	0	0	4	2	4	4	4	4	4	4	0	0	0	0	0
	080	0	0	0	4	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Stereotypie [Score] week 11	Faeces consistency [Score] week 11	Abnormal vocalisation [Score] week 11	Aggressiveness [Score] week 11	Animal sleeps [Score] week 12	Animal moving in cage [Score] week 12	Piloerection [Score] week 12	Vocalization [Score] week 12	Grooming [Score] week 12	Salivation [Score] week 12	Lacrimation [Score] week 12	Changes in skin [Score] week 12	Cyanosis [Score] week 12	Exophthalmos [Score] week 12	Eyes opening [Score] week 12	Resiration [Score] week 12
HD / F	071	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	072	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	073	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	074	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	075	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	076	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	077	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	078	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	079	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4
	080	0	4	0	0	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Small

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	response to handling [Score] week 12	Arousal [Score] week 12	Fear [Score] week 12	Finger approach [Score] week 12	Head touch [Score] week 12	Body position [Score] week 12	Spontaneous activity [Score] week 12	Ataxic gait [Score] week 12	Hypotonic gait [Score] week 12	Twitches [Score] week 12	Tremors [Score] week 12	Seizures [Score] week 12	Stereotypie [Score] week 12	Faeces consistency [Score] week 12	Abnormal vocalisation [Score] week 12	Aggressiveness [Score] week 12
HD / F	071	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	072	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	073	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	074	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	075	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	076	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	077	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	078	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	079	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0
	080	4	4	4	4	4	4	4	0	0	0	0	0	0	4	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
C / M	001	1	0	0	0	0	4	0	0	0	0	0	4
	002	1	0	0	0	0	4	0	0	0	0	0	4
	003	1	0	0	0	0	4	0	0	0	0	0	4
	004	1	0	0	0	0	4	0	0	0	0	0	4
	005	1	0	0	0	0	4	0	0	0	0	0	4
	006	1	0	0	0	0	4	0	0	0	0	0	4
	007	1	0	0	0	0	4	0	0	0	0	0	4
	008	1	0	0	0	0	4	0	0	0	0	0	4
	009	1	0	0	0	0	4	0	0	0	0	0	4
	010	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
C / M	001	4	4	4	4	4	4	4	0	0	0	0	0
	002	4	4	4	4	4	4	4	0	0	0	0	0
	003	4	4	4	4	4	4	4	0	0	0	0	0
	004	4	4	4	4	4	4	4	0	0	0	0	0
	005	4	4	4	4	4	4	4	0	0	0	0	0
	006	4	4	4	4	4	4	4	0	0	0	0	0
	007	4	4	4	4	4	4	4	0	0	0	0	0
	008	4	4	4	4	4	4	4	0	0	0	0	0
	009	4	4	4	4	4	4	4	0	0	0	0	0
	010	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
C / M	001	0	0	6	0	0	0	4	0	0	4	4	4
	002	0	0	7	0	0	0	4	0	0	4	4	4
	003	0	0	4	0	0	0	4	0	0	4	4	4
	004	0	0	8	0	0	0	4	0	0	4	4	4
	005	0	0	6	0	0	0	4	0	0	4	4	4
	006	0	0	9	0	0	0	4	0	0	4	4	4
	007	0	0	9	0	0	0	4	0	0	4	4	4
	008	0	0	6	0	0	0	4	0	0	4	4	4
	009	0	0	6	0	0	3	4	0	0	4	4	4
	010	0	0	8	0	0	0	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
C / M	001	4	4	4	4	4	4	0	0	4	379.0	0	0
	002	4	4	4	4	4	4	0	0	0	381.0	0	0
	003	4	4	4	4	4	4	0	0	4	380.0	0	0
	004	4	4	4	4	4	4	0	0	4	376.0	0	0
	005	4	4	4	4	4	4	0	0	4	382.0	0	0
	006	4	4	4	4	4	4	0	0	4	38.1	0	0
	007	4	4	4	4	4	4	0	0	4	39.0	0	0
	008	4	4	4	4	4	4	0	0	4	37.7	0	0
	009	4	4	4	4	4	4	0	0	4	37.9	0	0
	010	4	4	4	4	4	4	0	0	4	37.8	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
C / M	001	0	1	0	0	0	4	0	0	0	0	0	4
	002	0	1	0	0	0	4	0	0	0	0	0	4
	003	0	1	0	0	0	4	0	0	0	0	0	4
	004	0	1	0	0	0	4	0	0	0	0	0	4
	005	0	1	0	0	0	4	0	0	0	0	0	4
	006	0	1	0	0	0	4	0	0	0	0	0	4
	007	0	1	0	0	0	4	0	0	0	0	0	4
	008	0	1	0	0	0	4	0	0	0	0	0	4
	009	0	1	0	0	0	4	0	0	0	0	0	4
	010	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
C / M	001	4	4	4	4	4	4	4	0	0	0	0	0
	002	4	4	4	4	4	4	4	0	0	0	0	0
	003	4	4	4	4	4	4	3	0	0	0	0	0
	004	4	4	4	4	4	4	3	0	0	0	0	0
	005	4	4	4	4	4	4	3	0	0	0	0	0
	006	4	4	4	4	4	4	4	0	0	0	0	0
	007	4	4	4	4	4	4	4	0	0	0	0	0
	008	4	4	4	4	4	4	4	0	0	0	0	0
	009	4	4	4	4	4	4	4	0	0	0	0	0
	010	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
C / M	001	0	0	1	0	0	0	4	0	0	4	4	4
	002	0	0	2	0	0	0	4	0	0	4	4	4
	003	0	0	1	1	0	0	4	0	0	4	4	4
	004	0	0	1	0	0	1	4	0	0	4	4	4
	005	0	0	1	0	0	1	4	0	0	4	4	4
	006	0	0	1	0	0	0	4	0	0	4	4	4
	007	0	0	0	0	0	0	4	0	0	4	4	4
	008	0	0	2	0	0	0	4	0	0	4	4	4
	009	0	0	1	2	0	1	4	0	0	4	4	4
	010	0	0	2	0	0	0	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
C / M	001	4	4	4	4	4	4	0	0	4	37.9	0	0
	002	4	4	4	4	4	4	0	0	4	38.1	0	0
	003	4	4	4	4	4	4	0	0	4	38.5	0	0
	004	4	4	4	4	4	4	0	0	4	38.2	0	0
	005	4	4	4	4	4	4	0	0	4	37.8	0	0
	006	4	4	4	4	4	4	0	0	4	37.8	0	0
	007	4	4	4	4	4	4	0	0	4	38.2	0	0
	008	4	4	4	4	4	4	0	0	4	38.8	0	0
	009	4	4	4	4	4	4	0	0	4	38.2	0	0
	010	4	4	4	4	4	4	0	0	4	38.9	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
C / F	041	1	0	0	0	0	4	0	0	0	0	0	4
	042	1	0	0	0	0	4	0	0	0	0	0	4
	043	1	0	0	0	0	4	0	0	0	0	0	4
	044	1	0	0	0	0	4	0	0	0	0	0	4
	045	1	0	0	0	0	4	0	0	0	0	0	4
	046	1	0	0	0	0	4	0	0	0	0	0	4
	047	1	0	0	0	0	4	0	0	0	0	0	4
	048	1	0	0	0	0	4	0	0	0	0	0	4
	049	1	0	0	0	0	4	0	0	0	0	0	4
	050	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
C / F	041	4	4	4	4	4	4	4	0	0	0	0	0
	042	4	4	4	4	4	4	3	0	0	0	0	0
	043	4	4	4	4	4	4	4	0	0	0	0	0
	044	4	4	4	4	4	4	4	0	0	0	0	0
	045	4	4	4	4	4	4	4	0	0	0	0	0
	046	4	4	4	4	4	4	4	0	0	0	0	0
	047	4	4	4	4	4	4	4	0	0	0	0	0
	048	4	4	4	4	4	4	4	0	0	0	0	0
	049	4	4	4	4	4	4	4	0	0	0	0	0
	050	4	4	4	4	4	4	3	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
C / F	041	0	0	10	0	0	2	4	0	0	4	4	4
	042	0	0	6	0	0	0	4	0	0	4	4	4
	043	0	0	6	0	0	0	4	0	0	4	4	4
	044	0	0	11	0	0	3	4	0	0	4	4	4
	045	0	0	8	0	0	0	4	0	0	4	4	4
	046	0	0	6	0	0	0	4	0	0	4	4	4
	047	0	0	8	0	0	0	4	0	0	4	4	4
	048	0	0	11	0	0	0	4	0	0	4	4	4
	049	0	0	6	0	0	0	4	0	0	4	4	4
	050	0	0	7	2	0	0	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
C / F	041	4	4	4	4	4	4	0	0	4	38.1	0	0
	042	4	4	4	4	4	4	0	0	4	37.6	0	0
	043	4	4	4	4	4	4	0	0	4	38.2	0	0
	044	4	4	4	4	4	4	0	0	4	38.1	0	0
	045	4	4	4	4	4	4	0	0	4	38.2	0	0
	046	4	4	4	4	4	4	0	0	4	38.1	0	0
	047	4	4	4	4	4	4	0	0	4	38.2	0	0
	048	4	4	4	4	4	4	0	0	4	37.9	0	0
	049	4	4	4	4	4	4	0	0	4	38.3	0	0
	050	4	4	4	4	4	4	0	0	4	38.2	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
C / F	041	0	1	0	0	0	4	0	0	0	0	0	4
	042	0	1	0	0	0	4	0	0	0	0	0	4
	043	0	1	0	0	0	4	0	0	0	0	0	4
	044	0	1	0	0	0	4	0	0	0	0	0	4
	045	0	1	0	0	0	4	0	0	0	0	0	4
	046	0	1	0	0	0	4	0	0	0	0	0	4
	047	0	1	0	0	0	4	0	0	0	0	0	4
	048	0	1	0	0	0	4	0	0	0	0	0	4
	049	0	1	0	0	0	4	0	0	0	0	0	4
	050	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
C / F	041	4	4	4	4	4	4	4	0	0	0	0	0
	042	4	4	4	4	4	4	4	0	0	0	0	0
	043	4	4	4	4	4	4	4	0	0	0	0	0
	044	4	4	4	4	4	4	4	0	0	0	0	0
	045	4	4	4	4	4	4	4	0	0	0	0	0
	046	4	4	4	4	4	4	4	0	0	0	0	0
	047	4	4	4	4	4	4	4	0	0	0	0	0
	048	4	4	4	4	4	4	4	0	0	0	0	0
	049	4	4	4	4	4	4	4	0	0	0	0	0
	050	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
C / F	041	0	0	2	0	0	0	4	0	0	4	4	4
	042	0	0	3	1	0	0	4	0	0	4	4	4
	043	0	0	5	2	0	0	4	0	0	4	4	4
	044	0	0	6	3	1	1	4	0	0	4	4	4
	045	0	0	0	5	0	0	4	0	0	4	4	4
	046	0	0	5	1	0	2	4	0	0	4	4	4
	047	0	0	4	1	1	3	4	0	0	4	4	4
	048	0	0	6	1	0	0	4	0	0	4	4	4
	049	0	0	4	1	0	2	4	0	0	4	4	4
	050	0	0	4	1	0	1	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
C / F	041	4	4	4	4	4	4	0	0	4	38.0	0	0
	042	4	4	4	4	4	4	0	0	4	38.6	0	0
	043	4	4	4	4	4	4	0	0	4	38.9	0	0
	044	4	4	4	4	4	4	0	0	4	38.7	0	0
	045	4	4	4	4	4	4	0	0	4	39.0	0	0
	046	4	4	4	4	4	4	0	0	4	38.3	0	0
	047	4	4	4	4	4	4	0	0	4	38.2	0	0
	048	4	4	4	4	4	4	0	0	4	38.1	0	0
	049	4	4	4	4	4	4	0	0	4	38.5	0	0
	050	4	4	4	4	4	4	0	0	4	37.9	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
LD / M	011	1	0	0	0	0	4	0	0	0	0	0	4
	012	1	0	0	0	0	4	0	0	0	0	0	4
	013	1	0	0	0	0	4	0	0	0	0	0	4
	014	1	0	0	0	0	4	0	0	0	0	0	4
	015	1	0	0	0	0	4	0	0	0	0	0	4
	016	1	0	0	0	0	4	0	0	0	0	0	4
	017	1	0	0	0	0	4	0	0	0	0	0	4
	018	1	0	0	0	0	4	0	0	0	0	0	4
	019	1	0	0	0	0	4	0	0	0	0	0	4
	020	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
LD / M	011	4	4	4	4	4	4	4	0	0	0	0	0
	012	4	4	4	4	4	4	4	0	0	0	0	0
	013	4	4	4	4	4	4	4	0	0	0	0	0
	014	4	4	4	4	4	4	4	0	0	0	0	0
	015	4	4	4	4	4	4	3	0	0	0	0	0
	016	4	4	4	4	4	4	4	0	0	0	0	0
	017	4	4	4	4	4	4	4	0	0	0	0	0
	018	4	4	4	4	4	4	4	0	0	0	0	0
	019	4	4	4	4	4	4	4	0	0	0	0	0
	020	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
LD / M	011	0	0	9	0	0	0	4	0	0	4	4	4
	012	0	0	6	1	0	0	4	0	0	4	4	4
	013	0	0	11	0	0	0	4	0	0	4	4	4
	014	0	0	7	0	0	0	4	0	0	4	4	4
	015	0	0	4	0	0	0	4	0	0	4	4	4
	016	0	0	6	0	0	0	4	0	0	4	4	4
	017	0	0	4	0	0	0	4	0	0	4	4	4
	018	0	0	6	0	0	0	4	0	0	4	4	4
	019	0	0	6	0	0	0	4	0	0	4	4	4
	020	0	0	8	0	0	0	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
LD / M	011	4	4	4	4	4	4	0	0	4	384.0	0	0
	012	4	4	4	4	4	4	0	0	4	379.0	0	0
	013	4	4	4	4	4	4	0	0	4	390.0	0	0
	014	4	4	4	4	4	4	0	0	4	383.0	0	0
	015	4	4	4	4	4	4	0	0	4	386.0	0	0
	016	4	4	4	4	4	4	0	0	4	38.2	0	0
	017	4	4	4	4	4	4	0	0	4	38.3	0	0
	018	4	4	4	4	4	4	0	0	4	37.9	0	0
	019	4	4	4	4	4	4	0	0	4	36.8	0	0
	020	4	4	4	4	4	4	0	0	4	37.8	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
LD / M	011	0	1	0	0	0	4	0	0	0	0	0	4
	012	0	1	0	0	0	4	0	0	0	0	0	4
	013	0	1	0	0	0	4	0	0	0	0	0	4
	014	0	1	0	0	0	4	0	0	0	0	0	4
	015	0	1	0	0	0	4	0	0	0	0	0	4
	016	0	1	0	0	0	4	0	0	0	0	0	4
	017	0	1	0	0	0	4	0	0	0	0	0	4
	018	0	1	0	0	0	4	0	0	0	0	0	4
	019	0	1	0	0	0	4	0	0	0	0	0	4
	020	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
LD / M	011	4	4	4	4	4	4	4	0	0	0	0	0
	012	4	4	4	4	4	4	3	0	0	0	0	0
	013	4	4	4	4	4	4	4	0	0	0	0	0
	014	4	4	4	4	4	4	3	0	0	0	0	0
	015	4	4	4	4	4	4	3	0	0	0	0	0
	016	4	4	4	4	4	4	4	0	0	0	0	0
	017	4	4	4	4	4	4	4	0	0	0	0	0
	018	4	4	4	4	4	4	4	0	0	0	0	0
	019	4	4	4	4	4	4	4	0	0	0	0	0
	020	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
LD / M	011	0	0	3	0	0	0	4	0	0	4	4	4
	012	0	0	0	0	0	1	4	0	0	4	4	4
	013	0	0	2	1	0	0	4	0	0	4	4	4
	014	0	0	3	0	0	0	4	0	0	4	4	4
	015	0	0	1	1	0	0	4	0	0	4	4	4
	016	0	0	1	1	1	2	4	0	0	4	4	4
	017	0	0	2	0	0	1	4	0	0	4	4	4
	018	0	0	1	0	0	1	4	0	0	4	4	4
	019	0	0	3	0	0	0	4	0	0	4	4	4
	020	0	0	0	0	0	1	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
LD / M	011	4	4	4	4	4	4	0	0	4	38.7	0	0
	012	4	4	4	4	4	4	0	0	4	38.2	0	0
	013	4	4	4	4	4	4	0	0	4	38.9	0	0
	014	4	4	4	4	4	4	0	0	4	38.9	0	0
	015	4	4	4	4	4	4	0	0	4	38.1	0	0
	016	4	4	4	4	4	4	0	0	4	38.6	0	0
	017	4	4	4	4	4	4	0	0	4	37.9	0	0
	018	4	4	4	4	4	5	0	0	4	38.3	0	0
	019	4	4	4	4	4	4	0	0	4	38.0	0	0
	020	4	4	4	4	4	4	0	0	4	38.7	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
LD / F	051	1	0	0	0	0	4	0	0	0	0	0	4
	052	1	0	0	0	0	4	0	0	0	0	0	4
	053	1	0	0	0	0	4	0	0	0	0	0	4
	054	1	0	0	0	0	4	0	0	0	0	0	4
	055	1	0	0	0	0	4	0	0	0	0	0	4
	056	1	0	0	0	0	4	0	0	0	0	0	4
	057	1	0	0	0	0	4	0	0	0	0	0	4
	058	1	0	0	0	0	4	0	0	0	0	0	4
	059	1	0	0	0	0	4	0	0	0	0	0	4
	060	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
LD / F	051	4	4	4	4	4	4	4	0	0	0	0	0
	052	4	4	4	4	4	4	4	0	0	0	0	0
	053	4	4	4	4	4	4	4	0	0	0	0	0
	054	4	4	4	4	4	4	4	0	0	0	0	0
	055	4	4	4	4	4	4	4	0	0	0	0	0
	056	4	4	4	4	4	4	4	0	0	0	0	0
	057	4	4	4	4	4	4	4	0	0	0	0	0
	058	4	4	4	4	4	4	4	0	0	0	0	0
	059	4	4	4	4	4	4	4	0	0	0	0	0
	060	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
LD / F	051	0	0	6	0	0	0	4	0	0	4	4	4
	052	0	0	8	0	0	0	4	0	0	4	4	4
	053	0	0	8	0	0	0	4	0	0	4	4	4
	054	0	0	9	0	0	0	4	0	0	4	4	4
	055	0	0	8	0	0	0	4	0	0	4	4	4
	056	0	0	8	0	0	0	4	0	0	2	4	4
	057	0	0	8	0	0	0	4	0	0	4	4	4
	058	0	0	8	0	0	0	4	0	0	4	4	4
	059	0	0	12	0	0	0	4	0	0	4	4	4
	060	0	0	8	0	0	0	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
LD / F	051	4	4	4	4	4	4	0	0	4	38.2	0	0
	052	4	4	4	4	4	4	0	0	4	38.6	0	0
	053	4	4	4	4	4	4	0	0	4	39.0	0	0
	054	4	4	4	4	4	4	0	0	4	39.0	0	0
	055	4	4	4	4	4	4	0	0	4	38.4	0	0
	056	4	4	4	4	4	4	0	0	4	38.1	0	0
	057	4	4	4	4	4	4	4	0	0	38.4	0	0
	058	4	4	4	4	4	4	0	0	4	38.1	0	0
	059	4	4	4	4	4	4	0	0	4	38.1	0	0
	060	4	4	4	4	4	4	0	0	4	38.6	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
LD / F	051	0	1	0	0	0	4	0	0	0	0	0	4
	052	0	1	0	0	0	4	0	0	0	0	0	4
	053	0	1	0	0	0	4	0	0	0	0	0	4
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	1	0	0	0	4	0	0	0	0	0	4
	056	0	1	0	0	0	4	0	0	0	0	0	4
	057	0	1	0	0	0	4	0	0	0	0	0	4
	058	0	1	0	0	0	4	0	0	0	0	0	4
	059	0	1	0	0	0	4	0	0	0	0	0	4
	060	0	1	0	0	0	4	0	0	0	0	0	4

NS = No More Scheduled

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
LD / F	051	4	4	4	4	4	4	4	0	0	0	0	0
	052	4	4	4	4	4	4	4	0	0	0	0	0
	053	4	4	4	4	4	4	4	0	0	0	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	4	4	4	4	4	4	4	0	0	0	0	0
	056	4	4	4	4	4	4	4	0	0	0	0	0
	057	4	4	4	44	4	4	4	0	0	0	0	0
	058	4	4	4	4	4	4	4	0	0	0	0	0
	059	4	4	4	4	4	4	4	0	0	0	0	0
	060	4	4	4	4	4	4	4	0	0	0	0	0

NS = No More Scheduled

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
LD / F	051	0	0	2	0	0	0	4	0	0	4	4	4
	052	0	0	6	1	0	1	4	0	0	4	4	4
	053	0	0	5	0	0	0	4	0	0	4	4	4
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	0	0	3	0	0	0	4	0	0	4	4	4
	056	0	0	4	1	0	0	4	0	0	4	4	4
	057	0	0	2	0	0	0	4	0	0	4	4	4
	058	0	0	5	1	2	3	4	0	0	4	4	4
	059	0	0	3	2	1	2	4	0	0	4	4	4
	060	0	0	4	0	0	0	4	0	0	4	4	4

NS = No More Scheduled

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
LD / F	051	4	4	4	4	4	4	0	0	4	38.4	0	0
	052	4	4	4	4	4	4	0	0	4	38.7	0	0
	053	4	4	4	4	4	4	0	0	4	38.5	0	0
	054	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	4	4	4	4	4	4	0	0	4	37.9	0	0
	056	4	4	4	4	4	4	0	0	4	38.5	0	0
	057	4	4	4	4	4	4	0	0	4	38.2	0	0
	058	4	4	4	4	4	4	0	0	4	38.1	0	0
	059	4	4	4	4	4	4	0	0	4	37.9	0	0
	060	4	4	4	4	4	4	0	0	4	38.4	0	0

NS = No More Scheduled

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
MD / M	021	1	0	0	0	0	4	0	0	0	0	0	4
	022	1	0	0	0	0	4	0	0	0	0	0	4
	023	1	0	0	0	0	4	0	0	0	0	0	4
	024	1	0	0	0	0	4	0	0	0	0	0	4
	025	0	1	0	0	0	4	0	0	0	0	0	4
	026	1	0	0	0	0	4	0	0	0	0	0	4
	027	1	0	0	0	0	4	0	0	0	0	0	4
	028	1	0	0	0	0	4	0	0	0	0	0	4
	029	1	0	0	0	0	4	0	0	0	0	0	4
	030	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
MD / M	021	4	4	4	4	4	4	4	0	0	0	0	0
	022	4	4	4	4	4	4	4	0	0	0	0	0
	023	4	4	4	4	4	4	4	0	0	0	0	0
	024	4	4	4	4	4	4	3	0	0	0	0	0
	025	4	4	4	4	4	4	4	0	0	0	0	0
	026	4	4	4	4	4	4	4	0	0	0	0	0
	027	4	4	4	4	4	4	4	0	0	0	0	0
	028	4	4	4	4	4	4	4	0	0	0	0	0
	029	4	4	4	4	4	4	4	0	0	0	0	0
	030	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
MD / M	021	0	0	5	0	0	0	4	0	0	4	4	4
	022	0	0	3	0	0	0	4	0	0	4	4	4
	023	0	0	4	0	0	0	4	0	0	4	4	4
	024	0	0	2	0	0	0	4	0	0	4	4	4
	025	0	0	6	0	0	0	4	0	0	4	4	4
	026	0	0	0	2	0	0	4	0	0	4	4	4
	027	0	0	8	0	0	0	4	0	0	4	4	4
	028	0	0	6	1	0	2	4	0	0	4	4	4
	029	0	0	3	0	0	0	4	0	0	2	4	4
	030	0	0	4	0	0	0	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
MD / M	021	4	4	4	4	4	4	0	0	4	381.0	0	0
	022	4	4	4	4	4	4	0	0	4	379.0	0	0
	023	4	4	4	4	4	4	0	0	4	380.0	0	0
	024	4	4	4	4	4	4	0	0	4	382.0	0	0
	025	4	4	4	4	4	4	0	0	4	376.0	0	0
	026	4	4	4	4	4	4	0	0	4	376.0	0	0
	027	4	4	4	4	4	4	0	0	4	388.0	0	0
	028	4	4	4	4	4	4	0	0	4	381.0	0	0
	029	4	4	4	4	4	4	0	0	4	379.0	0	0
	030	4	4	4	4	4	4	0	0	4	381.0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
MD / M	021	0	1	0	0	0	4	0	0	0	0	0	4
	022	0	1	0	0	0	4	0	0	0	0	0	4
	023	0	1	0	0	0	4	0	0	0	0	0	4
	024	0	1	0	0	0	4	0	0	0	0	0	4
	025	0	1	0	0	0	4	0	0	0	0	0	4
	026	0	1	0	0	0	4	0	0	0	0	0	4
	027	0	1	0	0	0	4	0	0	0	0	0	4
	028	0	1	0	0	0	4	0	0	0	0	0	4
	029	0	1	0	0	0	4	0	0	0	0	0	4
	030	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
MD / M	021	4	4	4	4	4	4	3	0	0	0	0	0
	022	4	4	4	4	4	4	4	0	0	0	0	0
	023	4	4	4	4	4	4	3	0	0	0	0	0
	024	4	4	4	4	4	4	4	0	0	0	0	0
	025	4	4	4	4	4	4	4	0	0	0	0	0
	026	4	4	4	4	4	4	4	0	0	0	0	0
	027	4	4	4	4	4	4	4	0	0	0	0	0
	028	4	4	4	4	4	4	4	0	0	0	0	0
	029	4	4	4	4	4	4	4	0	0	0	0	0
	030	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
MD / M	021	0	0	1	0	0	0	4	0	0	4	4	4
	022	0	0	3	0	0	0	4	0	0	4	4	4
	023	0	0	3	0	0	0	4	0	0	4	4	4
	024	0	0	1	1	0	1	4	0	0	4	4	4
	025	0	0	0	0	0	0	4	0	0	4	4	4
	026	0	0	1	0	0	0	4	0	0	4	4	4
	027	0	0	2	0	0	0	4	0	0	4	4	4
	028	0	0	4	1	0	0	4	0	0	4	4	4
	029	0	0	5	2	0	1	4	0	0	4	4	4
	030	0	0	3	0	0	1	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
MD / M	021	4	4	4	4	4	4	0	0	4	37.6	0	0
	022	4	4	4	4	4	4	0	0	4	38.5	0	0
	023	4	4	4	4	4	4	0	0	4	37.9	0	0
	024	4	4	4	4	4	4	0	0	4	39.0	0	0
	025	4	4	4	4	4	4	0	0	4	38.6	0	0
	026	4	4	4	4	4	4	0	0	4	38.9	0	0
	027	4	4	4	4	4	4	0	0	4	38.2	0	0
	028	4	4	4	4	4	4	0	0	4	38.6	0	0
	029	4	4	4	4	4	4	0	0	4	37.7	0	0
	030	4	4	4	4	4	4	0	0	4	38.0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
MD / F	061	1	0	0	0	0	4	0	0	0	0	0	4
	062	1	0	0	0	0	4	0	0	0	0	0	4
	063	1	0	0	0	0	4	0	0	0	0	0	4
	064	1	0	0	0	0	0	4	0	0	0	0	4
	065	1	0	0	0	0	4	0	0	0	0	0	4
	066	1	0	0	0	0	4	0	0	0	0	0	4
	067	1	0	0	0	0	4	0	0	0	0	0	4
	068	1	0	0	0	0	4	0	0	0	0	0	4
	069	1	0	0	0	0	4	0	0	0	0	0	4
	070	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
MD / F	061	4	4	4	4	4	4	4	0	0	0	0	0
	062	4	4	4	4	4	4	4	0	0	0	0	0
	063	4	4	4	4	4	4	4	0	0	0	0	0
	064	4	4	4	4	4	4	4	0	0	0	0	0
	065	4	4	4	4	4	4	4	0	0	0	0	0
	066	4	4	4	4	4	4	4	0	0	0	0	0
	067	4	4	4	4	4	4	4	0	0	0	0	0
	068	4	4	4	4	4	4	4	0	0	0	0	0
	069	4	4	4	4	4	4	4	0	0	0	0	0
	070	4	4	4	4	4	4	4	4	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
MD / F	061	0	0	8	0	0	0	4	0	0	4	4	4
	062	0	0	6	0	0	0	4	0	0	4	4	4
	063	0	0	7	0	0	0	4	0	0	4	4	4
	064	0	0	8	0	0	2	4	0	0	4	4	4
	065	0	0	10	2	0	0	4	0	0	4	4	4
	066	0	0	8	0	0	0	4	0	0	4	4	4
	067	0	0	9	0	0	0	4	0	0	4	4	4
	068	0	0	5	0	0	0	4	0	0	4	4	4
	069	0	0	6	2	0	4	4	0	0	4	4	4
	070	0	0	8	0	0	0	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
MD / F	061	4	4	4	4	4	4	0	0	4	37.7	0	0
	062	4	4	4	4	4	4	0	0	4	38.4	0	0
	063	4	4	4	4	4	4	0	0	4	39.0	0	0
	064	4	4	4	4	4	4	0	0	4	38.5	0	0
	065	4	4	4	4	4	4	0	0	4	37.9	0	0
	066	4	4	4	4	4	4	0	0	4	39.0	0	0
	067	4	4	4	4	4	4	0	0	4	38.7	0	0
	068	4	4	4	4	4	4	0	0	4	39.1	0	0
	069	4	4	4	4	4	4	0	0	4	37.9	0	0
	070	4	4	4	4	4	4	0	0	4	38.2	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
MD / F	061	0	1	0	0	0	4	0	0	0	0	0	4
	062	0	1	0	0	0	4	0	0	0	0	0	4
	063	0	1	0	0	0	4	0	0	0	0	0	4
	064	0	1	0	0	0	4	0	0	0	0	0	4
	065	0	1	0	0	0	4	0	0	0	0	0	4
	066	0	1	0	0	0	4	0	0	0	0	0	4
	067	0	1	0	0	0	4	0	0	0	0	0	4
	068	0	1	0	0	0	4	0	0	0	0	0	4
	069	0	1	0	0	0	4	0	0	0	0	0	4
	070	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
MD / F	061	4	4	4	4	4	4	4	0	0	0	0	0
	062	4	4	4	4	4	4	4	0	0	0	0	0
	063	4	4	4	4	4	4	4	0	0	0	0	0
	064	4	4	4	4	4	4	4	0	0	0	0	0
	065	4	4	4	4	4	4	4	0	0	0	0	0
	066	4	4	4	4	4	4	4	0	0	0	0	0
	067	4	4	4	4	4	4	4	0	0	0	0	0
	068	4	4	4	4	4	4	4	0	0	0	0	0
	069	4	4	4	4	4	4	4	0	0	0	0	0
	070	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
MD / F	061	0	0	5	0	0	0	4	0	0	4	4	4
	062	0	0	6	0	0	0	4	0	0	4	4	4
	063	0	0	4	0	0	1	4	0	0	4	4	4
	064	0	0	2	0	0	0	4	0	0	4	4	4
	065	0	0	1	1	0	0	4	0	0	4	4	4
	066	0	0	4	1	2	3	4	0	0	4	4	4
	067	0	0	4	1	0	2	4	0	0	4	4	4
	068	0	0	3	1	0	0	4	0	0	4	4	4
	069	0	0	5	0	0	3	4	0	0	4	4	4
	070	0	0	6	0	0	1	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
MD / F	061	4	4	4	4	4	4	0	0	4	38.9	0	0
	062	4	4	4	4	4	4	0	0	4	39.2	0	0
	063	4	4	4	4	4	4	0	0	4	39.0	0	0
	064	4	4	4	4	4	4	0	0	4	38.8	0	0
	065	4	4	4	4	4	4	0	0	4	38.5	0	0
	066	4	4	4	4	4	4	0	0	4	38.3	0	0
	067	4	4	4	4	4	4	0	0	4	37.8	0	0
	068	4	4	4	4	4	4	0	0	4	37.9	0	0
	069	4	4	4	4	4	4	0	0	4	38.2	0	0
	070	4	4	4	4	4	4	0	0	4	38.0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
HD / M	031	1	0	0	0	0	4	0	0	0	0	0	4
	032	1	0	0	0	0	4	0	0	0	0	0	4
	033	1	0	0	0	0	4	0	0	0	0	0	4
	034	1	0	0	0	0	4	0	0	0	0	0	4
	035	0	1	0	0	0	4	0	0	0	0	0	4
	036	1	0	0	0	0	4	0	0	0	0	0	4
	037	1	0	0	0	0	4	0	0	0	0	0	4
	038	1	0	0	0	0	4	0	0	0	0	0	4
	039	1	0	0	0	0	4	0	0	0	0	0	4
	040	1	0	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
HD / M	031	4	4	4	4	4	4	4	0	0	0	0	0
	032	4	4	4	4	4	4	4	0	0	0	0	0
	033	4	4	4	4	4	4	4	0	0	0	0	0
	034	4	4	4	4	4	4	4	0	0	0	0	0
	035	4	4	4	4	4	4	4	0	0	0	0	0
	036	4	4	4	4	4	4	4	0	0	0	0	0
	037	4	4	4	4	4	4	4	0	0	0	0	0
	038	4	4	4	4	4	4	4	0	0	0	0	0
	039	4	4	4	4	4	4	4	0	0	0	0	0
	040	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
HD / M	031	0	0	6	0	0	0	4	0	0	4	4	4
	032	0	0	3	0	0	0	4	0	0	4	4	4
	033	0	0	7	0	0	3	4	0	0	4	4	4
	034	0	0	5	0	0	0	4	0	0	4	4	4
	035	0	0	1	0	0	0	4	0	0	4	4	4
	036	0	0	3	0	1	0	4	0	0	4	4	4
	037	0	0	4	0	0	0	4	0	0	4	4	4
	038	0	0	6	0	0	0	4	0	0	4	4	4
	039	0	0	1	0	0	0	4	0	0	4	4	4
	040	0	0	5	0	0	0	4	0	0	2	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
HD / M	031	4	4	4	4	4	4	0	0	4	382.0	0	0
	032	4	4	4	4	4	4	0	0	4	390.0	0	0
	033	4	4	4	4	4	4	0	0	4	381.0	0	0
	034	4	4	4	4	4	4	0	0	4	369.0	0	0
	035	4	4	4	4	4	4	0	0	4	382.0	0	0
	036	4	4	4	4	4	4	0	0	4	381.0	0	0
	037	4	4	4	4	4	4	0	0	4	376.0	0	0
	038	4	4	4	4	4	4	0	0	4	384.0	0	0
	039	4	4	4	4	4	4	0	0	4	383.0	0	0
	040	4	4	4	4	4	4	0	0	4	380.0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
HD / M	031	0	1	0	0	0	4	0	0	0	0	0	4
	032	0	1	0	0	0	4	0	0	0	0	0	4
	033	0	1	0	0	0	4	0	0	0	0	0	4
	034	0	1	0	0	0	4	0	0	0	0	0	4
	035	0	1	0	0	0	4	0	0	0	0	0	4
	036	0	1	0	0	0	4	0	0	0	0	0	4
	037	0	1	0	0	0	4	0	0	0	0	0	4
	038	0	1	0	0	0	4	0	0	0	0	0	4
	039	0	1	0	0	0	4	0	0	0	0	0	4
	040	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
HD / M	031	4	4	4	4	4	4	3	0	0	0	0	0
	032	4	4	4	4	4	4	4	0	0	0	0	0
	033	4	4	4	4	4	4	3	0	0	0	0	0
	034	4	4	4	4	4	4	4	0	0	0	0	0
	035	4	4	4	4	4	4	4	0	0	0	0	0
	036	4	4	4	4	4	4	4	0	0	0	0	0
	037	4	4	4	4	4	4	4	0	0	0	0	0
	038	4	4	4	4	4	4	4	0	0	0	0	0
	039	4	4	4	4	4	4	4	0	0	0	0	0
	040	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
HD / M	031	0	0	0	1	0	0	4	0	0	4	4	4
	032	0	0	2	0	0	0	4	0	0	4	4	4
	033	0	0	1	2	0	0	4	0	0	4	4	4
	034	0	0	1	0	0	0	4	0	0	4	4	4
	035	0	0	1	0	0	0	4	0	0	4	4	4
	036	0	0	2	0	0	0	4	0	0	4	4	4
	037	0	0	4	0	0	0	4	0	0	4	4	4
	038	0	0	6	0	0	0	4	0	0	4	4	4
	039	0	0	1	0	0	0	4	0	0	4	4	4
	040	0	0	3	2	1	1	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
HD / M	031	4	4	4	4	4	4	0	0	4	38.9	0	0
	032	4	4	4	4	4	4	0	0	4	38.5	0	0
	033	4	4	4	4	4	4	0	0	4	38.2	0	0
	034	4	4	4	4	4	4	0	0	4	38.1	0	0
	035	4	4	4	4	4	4	0	0	4	38.3	0	0
	036	4	4	4	4	4	4	0	0	4	37.5	0	0
	037	4	4	4	4	4	4	0	0	4	37.8	0	0
	038	4	4	4	4	4	4	0	0	4	38.2	0	0
	039	4	4	4	4	4	4	0	0	4	37.9	0	0
	040	4	4	4	4	4	4	0	0	4	37.9	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week -1	Animal moving in cage [Score] week -1	Piloerection [Score] week -1	Vocalization [Score] week -1	O Grooming [Score] week -1	Salivation [Score] week -1	Lacrimation [Score] week -1	Changes in skin [Score] week -1	Cyanosis [Score] week -1	Exophthalmos [Score] week -1	Eyes opening [Score] week -1	Respiration [Score] week -1
HD / F	071	1	0	0	0	0	4	0	0	0	0	0	4
	072	1	0	0	0	0	4	0	0	0	0	0	4
	073	1	0	0	0	0	4	0	0	0	0	0	4
	074	1	0	0	0	0	4	0	0	0	0	0	4
	075	1	0	0	0	0	4	0	0	0	0	0	4
	076	1	0	0	0	0	4	0	0	0	0	0	4
	077	1	0	0	0	0	4	0	0	0	0	0	4
	078	0	1	0	0	0	4	0	0	0	0	0	4
	079	1	0	0	0	0	4	0	0	0	0	0	4
	080	0	1	0	0	0	4	0	0	0	0	0	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week -1	Arousal [Score] week -1	Fear [Score] week -1	Finger approach [Score] week -1	Head touch [Score] week -1	Body position [Score] week -1	Spontaneous activity [Score] week -1	Ataxic gait [Score] week -1	Hypotonic gait [Score] week -1	Twitches [Score] week -1	Tremors [Score] week -1	Seizures [Score] week -1
HD / F	071	4	4	4	4	4	4	4	0	0	0	0	0
	072	4	4	4	4	2	4	4	0	0	0	0	0
	073	4	4	4	4	4	4	4	0	0	0	0	0
	074	4	4	4	4	4	4	4	0	0	0	0	0
	075	4	4	4	4	4	4	4	0	0	0	0	0
	076	4	4	4	4	4	4	4	0	0	0	0	0
	077	4	4	4	4	2	4	4	0	0	0	0	0
	078	4	4	4	4	4	4	4	0	0	0	0	0
	079	4	4	4	4	4	4	4	0	0	0	0	0
	080	4	4	4	4	4	4	4	0	0	0	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week -1	Stereotypie [Score] week -1	Rearing supported [Score] week -1	Rearing not supported [Score] week -1	Urination [Score] week -1	Defecation [Score] week -1	Feaces consistency week -1	Abnormal vocalisation [Score] week -1	Aggressiveness [Score] week -1	Startle response [Score] week -1	Equilibrium reflex [Score] week -1	Positional passivity [Score] week -1
HD / F	071	0	0	8	0	0	0	4	0	0	4	4	4
	072	0	0	6	0	0	0	4	0	0	4	4	4
	073	0	0	8	0	0	0	4	0	0	4	4	4
	074	0	0	6	1	0	0	4	0	0	4	4	4
	075	0	0	11	0	1	0	4	0	0	4	4	4
	076	0	0	7	0	0	0	4	0	0	2	4	4
	077	0	0	13	2	0	0	4	0	0	4	4	4
	078	0	0	6	0	0	0	4	0	0	4	4	4
	079	0	0	9	0	0	0	4	0	0	4	4	4
	080	0	0	7	0	0	2	4	0	0	4	4	4

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week -1	Grip strength [Score] week -1	Pinching the tail [Score] week -1	Toe pinch reflex [Score] week -1	Limb tone [Score] week -1	Hind limb reflex [Score] week -1	Righting reflex ground [Score] week -1	Air righting reflex [Score] week -1	Pupil response [Score] week -1	Body temperature [°C] week -1	Anterior chamber of eye [Score] week -1	Fundus of the eye [Score] week -1
HD / F	071	4	4	4	4	4	4	0	0	4	38.5	0	0
	072	4	4	4	4	4	4	0	0	4	38.7	0	0
	073	4	4	4	4	4	4	0	0	4	38.6	0	0
	074	4	4	4	4	4	4	0	0	4	38.2	0	0
	075	4	4	4	4	4	4	0	0	4	38.2	0	0
	076	4	4	4	4	4	4	0	0	4	37.8	0	0
	077	4	4	4	4	4	4	0	0	4	38.6	0	0
	078	4	4	4	4	4	4	0	0	4	38.8	0	0
	079	4	4	4	4	4	4	0	0	4	38.3	0	0
	080	4	4	4	4	4	4	0	0	4	38.6	0	0

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Animal Sleeps [Score] week 13	Animal moving in cage [Score] week 13	Piloerection [Score] week 13	Vocalization [Score] week 13	O Grooming [Score] week 13	Salivation [Score] week 13	Lacrimation [Score] week 13	Changes in skin [Score] week 13	Cyanosis [Score] week 13	Exophthalmos [Score] week 13	Eyes opening [Score] week 13	Respiration [Score] week 13
HD / F	071	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	072	0	1	0	0	0	4	0	0	0	0	0	4
	073	0	1	0	0	0	4	0	0	0	0	0	4
	074	0	1	0	0	0	4	0	0	0	0	0	4
	075	0	1	0	0	0	4	0	0	0	0	0	4
	076	0	1	0	0	0	4	0	0	0	0	0	4
	077	0	1	0	0	0	4	0	0	0	0	0	4
	078	0	1	0	0	0	4	0	0	0	0	0	4
	079	0	1	0	0	0	4	0	0	0	0	0	4
	080	0	1	0	0	0	4	0	0	0	0	0	4

NS = No More Scheduled

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Response to handling [Score] week 13	Arousal [Score] week 13	Fear [Score] week 13	Finger approach [Score] week 13	Head touch [Score] week 13	Body position [Score] week 13	Spontaneous activity [Score] week 13	Ataxic gait [Score] week 13	Hypotonic gait [Score] week 13	Twitches [Score] week 13	Tremors [Score] week 13	Seizures [Score] week 13
HD / F	071	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	072	4	4	4	4	4	4	4	0	0	0	0	0
	073	4	4	4	4	4	4	4	0	0	0	0	0
	074	4	4	4	4	4	4	4	0	0	0	0	0
	075	4	4	4	4	4	4	4	0	0	0	0	0
	076	4	4	4	4	4	4	4	0	0	0	0	0
	077	4	4	4	4	4	4	4	0	0	0	0	0
	078	4	4	4	4	4	4	4	0	0	0	0	0
	079	4	4	4	4	4	4	4	0	0	0	0	0
	080	4	4	4	4	4	4	4	0	0	0	0	0

NS = No More Scheduled

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Unusual behavior [Score] week 13	Stereotypie [Score] week 13	Rearing supported [Score] week 13	Rearing not supported [Score] week 13	Urination [Score] week 13	Defecation [Score] week 13	Feaces consistency week 13	Abnormal vocalisation [Score] week 13	Aggressiveness [Score] week 13	Startle response [Score] week 13	Equilibrium reflex [Score] week 13	Positional passivity [Score] week 13
HD / F	071	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	072	0	0	3	0	0	0	4	0	0	4	4	4
	073	0	0	5	2	0	0	4	0	0	4	4	4
	074	0	0	4	2	0	0	4	0	0	4	4	4
	075	0	0	5	3	1	1	4	0	0	4	4	4
	076	0	0	2	1	2	3	4	0	0	4	4	4
	077	0	0	2	1	2	3	4	0	0	4	4	4
	078	0	0	6	0	0	1	4	0	0	4	4	4
	079	0	0	4	1	0	0	4	0	0	4	4	4
	080	0	0	6	0	0	0	4	0	0	4	4	4

NS = No More Scheduled

Individual Functional Observation Battery Big

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Visual placing [Score] week 13	Grip strength [Score] week 13	Pinching the tail [Score] week 13	Toe pinch reflex [Score] week 13	Limb tone [Score] week 13	Hind limb reflex [Score] week 13	Righting reflex ground [Score] week 13	Air righting reflex [Score] week 13	Pupil response [Score] week 13	Body temperature [°C] week 13	Anterior chamber of eye [Score] week 13	Fundus of the eye [Score] week 13
HD / F	071	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	072	4	4	4	4	4	4	0	0	4	38.8	0	0
	073	4	4	4	4	4	4	0	0	4	38.2	0	0
	074	4	4	4	4	4	4	0	0	4	38.6	0	0
	075	4	4	4	4	4	4	0	0	4	38.9	0	0
	076	4	4	4	4	4	4	0	0	4	37.6	0	0
	077	4	4	4	4	4	4	0	0	4	37.9	0	0
	078	4	4	4	4	4	4	0	0	4	38.5	0	0
	079	4	4	4	4	4	4	0	0	4	38.3	0	0
	080	4	4	4	4	4	4	0	0	4	38.3	0	0

NS = No More Scheduled

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
C / M	001	203.0	244.0	269.0	300.0	322.0	335.0	353.0	364.0	382.0	390.0	398.0	412.0	414.0	420.0
	002	211.0	248.0	281.0	310.0	332.0	350.0	367.0	374.0	390.0	401.0	410.0	430.0	434.0	438.0
	003	195.0	235.0	249.0	272.0	285.0	294.0	311.0	318.0	327.0	331.0	342.0	349.0	353.0	366.0
	004	205.0	244.0	271.0	292.0	314.0	324.0	344.0	349.0	357.0	361.0	371.0	384.0	391.0	399.0
	005	200.0	244.0	277.0	314.0	332.0	342.0	366.0	372.0	374.0	384.0	392.0	394.0	397.0	406.0
	006	199.0	240.0	268.0	298.0	312.0	327.0	340.0	342.0	349.0	356.0	369.0	379.0	378.0	380.0
	007	200.0	238.0	261.0	293.0	304.0	317.0	326.0	331.0	343.0	346.0	351.0	365.0	366.0	373.0
	008	221.0	260.0	286.0	323.0	336.0	352.0	374.0	377.0	383.0	392.0	403.0	412.0	416.0	417.0
	009	203.0	235.0	255.0	274.0	288.0	301.0	318.0	326.0	343.0	344.0	353.0	363.0	368.0	370.0
	010	205.0	239.0	263.0	285.0	302.0	319.0	335.0	340.0	356.0	363.0	375.0	384.0	393.0	395.0

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
LD / M	011	200.0	243.0	264.0	284.0	292.0	294.0	308.0	314.0	324.0	336.0	340.0	351.0	359.0	360.0
	012	208.0	242.0	254.0	270.0	283.0	293.0	312.0	311.0	321.0	327.0	332.0	348.0	344.0	351.0
	013	192.0	227.0	253.0	277.0	295.0	308.0	323.0	328.0	337.0	341.0	342.0	354.0	356.0	363.0
	014	223.0	256.0	290.0	311.0	326.0	342.0	354.0	364.0	368.0	373.0	382.0	393.0	396.0	402.0
	015	200.0	240.0	268.0	300.0	316.0	337.0	350.0	360.0	365.0	368.0	378.0	394.0	386.0	393.0
	016	204.0	233.0	259.0	273.0	294.0	308.0	318.0	325.0	331.0	334.0	342.0	355.0	357.0	357.0
	017	221.0	250.0	275.0	309.0	329.0	351.0	365.0	370.0	380.0	376.0	398.0	412.0	408.0	413.0
	018	220.0	251.0	272.0	297.0	314.0	329.0	343.0	343.0	359.0	359.0	375.0	388.0	392.0	399.0
	019	216.0	257.0	279.0	306.0	324.0	335.0	352.0	353.0	365.0	367.0	380.0	391.0	393.0	389.0
	020	205.0	244.0	282.0	309.0	329.0	345.0	360.0	371.0	384.0	388.0	404.0	420.0	423.0	421.0

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
MD / M	021	194.0	231.0	256.0	281.0	298.0	306.0	316.0	329.0	336.0	340.0	350.0	362.0	364.0	367.0
	022	195.0	222.0	247.0	265.0	270.0	276.0	282.0	287.0	293.0	297.0	310.0	320.0	323.0	326.0
	023	212.0	254.0	290.0	317.0	338.0	350.0	370.0	382.0	392.0	402.0	406.0	412.0	415.0	418.0
	024	192.0	228.0	253.0	278.0	290.0	302.0	324.0	333.0	338.0	352.0	361.0	367.0	369.0	375.0
	025	205.0	241.0	268.0	303.0	321.0	342.0	356.0	371.0	377.0	387.0	401.0	409.0	412.0	419.0
	026	211.0	239.0	260.0	281.0	305.0	318.0	332.0	340.0	352.0	362.0	366.0	381.0	381.0	381.0
	027	220.0	253.0	283.0	309.0	327.0	348.0	361.0	367.0	370.0	380.0	392.0	401.0	407.0	407.0
	028	220.0	254.0	279.0	304.0	326.0	341.0	355.0	367.0	377.0	383.0	397.0	411.0	409.0	414.0
	029	212.0	245.0	272.0	298.0	312.0	318.0	331.0	340.0	345.0	352.0	360.0	376.0	375.0	377.0
	030	211.0	244.0	263.0	292.0	308.0	326.0	344.0	350.0	364.0	369.0	376.0	392.0	393.0	397.0

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
HD / M	031	204.0	240.0	262.0	292.0	310.0	325.0	343.0	358.0	372.0	379.0	390.0	403.0	408.0	413.0
	032	199.0	228.0	249.0	273.0	293.0	305.0	316.0	322.0	331.0	340.0	350.0	358.0	362.0	369.0
	033	196.0	249.0	287.0	318.0	334.0	347.0	364.0	364.0	375.0	381.0	389.0	393.0	395.0	405.0
	034	202.0	240.0	272.0	299.0	310.0	320.0	334.0	340.0	348.0	353.0	363.0	368.0	370.0	373.0
	035	200.0	240.0	272.0	292.0	319.0	329.0	346.0	356.0	368.0	368.0	383.0	392.0	400.0	402.0
	036	212.0	248.0	276.0	305.0	318.0	333.0	348.0	358.0	374.0	374.0	374.0	389.0	392.0	399.0
	037	216.0	245.0	267.0	285.0	299.0	309.0	325.0	320.0	325.0	330.0	333.0	349.0	349.0	343.0
	038	217.0	244.0	264.0	331.0	303.0	315.0	325.0	328.0	343.0	356.0	366.0	373.0	377.0	378.0
	039	224.0	265.0	302.0	300.0	352.0	371.0	383.0	388.0	402.0	408.0	422.0	435.0	445.0	444.0
	040	212.0	244.0	268.0	290.0	305.0	317.0	326.0	327.0	340.0	340.0	346.0	357.0	352.0	357.0

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
C / F	041	163.0	174.0	192.0	191.0	215.0	216.0	215.0	215.0	218.0	227.0	228.0	225.0	233.0	225.0
	042	172.0	184.0	193.0	208.0	220.0	219.0	222.0	227.0	230.0	238.0	233.0	240.0	242.0	245.0
	043	164.0	177.0	195.0	204.0	212.0	205.0	217.0	225.0	223.0	228.0	230.0	237.0	238.0	239.0
	044	177.0	188.0	207.0	215.0	227.0	222.0	234.0	236.0	240.0	240.0	244.0	249.0	250.0	249.0
	045	169.0	181.0	190.0	200.0	213.0	217.0	210.0	225.0	223.0	229.0	224.0	229.0	234.0	231.0
	046	165.0	179.0	195.0	207.0	210.0	220.0	222.0	221.0	216.0	229.0	231.0	232.0	229.0	236.0
	047	155.0	179.0	189.0	183.0	200.0	207.0	212.0	207.0	222.0	226.0	224.0	223.0	231.0	222.0
	048	172.0	188.0	200.0	204.0	218.0	222.0	232.0	228.0	234.0	237.0	240.0	241.0	245.0	240.0
	049	153.0	164.0	174.0	182.0	198.0	200.0	200.0	197.0	204.0	209.0	210.0	209.0	213.0	207.0
	050	165.0	176.0	181.0	203.0	208.0	213.0	215.0	222.0	222.0	228.0	225.0	234.0	234.0	239.0

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
LD / F	051	152.0	166.0	185.0	192.0	189.0	202.0	211.0	217.0	211.0	222.0	226.0	225.0	219.0	231.0
	052	162.0	175.0	180.0	198.0	208.0	210.0	214.0	221.0	218.0	224.0	219.0	229.0	235.0	235.0
	053	163.0	175.0	185.0	190.0	210.0	220.0	213.0	226.0	225.0	230.0	233.0	242.0	242.0	246.0
	054	150.0	167.0	188.0	194.0	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	158.0	164.0	178.0	187.0	197.0	193.0	202.0	205.0	204.0	205.0	210.0	212.0	211.0	213.0
	056	171.0	181.0	190.0	195.0	206.0	208.0	213.0	210.0	224.0	224.0	230.0	232.0	237.0	228.0
	057	165.0	184.0	198.0	215.0	216.0	230.0	230.0	232.0	238.0	250.0	248.0	248.0	250.0	254.0
	058	172.0	180.0	191.0	200.0	200.0	208.0	205.0	215.0	214.0	224.0	226.0	230.0	224.0	232.0
	059	153.0	176.0	194.0	200.0	204.0	204.0	222.0	220.0	222.0	222.0	226.0	231.0	233.0	244.0
	060	168.0	191.0	205.0	219.0	214.0	228.0	233.0	232.0	231.0	235.0	235.0	238.0	239.0	244.0

NS = No More Scheduled

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
MD / F	061	162.0	171.0	190.0	193.0	205.0	208.0	214.0	215.0	217.0	222.0	228.0	228.0	237.0	233.0
	062	157.0	166.0	180.0	193.0	201.0	207.0	206.0	213.0	216.0	219.0	222.0	231.0	233.0	232.0
	063	162.0	175.0	196.0	208.0	216.0	215.0	228.0	230.0	230.0	230.0	234.0	242.0	244.0	246.0
	064	153.0	171.0	182.0	199.0	206.0	209.0	213.0	227.0	233.0	231.0	227.0	232.0	240.0	237.0
	065	153.0	176.0	190.0	196.0	211.0	207.0	216.0	222.0	218.0	227.0	225.0	233.0	230.0	239.0
	066	162.0	180.0	196.0	200.0	200.0	210.0	220.0	214.0	218.0	225.0	228.0	233.0	225.0	229.0
	067	169.0	183.0	192.0	209.0	212.0	213.0	217.0	226.0	232.0	234.0	230.0	237.0	242.0	239.0
	068	152.0	164.0	183.0	192.0	194.0	203.0	210.0	208.0	210.0	218.0	222.0	223.0	214.0	221.0
	069	166.0	180.0	191.0	212.0	218.0	223.0	223.0	232.0	240.0	240.0	230.0	243.0	249.0	245.0
	070	155.0	171.0	181.0	191.0	197.0	211.0	209.0	210.0	210.0	220.0	225.0	228.0	222.0	225.0

Individual Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	day 1	day 8	day 15	day 22	day 29	day 36	day 43	day 50	day 57	day 64	day 71	day 78	day 85	day 90
HD / F	071	170.0	181.0	189.0	208.0	212.0	218.0	218.0	226.0	228.0	230.0	231.0	238.0	NS	NS
	072	149.0	158.0	173.0	174.0	188.0	193.0	192.0	200.0	199.0	208.0	208.0	207.0	205.0	211.0
	073	157.0	171.0	181.0	186.0	197.0	206.0	205.0	213.0	219.0	222.0	225.0	222.0	227.0	224.0
	074	146.0	156.0	180.0	190.0	197.0	200.0	208.0	215.0	211.0	207.0	223.0	225.0	227.0	230.0
	075	173.0	192.0	208.0	209.0	226.0	235.0	236.0	239.0	242.0	250.0	250.0	251.0	258.0	253.0
	076	159.0	173.0	181.0	195.0	200.0	208.0	207.0	215.0	220.0	225.0	227.0	231.0	230.0	229.0
	077	159.0	172.0	180.0	200.0	200.0	212.0	217.0	218.0	215.0	225.0	228.0	235.0	225.0	218.0
	078	169.0	186.0	190.0	200.0	204.0	212.0	221.0	216.0	224.0	235.0	233.0	235.0	238.0	234.0
	079	160.0	177.0	188.0	197.0	204.0	213.0	217.0	217.0	224.0	230.0	230.0	230.0	235.0	236.0
	080	177.0	193.0	205.0	207.0	223.0	229.0	232.0	227.0	244.0	245.0	246.0	248.0	253.0	247.0

NS = No More Scheduled

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
C / M	001	41.0	25.0	31.0	22.0	13.0	18.0	11.0	18.0	8.0	8.0	14.0	2.0	6.0	217.0
	002	37.0	33.0	29.0	22.0	18.0	17.0	7.0	16.0	11.0	9.0	20.0	4.0	4.0	227.0
	003	40.0	14.0	23.0	13.0	9.0	17.0	7.0	9.0	4.0	11.0	7.0	4.0	13.0	171.0
	004	39.0	27.0	21.0	22.0	10.0	20.0	5.0	8.0	4.0	10.0	13.0	7.0	8.0	194.0
	005	44.0	33.0	37.0	18.0	10.0	24.0	6.0	2.0	10.0	8.0	2.0	3.0	9.0	206.0
	006	41.0	28.0	30.0	14.0	15.0	13.0	2.0	7.0	7.0	13.0	10.0	-1.0	2.0	181.0
	007	38.0	23.0	32.0	11.0	13.0	9.0	5.0	12.0	3.0	5.0	14.0	1.0	7.0	173.0
	008	39.0	26.0	37.0	13.0	16.0	22.0	3.0	6.0	9.0	11.0	9.0	4.0	1.0	196.0
	009	32.0	20.0	19.0	14.0	13.0	17.0	8.0	17.0	1.0	9.0	10.0	5.0	2.0	167.0
	010	34.0	24.0	22.0	17.0	17.0	16.0	5.0	16.0	7.0	12.0	9.0	9.0	2.0	190.0

d = day

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
LD / M	011	43.0	21.0	20.0	8.0	2.0	14.0	6.0	10.0	12.0	4.0	11.0	8.0	1.0	160.0
	012	34.0	12.0	16.0	13.0	10.0	19.0	-1.0	10.0	6.0	5.0	16.0	-4.0	7.0	143.0
	013	35.0	26.0	24.0	18.0	13.0	15.0	5.0	9.0	4.0	1.0	12.0	2.0	7.0	171.0
	014	33.0	34.0	21.0	15.0	16.0	12.0	10.0	4.0	5.0	9.0	11.0	3.0	6.0	179.0
	015	40.0	28.0	32.0	16.0	21.0	13.0	10.0	5.0	3.0	10.0	16.0	-8.0	7.0	193.0
	016	29.0	26.0	14.0	21.0	14.0	10.0	7.0	6.0	3.0	8.0	13.0	2.0	0.0	153.0
	017	29.0	25.0	34.0	20.0	22.0	14.0	5.0	10.0	-4.0	22.0	14.0	-4.0	5.0	192.0
	018	31.0	21.0	25.0	17.0	15.0	14.0	0.0	16.0	0.0	16.0	13.0	4.0	7.0	179.0
	019	41.0	22.0	27.0	18.0	11.0	17.0	1.0	12.0	2.0	13.0	11.0	2.0	-4.0	173.0
	020	39.0	38.0	27.0	20.0	16.0	15.0	11.0	13.0	4.0	16.0	16.0	3.0	-2.0	216.0

d = day

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
MD / M	021	37.0	25.0	25.0	17.0	8.0	10.0	13.0	7.0	4.0	10.0	12.0	2.0	3.0	173.0
	022	27.0	25.0	18.0	5.0	6.0	6.0	5.0	6.0	4.0	13.0	10.0	3.0	3.0	131.0
	023	42.0	36.0	27.0	21.0	12.0	20.0	12.0	10.0	10.0	4.0	6.0	3.0	3.0	206.0
	024	36.0	25.0	25.0	12.0	12.0	22.0	9.0	5.0	14.0	9.0	6.0	2.0	6.0	183.0
	025	36.0	27.0	35.0	18.0	21.0	14.0	15.0	6.0	10.0	14.0	8.0	3.0	7.0	214.0
	026	28.0	21.0	21.0	24.0	13.0	14.0	8.0	12.0	10.0	4.0	15.0	0.0	0.0	170.0
	027	33.0	30.0	26.0	18.0	21.0	13.0	6.0	3.0	10.0	12.0	9.0	6.0	0.0	187.0
	028	34.0	25.0	25.0	22.0	15.0	14.0	12.0	10.0	6.0	14.0	14.0	-2.0	5.0	194.0
	029	33.0	27.0	26.0	14.0	6.0	13.0	9.0	5.0	7.0	8.0	16.0	-1.0	2.0	165.0
	030	33.0	19.0	29.0	16.0	18.0	18.0	6.0	14.0	5.0	7.0	16.0	1.0	4.0	186.0

d = day

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
HD / M	031	36.0	22.0	30.0	18.0	15.0	18.0	15.0	14.0	7.0	11.0	13.0	5.0	5.0	209.0
	032	29.0	21.0	24.0	20.0	12.0	11.0	6.0	9.0	9.0	10.0	8.0	4.0	7.0	170.0
	033	53.0	38.0	31.0	16.0	13.0	17.0	0.0	11.0	6.0	8.0	4.0	2.0	10.0	209.0
	034	38.0	32.0	27.0	11.0	10.0	14.0	6.0	8.0	5.0	10.0	5.0	2.0	3.0	171.0
	035	40.0	32.0	20.0	27.0	10.0	17.0	10.0	12.0	0.0	15.0	9.0	8.0	2.0	202.0
	036	36.0	28.0	29.0	13.0	15.0	15.0	10.0	16.0	0.0	0.0	15.0	3.0	7.0	187.0
	037	29.0	22.0	18.0	14.0	10.0	16.0	-5.0	5.0	5.0	3.0	16.0	0.0	-6.0	127.0
	038	27.0	20.0	67.0	-28.0	12.0	10.0	3.0	15.0	13.0	10.0	7.0	4.0	1.0	161.0
	039	41.0	37.0	-2.0	52.0	19.0	12.0	5.0	14.0	6.0	14.0	13.0	10.0	-1.0	220.0
	040	32.0	24.0	22.0	15.0	12.0	9.0	1.0	13.0	0.0	6.0	11.0	-5.0	5.0	145.0

d = day

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
C / F	041	11.0	18.0	-1.0	24.0	1.0	-1.0	0.0	3.0	9.0	1.0	-3.0	8.0	-8.0	62.0
	042	12.0	9.0	15.0	12.0	-1.0	3.0	5.0	3.0	8.0	-5.0	7.0	2.0	3.0	73.0
	043	13.0	18.0	9.0	8.0	-7.0	12.0	8.0	-2.0	5.0	2.0	7.0	1.0	1.0	75.0
	044	11.0	19.0	8.0	12.0	-5.0	12.0	2.0	4.0	0.0	4.0	5.0	1.0	-1.0	72.0
	045	12.0	9.0	10.0	13.0	4.0	-7.0	15.0	-2.0	6.0	-5.0	5.0	5.0	-3.0	62.0
	046	14.0	16.0	12.0	3.0	10.0	2.0	-1.0	-5.0	13.0	2.0	1.0	-3.0	7.0	71.0
	047	24.0	10.0	-6.0	17.0	7.0	5.0	-5.0	15.0	4.0	-2.0	-1.0	8.0	-9.0	67.0
	048	16.0	12.0	4.0	14.0	4.0	10.0	-4.0	6.0	3.0	3.0	1.0	4.0	-5.0	68.0
	049	11.0	10.0	8.0	16.0	2.0	0.0	-3.0	7.0	5.0	1.0	-1.0	4.0	-6.0	54.0
	050	11.0	5.0	22.0	5.0	5.0	2.0	7.0	0.0	6.0	-3.0	9.0	0.0	5.0	74.0

d = day

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
LD / F	051	14.0	19.0	7.0	-3.0	13.0	9.0	6.0	-6.0	11.0	4.0	-1.0	-6.0	12.0	79.0
	052	13.0	5.0	18.0	10.0	2.0	4.0	7.0	-3.0	6.0	-5.0	10.0	6.0	0.0	73.0
	053	12.0	10.0	5.0	20.0	10.0	-7.0	13.0	-1.0	5.0	3.0	9.0	0.0	4.0	83.0
	054	17.0	21.0	6.0	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	055	6.0	14.0	9.0	10.0	-4.0	9.0	3.0	-1.0	1.0	5.0	2.0	-1.0	2.0	55.0
	056	10.0	9.0	5.0	11.0	2.0	5.0	-3.0	14.0	0.0	6.0	2.0	5.0	-9.0	57.0
	057	19.0	14.0	17.0	1.0	14.0	0.0	2.0	6.0	12.0	-2.0	0.0	2.0	4.0	89.0
	058	8.0	11.0	9.0	0.0	8.0	-3.0	10.0	-1.0	10.0	2.0	4.0	-6.0	8.0	60.0
	059	23.0	18.0	6.0	4.0	0.0	18.0	-2.0	2.0	0.0	4.0	5.0	2.0	11.0	91.0
	060	23.0	14.0	14.0	-5.0	14.0	5.0	-1.0	-1.0	4.0	0.0	3.0	1.0	5.0	76.0

d = day; NS = No More Scheduled

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
MD / F	061	9.0	19.0	3.0	12.0	3.0	6.0	1.0	2.0	5.0	6.0	0.0	9.0	-4.0	71.0
	062	9.0	14.0	13.0	8.0	6.0	-1.0	7.0	3.0	3.0	3.0	9.0	2.0	-1.0	75.0
	063	13.0	21.0	12.0	8.0	-1.0	13.0	2.0	0.0	0.0	4.0	8.0	2.0	2.0	84.0
	064	18.0	11.0	17.0	7.0	3.0	4.0	14.0	6.0	-2.0	-4.0	5.0	8.0	-3.0	84.0
	065	23.0	14.0	6.0	15.0	-4.0	9.0	6.0	-4.0	9.0	-2.0	8.0	-3.0	9.0	86.0
	066	18.0	16.0	4.0	0.0	10.0	10.0	-6.0	4.0	7.0	3.0	5.0	-8.0	4.0	67.0
	067	14.0	9.0	17.0	3.0	1.0	4.0	9.0	6.0	2.0	-4.0	7.0	5.0	-3.0	70.0
	068	12.0	19.0	9.0	2.0	9.0	7.0	-2.0	2.0	8.0	4.0	1.0	-9.0	7.0	69.0
	069	14.0	11.0	21.0	6.0	5.0	0.0	9.0	8.0	0.0	-10.0	13.0	6.0	-4.0	79.0
	070	16.0	10.0	10.0	6.0	14.0	-2.0	1.0	0.0	10.0	5.0	3.0	-6.0	3.0	70.0

d = day

Individual Changes Body Weights - BW / Body Weights [g]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90	d 1 -> 90
HD / F	071	11.0	8.0	19.0	4.0	6.0	0.0	8.0	2.0	2.0	1.0	7.0	NS	NS	NS
	072	9.0	15.0	1.0	14.0	5.0	-1.0	8.0	-1.0	9.0	0.0	-1.0	-2.0	6.0	62.0
	073	14.0	10.0	5.0	11.0	9.0	-1.0	8.0	6.0	3.0	3.0	-3.0	5.0	-3.0	67.0
	074	10.0	24.0	10.0	7.0	3.0	8.0	7.0	-4.0	-4.0	16.0	2.0	2.0	3.0	84.0
	075	19.0	16.0	1.0	17.0	9.0	1.0	3.0	3.0	8.0	0.0	1.0	7.0	-5.0	80.0
	076	14.0	8.0	14.0	5.0	8.0	-1.0	8.0	5.0	5.0	2.0	4.0	-1.0	-1.0	70.0
	077	13.0	8.0	20.0	0.0	12.0	5.0	1.0	-3.0	10.0	3.0	7.0	-10.0	-7.0	59.0
	078	17.0	4.0	10.0	4.0	8.0	9.0	-5.0	8.0	11.0	-2.0	2.0	3.0	-4.0	65.0
	079	17.0	11.0	9.0	7.0	9.0	4.0	0.0	7.0	6.0	0.0	0.0	5.0	1.0	76.0
	080	16.0	12.0	2.0	16.0	6.0	3.0	-5.0	17.0	1.0	1.0	2.0	5.0	-6.0	70.0

d = day; NS = No More Scheduled

Individual Food Consumption [g/kg/Day]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Group	Cage	Animals	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50
C / M	001	005, 004, 002, 001, 003	97.5	92.4	84.9	82.6	75.2	72.4	68.3
	002	008, 010, 006, 007, 009	97.4	91.3	83.3	77.5	74.2	69.2	68.1
LD / M	003	015, 012, 013, 011, 014	95.4	90.5	80.8	76.9	71.9	69.3	66.0
	004	019, 016, 020, 017, 018	99.1	91.2	82.4	77.5	71.9	67.9	68.3
MD / M	005	024, 025, 022, 023, 021	97.5	97.1	86.1	78.7	72.1	70.6	68.7
	006	029, 028, 030, 026, 027	96.3	90.1	80.3	79.0	74.6	70.7	70.0
HD / M	007	034, 032, 033, 031, 035	96.5	94.0	83.2	77.3	74.7	71.1	70.3
	008	038, 036, 039, 040, 037	97.6	93.7	82.7	80.4	74.8	71.1	71.4

d = day

Individual Food Consumption [g/kg/Day]

Ascentos™ 1.1

Sex: **Male** - Phase: **In-life**

Group	Cage	Animals	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90
C / M	001	005, 004, 002, 001, 003	65.3	63.5	63.0	59.5	58.8	59.3
	002	008, 010, 006, 007, 009	65.0	65.4	62.2	59.0	57.6	56.4
LD / M	003	015, 012, 013, 011, 014	64.5	62.1	61.8	59.5	60.7	59.3
	004	019, 016, 020, 017, 018	64.4	64.5	61.9	59.1	58.5	55.9
MD / M	005	024, 025, 022, 023, 021	65.5	63.7	63.9	60.3	61.5	60.1
	006	029, 028, 030, 026, 027	66.5	66.6	61.9	60.4	58.9	56.9
HD / M	007	034, 032, 033, 031, 035	66.2	65.6	62.9	60.4	60.3	59.4
	008	038, 036, 039, 040, 037	69.0	69.6	65.0	64.3	61.0	60.1

d = day

Individual Food Consumption [g/kg/Day]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Group	Cage	Animals	d 1 -> 8	d 8 -> 15	d 15 -> 22	d 22 -> 29	d 29 -> 36	d 36 -> 43	d 43 -> 50
C / F	009	042, 044, 045, 041, 043	93.1	93.1	85.4	86.1	80.7	80.3	80.3
	010	049, 050, 046, 048, 047	93.2	94.1	89.8	87.4	81.0	78.7	78.2
LD / F	011	055, 051, 052, 053, 054	100.1	97.9	87.7	86.4	86.6	81.9	82.4
	012	057, 059, 060, 058, 056	97.5	94.0	90.1	87.4	82.8	78.6	76.9
MD / F	013	061, 064, 063, 062, 065	98.8	101.0	95.3	91.3	85.2	86.3	86.5
	014	068, 066, 067, 069, 070	98.0	99.3	94.2	89.0	86.9	84.3	83.3
HD / F	015	075, 071, 073, 074, 072	98.0	95.5	92.0	86.7	83.4	81.1	82.3
	016	076, 079, 080, 078, 077	96.7	94.9	101.2	88.0	85.1	82.8	81.8

d = day

Individual Food Consumption [g/kg/Day]

Ascentos™ 1.1

Sex: **Female** - Phase: **In-life**

Group	Cage	Animals	d 50 -> 57	d 57 -> 64	d 64 -> 71	d 71 -> 78	d 78 -> 85	d 85 -> 90
C / F	009	042, 044, 045, 041, 043	76.2	78.9	73.5	73.7	68.4	72.9
	010	049, 050, 046, 048, 047	76.0	77.0	74.4	74.9	71.7	73.9
LD / F	011	055, 051, 052, 053, 054	77.4	82.6	75.7	75.4	70.5	74.9
	012	057, 059, 060, 058, 056	79.2	78.7	EX	EX	74.3	74.6
MD / F	013	061, 064, 063, 062, 065	82.6	86.6	79.2	79.4	73.8	76.8
	014	068, 066, 067, 069, 070	80.5	85.8	79.9	78.5	76.4	76.8
HD / F	015	075, 071, 073, 074, 072	77.7	82.5	77.7	74.3	67.7	76.3
	016	076, 079, 080, 078, 077	81.6	83.0	78.8	78.9	73.0	72.5

d = day; EX = Exclude

Individual Haematology - Males

Group	Animal No.	RBC	Hb	Hct	MCV	MCH	MCHC	PLT	WBC	Neu	Lym	Mono	Eos	Baso	Luc	RE
	Units	10^{12}/L	g/dL	%	fL	pg/Ery	g/L	10^{9}/L	10^{9}/L	%	%	%	%	%	%	%
C	1	9.01	16.2	47.7	53.0	18.0	33.9	820	5.35	30.8	65.5	2.7	1.0	0.0	0.1	1.52
	2	9.01	15.1	46.1	51.2	16.7	32.7	824	4.90	18.5	78.3	2.5	0.4	0.1	0.2	1.80
	3	9.08	15.1	45.7	50.3	16.6	32.9	832	5.92	20.8	75.4	2.7	0.8	0.1	0.1	1.68
	4	9.13	16.7	50.0	54.7	18.3	33.4	767	4.72	36.9	58.6	3.8	0.4	0.0	0.2	1.88
	5	8.88	15.4	47.0	52.9	17.4	32.9	803	4.10	18.6	78.5	2.3	0.3	0.0	0.3	1.57
	6	8.36	15.8	45.4	54.4	18.9	34.8	654	4.05	12.8	85.0	1.4	0.5	0.1	0.2	1.17
	7	9.18	15.7	46.1	50.3	17.1	34.1	760	4.55	31.4	65.1	2.7	0.7	0.0	0.1	1.76
	8	8.90	15.9	46.7	52.5	17.9	34.0	706	3.73	26.1	71.0	2.0	0.6	0.0	0.2	1.49
	9	9.03	16.1	46.9	52.0	17.9	34.4	716	4.49	23.9	72.4	2.7	0.7	0.1	0.3	1.76
	10	9.60	16.3	49.0	51.0	17.0	33.4	778	2.24	23.0	72.3	3.9	0.4	0.1	0.4	1.60
LD	11	9.06	16.3	48.1	53.1	18.0	33.8	889	3.82	29.4	68.1	1.9	0.5	0.0	0.1	1.47
	12	8.78	15.8	45.7	52.1	18.0	34.6	797	2.40	32.8	65.5	1.5	0.1	0.0	0.1	1.75
	13	9.08	15.5	46.5	51.2	17.1	33.3	863	4.55	30.0	66.9	2.0	0.9	0.1	0.2	1.58
	14	9.25	15.3	46.9	50.6	16.5	32.6	743	4.06	18.3	79.3	2.2	0.1	0.0	0.2	1.63
	15	9.08	16.1	47.3	52.1	17.7	33.9	760	4.07	25.8	70.8	2.8	0.4	0.1	0.1	1.52
	16	9.21	16.4	47.0	51.1	17.8	34.8	752	2.87	29.0	68.1	2.2	0.5	0.1	0.1	1.45
	17	8.43	14.9	43.4	51.5	17.7	34.4	777	4.35	23.1	71.3	4.5	0.7	0.1	0.3	1.49
	18	8.59	16.4	44.9	52.3	19.1	36.5	728	2.81	40.8	54.1	4.2	0.7	0.1	0.2	1.72
	19	9.19	16.2	47.1	51.3	17.6	34.4	798	5.56	30.9	64.0	3.9	0.6	0.1	0.5	1.29
	20	9.12	16.0	46.1	50.5	17.5	34.7	898	4.86	18.9	77.9	2.5	0.4	0.0	0.2	1.22

Individual Haematology – Males (Continued)

Group	Animal No.	RBC	Hb	Hct	MCV	MCH	MCHC	PLT	WBC	Neu	Lym	Mono	Eos	Baso	Luc	RE
	Units	10^{12}/L	g/dL	%	fL	pg/Ery	g/L	10^{9}/L	10^{9}/L	%	%	%	%	%	%	%
MD	21	9.29	15.7	48.1	51.7	17.0	32.8	831	3.39	42.2	53.5	3.4	0.8	0.0	0.1	1.38
	22	8.94	15.8	46.8	52.4	17.7	33.7	750	3.35	30.1	67.8	1.5	0.5	0.0	0.1	1.09
	23	9.31	15.7	47.6	51.2	16.9	33.0	737	3.54	27.4	67.7	4.1	0.4	0.1	0.4	1.63
	24	8.86	15.5	46.7	52.7	17.5	33.2	794	4.18	36.5	58.4	3.6	1.2	0.1	0.1	1.35
	25	8.66	15.6	46.5	53.7	18.0	33.5	774	4.53	21.1	75.5	3.0	0.3	0.1	0.1	1.84
	26	9.30	16.5	47.6	51.1	17.8	34.8	764	3.12	26.1	71.1	1.9	0.8	0.0	0.1	1.30
	27	8.76	15.8	45.8	52.3	18.0	34.5	706	3.14	25.4	71.6	2.6	0.4	0.0	0.1	1.73
	28	8.67	15.8	46.3	53.4	18.2	34.2	731	3.53	26.7	70.9	1.8	0.2	0.1	0.4	1.27
	29	9.02	16.3	46.2	51.3	18.1	35.3	693	5.16	18.8	76.5	3.5	0.5	0.1	0.5	1.44
	30	9.36	16.7	49.0	52.3	17.8	34.1	878	4.03	31.6	63.3	4.6	0.4	0.1	0.1	1.30
HD	31	9.02	15.3	47.4	52.6	16.9	32.2	811	4.24	31.7	64.0	3.7	0.4	0.1	0.1	1.96
	32	8.82	16.4	49.3	56.0	18.6	33.3	698	5.09	15.8	78.9	4.0	0.7	0.1	0.4	1.59
	33	9.37	16.6	48.2	51.4	17.7	34.5	774	4.65	20.9	76.5	2.0	0.4	0.1	0.1	1.48
	34	9.61	16.6	49.5	51.5	17.2	33.5	708	4.95	28.5	68.2	2.5	0.6	0.1	0.1	1.60
	35	9.17	16.4	48.8	53.1	17.9	33.7	445	2.54	30.1	67.0	2.1	0.5	0.1	0.0	1.54
	36	8.66	15.3	45.3	52.3	17.6	33.7	739	3.49	20.0	77.8	1.6	0.2	0.0	0.3	1.04
	37	9.66	17.2	50.8	52.6	17.8	33.8	633	5.02	17.8	79.0	2.3	0.6	0.1	0.2	1.17
	38	9.70	16.5	47.8	49.3	17.0	34.5	857	3.41	29.6	65.2	4.5	0.4	0.1	0.3	1.37
	39	9.22	15.9	46.7	50.6	17.2	34.0	860	5.55	29.5	65.3	4.6	0.3	0.2	0.3	1.99
	40	9.12	16.2	47.2	51.7	17.8	34.3	758	6.16	17.7	78.7	2.9	0.2	0.1	0.4	1.54

Individual Haematology - Females

Group	Animal No.	RBC	Hb	Hct	MCV	MCH	MCHC	PLT	WBC	Neu	Lym	Mono	Eos	Baso	Luc	RE
	Units	10^{12}/L	g/dL	%	fL	pg/Ery	g/dL	10^{9}/L	10^{9}/L	%	%	%	%	%	%	%
C	41	8.12	16.0	46.3	57.0	19.7	34.5	954	2.00	17.7	79.7	1.9	0.6	0.0	0.1	1.93
	42	8.07	15.2	44.8	55.5	18.9	34.0	694	2.34	28.0	67.8	3.7	0.4	0.0	0.1	2.41
	43	8.30	15.7	45.5	54.8	18.9	34.4	563	2.65	14.0	83.0	1.8	1.1	0.0	0.1	2.07
	44	7.99	14.6	43.1	54.0	18.3	33.9	884	2.00	24.8	70.4	4.0	0.7	0.0	0.1	1.97
	45	8.74	16.0	45.9	52.5	18.3	34.9	735	2.03	22.0	75.8	1.6	0.4	0.1	0.1	1.94
	46	7.82	14.6	43.6	55.7	18.7	33.5	791	1.60	15.9	80.9	2.3	0.5	0.1	0.2	1.97
	47	8.03	15.4	44.8	55.7	19.2	34.4	795	1.02	26.7	71.0	1.6	0.3	0.2	0.1	1.82
	48	8.86	16.0	47.4	53.5	18.1	33.8	647	3.55	15.3	82.2	2.1	0.3	0.1	0.1	2.10
	49	8.42	15.2	46.0	54.6	18.0	33.1	842	2.66	21.8	75.2	2.4	0.3	0.0	0.2	1.36
	50	8.31	15.5	44.9	54.0	18.6	34.5	782	3.32	15.0	82.0	2.5	0.3	0.0	0.2	2.27
LD	51	8.58	16.4	45.7	53.3	19.1	35.9	814	1.70	21.4	75.3	2.6	0.5	0.1	0.2	1.35
	52	8.13	15.4	44.7	55.0	18.9	34.4	765	1.80	26.4	71.2	1.8	0.4	0.1	0.1	2.00
	53	8.43	15.8	46.3	54.9	18.8	34.2	709	4.24	12.6	85.1	1.7	0.2	0.2	0.2	1.69
	54	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
	55	8.48	15.5	45.7	53.9	18.3	33.9	874	2.57	20.2	75.6	3.3	0.6	0.0	0.2	2.14
	56	7.89	15.6	43.7	55.3	19.8	35.8	722	2.99	17.4	79.2	3.0	0.3	0.2	0.0	1.80
	57	8.49	15.1	44.4	52.3	17.8	34.1	696	3.14	17.8	78.9	2.6	0.4	0.1	0.2	1.66
	58	8.33	15.4	44.7	53.7	18.5	34.4	818	3.69	11.5	84.6	3.4	0.2	0.1	0.2	1.68
	59	8.20	15.3	43.7	53.3	18.7	35.1	771	2.02	14.5	82.6	2.3	0.3	0.1	0.2	1.89
	60	8.81	16.2	46.8	53.0	18.3	34.6	895	3.60	14.3	80.7	4.2	0.5	0.1	0.2	1.48

n.a. = no data available

Individual Haematology – Females (Continued)

Group	Animal No.	RBC	Hb	Hct	MCV	MCH	MCHC	PLT	WBC	Neu	Lym	Mono	Eos	Baso	Luc	RE
	Units	10^{12}/L	g/dL	%	fL	pg/Ery	g/dL	10^{9}/L	10^{9}/L	%	%	%	%	%	%	%
MD	61	7.86	15.0	42.7	54.3	19.0	35.1	768	3.34	18.5	77.3	2.7	1.4	0.1	0.0	1.25
	62	7.81	14.8	43.0	55.0	19.0	34.5	753	2.79	19.0	77.4	2.8	0.6	0.0	0.2	2.04
	63	8.09	15.0	44.1	54.5	18.5	33.9	864	3.21	14.6	82.4	2.6	0.3	0.1	0.2	2.14
	64	8.27	15.1	44.4	53.7	18.3	34.0	836	1.94	18.6	77.3	3.2	0.4	0.1	0.4	2.06
	65	8.99	16.3	48.0	53.4	18.1	34.0	696	4.16	15.1	81.9	2.4	0.3	0.1	0.3	2.15
	66	8.49	15.1	45.3	53.4	17.8	33.4	588	1.82	22.4	75.1	2.0	0.4	0.1	0.0	1.02
	67	7.83	15.2	42.4	54.2	19.4	35.9	676	2.65	14.6	83.2	2.0	0.0	0.1	0.1	2.04
	68	9.13	16.7	47.6	52.1	18.3	35.0	896	2.13	20.8	74.4	4.4	0.2	0.0	0.2	1.37
	69	8.41	16.1	46.1	54.8	19.1	34.8	726	4.34	13.4	83.7	2.2	0.3	0.1	0.4	2.41
	70	9.02	16.0	46.7	51.8	17.8	34.3	691	2.66	16.7	76.5	6.3	0.2	0.0	0.4	1.57
HD	71	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
	72	8.78	15.6	45.8	52.1	17.8	34.1	641	1.94	19.8	77.2	2.4	0.4	0.2	0.1	1.80
	73	8.76	15.7	46.2	52.8	17.9	34.0	559	1.60	16.0	81.2	2.1	0.5	0.0	0.1	1.94
	74	8.13	14.7	43.9	54.0	18.1	33.5	704	1.45	13.3	84.4	1.7	0.2	0.1	0.2	1.65
	75	8.22	14.9	43.9	53.4	18.1	34.0	704	2.62	14.3	82.5	2.6	0.3	0.1	0.2	2.10
	76	8.09	14.5	42.7	52.8	18.0	34.0	706	1.88	21.5	75.4	2.7	0.2	0.1	0.2	2.07
	77	8.45	15.6	45.7	54.1	18.4	34.0	1048	4.88	56.4	40.2	3.2	0.2	0.0	0.0	1.48
	78	8.89	16.9	47.8	53.8	19.1	35.4	666	3.55	11.8	86.2	1.5	0.2	0.1	0.2	1.80
	79	8.53	15.5	45.8	53.7	18.2	34.0	839	2.44	33.1	62.8	3.5	0.3	0.0	0.3	2.26
	80	7.98	15.7	45.4	56.9	19.7	34.7	869	2.68	21.8	75.2	2.3	0.6	0.0	0.2	1.96

n.a. = no data available

Individual Coagulation – Males

Group	Animal no.	PT	aPTT
	Units	sec	sec
C	1	22.1	17.9
	2	25.7	16.1
	3	24.6	17.6
	4	23.3	14.5
	5	25.1	14.1
	6	21.3	14.3
	7	19.9	14.2
	8	23.5	15.5
	9	24.0	15.1
	10	25.2	13.3
LD	11	24.2	14.6
	12	23.3	16.0
	13	23.7	15.1
	14	24.2	15.7
	15	27.8	21.3
	16	22.8	14.1
	17	21.6	14.4
	18	24.2	13.4
	19	22.8	14.8
	20	24.2	19.9
MD	21	25.9	16.9
	22	24.6	16.2
	23	25.8	15.8
	24	24.1	15.5
	25	27.0	20.3
	26	22.9	14.3
	27	24.0	15.1
	28	23.9	16.9
	29	23.8	15.7
	30	23.0	14.5
HD	31	22.8	13.1
	32	23.5	16.0
	33	24.1	15.6
	34	22.8	15.5
	35	25.6	35.4
	36	23.6	13.1
	37	23.5	14.5
	38	21.7	14.4
	39	22.9	14.6
	40	23.8	20.8

Individual Coagulation – Females

Group	Animal no.	PT	aPTT
	Units	sec	sec
C	41	25.9	13.8
	42	24.2	17.4
	43	26.7	15.5
	44	25.9	14.5
	45	25.4	17.4
	46	26.6	15.2
	47	26.0	15.1
	48	25.2	15.2
	49	24.3	14.1
	50	25.6	12.1
LD	51	26.0	14.7
	52	27.0	15.7
	53	25.1	14.5
	54	n.a.	n.a.
	55	24.3	14.0
	56	28.3	18.7
	57	26.5	13.2
	58	26.8	14.7
	59	26.0	15.9
	60	26.4	16.6
MD	61	27.1	14.6
	62	25.8	16.3
	63	23.5	13.2
	64	24.1	14.3
	65	24.4	14.9
	66	25.8	8.2
	67	28.0	11.2
	68	26.4	17.1
	69	28.8	17.8
	70	25.0	15.3
HD	71	n.a.	n.a.
	72	24.8	16.4
	73	24.8	15.5
	74	25.0	16.2
	75	25.8	15.5
	76	26.2	20.3
	77	28.0	14.2
	78	24.2	13.2
	79	24.7	15.5
	80	25.3	12.5

n.a. = no data available

Individual Clinical Biochemistry - Males

Group	Animal No.	ASAT	ALAT	AP	GGT	Crea	TP	Alb	Urea	TBIL	Chol	Gluc	Na	K	Ca	P	Cl
	Units	U/L	U/L	U/L	U/L	µmol/L	g/L	g/L	mmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
C	1	69.9	24.6	89.17	0.18	16	46.0	24.65	5.05	2.5	1.64	6.05	105	3.01	2.01	1.48	77
	2	46.9	21.9	69.72	0.85	15	47.6	23.65	5.97	1.9	1.73	6.86	85	2.51	2.07	1.65	63
	3	70.2	27.3	104.26	0.45	16	55.2	31.14	6.53	2.2	2.08	7.48	127	3.52	2.14	1.48	98
	4	55.1	20.6	46.70	bllq	15	48.5	24.20	5.46	2.5	1.22	5.83	84	2.39	2.24	1.57	62
	5	24.3	12.3	35.75	0.02	11	34.4	bllq	5.22	1.6	1.06	4.87	57	1.74	1.67	1.55	bllq
	6	83.2	49.0	96.61	bllq	18	61.3	35.16	6.93	2.8	1.94	10.52	144	4.06	2.25	1.65	106
	7	98.6	43.1	167.59	0.41	24	61.0	34.32	6.70	2.2	1.46	10.72	143	3.98	2.29	1.75	106
	8	83.8	44.9	164.26	0.04	22	64.5	37.31	6.54	2.6	1.71	9.70	144	4.00	2.42	1.82	107
	9	82.1	48.1	85.75	0.32	22	59.4	34.37	6.93	2.9	2.00	7.99	144	3.93	2.29	1.77	107
	10*	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
LD	11	65.0	25.9	43.46	0.36	15	45.3	22.62	5.32	2.5	1.17	3.83	87	2.36	2.10	1.33	65
	12	68.4	33.6	98.11	bllq	16	45.9	27.02	6.23	1.9	1.27	5.15	111	3.03	2.05	1.34	84
	13	46.4	22.6	73.99	0.12	11	49.0	22.19	6.41	2.6	1.10	5.13	80	2.43	2.37	2.34	62
	14	40.2	19.1	74.24	0.59	18	44.7	22.75	6.43	2.6	1.38	5.61	80	2.27	2.21	1.88	60
	15	38.3	29.7	105.54	0.04	5	34.9	18.03	4.47	1.9	0.83	4.01	74	2.23	1.90	1.60	56
	16	82.1	36.8	111.73	0.16	24	59.0	34.50	6.46	1.6	1.22	10.35	143	4.01	2.30	1.40	109
	17	78.0	44.4	118.50	0.55	32	59.0	34.60	6.84	2.5	1.80	11.25	143	3.93	2.26	1.45	108
	18	65.8	39.4	121.05	bllq	20	61.0	36.64	6.43	2.6	1.54	10.16	142	3.85	2.35	1.82	110
	19	64.6	30.9	185.29	bllq	18	57.4	32.93	6.87	3.2	1.50	8.77	142	3.80	2.30	1.85	108
	20	71.6	49.2	132.15	0.04	22	63.9	35.88	6.91	3.5	2.02	10.37	136	3.83	2.47	2.00	99

* = haemolytic sample; n.d. = not determined; bllq = below lower level of quantification (GGT < 0 U/L; Alb < 15 g/L; Cl <50 mmol/L)

Individual Clinical Biochemistry – Males (Continued)

Group	Animal No.	ASAT	ALAT	AP	GGT	Crea	TP	Alb	Urea	TBIL	Chol	Gluc	Na	K	Ca	P	Cl
	Units	U/L	U/L	U/L	U/L	µmol/L	g/L	g/L	mmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
MD	21	80.7	41.1	150.13	0.61	18	54.5	29.63	6.78	2.3	1.09	6.64	122	3.52	2.18	1.76	93
	22	69.2	33.8	77.87	0.22	15	45.8	25.05	5.29	1.6	1.22	4.31	100	2.78	1.89	1.27	76
	23	32.8	16.1	61.69	bllq	11	35.9	16.49	4.85	2.2	1.00	5.39	66	2.22	1.90	1.64	bllq
	24	50.3	29.5	54.25	bllq	15	41.6	21.20	4.86	1.4	0.85	5.57	81	2.45	1.93	1.79	61
	25	65.3	44.1	137.31	bllq	28	59.7	34.90	7.61	3.2	1.67	10.77	143	4.47	2.47	2.29	107
	26	85.0	48.0	129.27	0.16	24	61.2	35.82	6.37	2.9	1.80	9.50	145	3.76	2.32	1.48	107
	27	88.5	41.9	87.76	0.55	26	59.5	35.26	5.73	3.1	1.43	8.80	144	3.80	2.26	1.39	109
	28	81.5	42.2	141.59	0.08	24	60.7	35.15	7.02	2.3	1.75	7.18	143	4.07	2.37	1.94	108
	29	69.3	43.0	124.77	0.34	18	59.6	35.17	6.75	2.8	2.50	8.13	144	3.86	2.42	2.14	108
	30	62.5	45.5	130.20	0.26	18	63.9	36.35	6.90	3.1	1.75	9.60	138	4.00	2.40	1.92	103
HD	31	53.2	21.2	115.16	0.28	20	40.6	21.20	5.68	2.0	1.49	5.11	85	2.69	1.80	1.42	62
	32	83.6	35.0	145.60	bllq	22	57.8	31.76	7.58	2.8	1.74	5.78	127	3.47	2.33	1.76	96
	33	79.6	37.8	119.29	bllq	20	56.5	31.42	6.69	2.5	1.45	8.26	137	3.83	2.23	1.83	106
	34	52.9	22.8	92.17	bllq	11	45.2	22.64	6.05	2.0	1.33	5.18	87	2.34	2.04	1.67	64
	35	54.1	35.0	127.24	bllq	15	53.2	27.42	6.40	2.3	1.41	7.31	109	3.27	2.30	2.28	83
	36	72.0	48.2	133.97	0.38	26	59.8	35.17	7.71	2.2	1.89	12.15	144	4.25	2.31	1.70	105
	37	90.1	54.6	221.48	0.24	24	61.2	35.07	9.81	2.9	1.78	9.72	142	3.99	2.30	1.72	109
	38	95.0	52.0	167.73	0.38	20	63.1	35.71	6.63	2.8	2.23	8.88	143	3.78	2.42	1.97	108
	39	68.3	32.4	169.97	bllq	26	60.7	34.04	6.76	2.5	2.28	10.34	143	4.23	2.43	1.94	105
	40	62.9	44.6	130.69	0.61	20	64.1	36.52	6.96	3.2	1.75	9.74	143	4.16	2.41	1.87	108

bllq = below lower level of quantification (GGT < 0 U/L; Alb < 15 g/L; Cl <50 mmol/L)

Individual Clinical Biochemistry - Females

Group	Animal No.	ASAT	ALAT	AP	GGT	Crea	TP	Alb	Urea	TBIL	Chol	Gluc	Na	K	Ca	P	Cl
	Units	U/L	U/L	U/L	U/L	µmol/L	g/L	g/L	mmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
C	41	78.6	31.1	40.87	bllq	24	59.8	35.76	7.48	2.9	1.15	5.87	136	3.71	2.31	1.78	104
	42	78.4	25.1	75.13	0.38	24	67.7	40.77	8.12	4.6	1.57	7.02	135	3.55	2.42	1.45	101
	43	82.2	22.9	63.24	0.40	22	63.9	38.30	7.18	3.4	1.26	6.73	136	3.65	2.42	2.05	101
	44	73.1	26.1	66.47	0.69	16	63.0	38.13	6.54	4.3	1.37	7.78	136	3.67	2.41	1.75	101
	45	74.1	24.9	43.94	0.24	22	60.4	36.93	5.59	3.4	1.06	7.90	134	3.33	2.42	1.74	100
	46	75.0	28.5	39.52	0.32	18	3.8	38.68	5.89	3.8	1.19	8.94	135	3.40	2.42	1.13	102
	47	108.2	44.1	62.59	0.30	24	58.5	35.31	6.74	2.8	1.37	9.16	135	3.36	2.26	1.26	103
	48	75.7	21.9	33.89	bllq	16	61.0	36.68	6.54	2.9	1.40	8.18	134	3.59	2.34	1.64	101
	49	80.1	35.9	57.14	0.32	16	60.2	36.77	6.79	3.1	1.26	7.95	135	3.51	2.35	2.19	101
	50	62.6	21.1	68.59	0.55	16	61.2	36.99	7.24	2.8	0.82	7.21	132	3.67	2.39	1.89	101
LD	51	80.6	37.7	80.37	0.65	26	56.2	34.48	8.15	2.8	1.15	4.92	136	3.64	2.31	1.70	103
	52	78.2	30.7	39.52	bllq	26	62.8	38.95	7.29	4.4	1.11	7.48	135	3.51	2.32	1.41	102
	53	83.4	25.3	98.91	bllq	18	57.0	34.01	6.82	4.6	1.38	6.56	134	3.44	2.43	1.97	99
	54	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
	55	70.9	25.7	71.81	0.30	16	62.7	37.65	6.47	3.4	0.87	6.39	136	3.42	2.42	1.89	103
	56	75.1	38.5	50.11	0.02	16	63.3	37.96	6.71	3.2	1.10	7.09	134	3.22	2.45	1.54	101
	57	109.3	91.6	85.35	bllq	20	61.3	36.01	7.18	2.8	1.66	8.64	135	3.36	2.43	1.62	102
	58	63.6	24.9	53.33	0.47	13	60.4	37.39	6.32	3.4	0.79	7.28	136	3.44	2.43	1.89	102
	59	65.3	34.7	41.11	bllq	16	65.1	39.50	6.73	4.0	1.33	7.40	135	3.21	2.45	1.46	103
	60	79.3	61.0	49.46	bllq	13	64.1	38.62	6.24	3.4	1.32	7.94	135	3.42	2.49	1.91	103

n.a. = no data available; bllq = below lower level of quantification (GGT < 0 U/L)

Individual Clinical Biochemistry – Females (Continued)

Group	Animal No.	ASAT	ALAT	AP	GGT	Crea	TP	Alb	Urea	TBIL	Chol	Gluc	Na	K	Ca	P	Cl
	Units	U/L	U/L	U/L	U/L	µmol/L	g/L	g/L	mmol/L	µmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
MD	61	91.8	36.7	101.44	0.36	40	55.3	33.25	9.23	3.2	1.55	8.12	134	3.86	2.36	2.12	101
	62	66.3	28.3	78.46	0.71	20	66.0	39.03	6.03	5.5	1.00	11.01	135	4.10	2.43	1.61	101
	63	65.5	27.9	72.37	0.18	24	60.6	37.79	7.62	4.6	0.74	5.05	135	3.80	2.50	2.06	100
	64	66.3	25.1	67.63	0.30	26	64.0	37.75	7.55	5.0	0.81	6.59	134	3.86	2.43	1.76	102
	65	95.3	26.5	34.15	0.00	20	60.5	36.39	7.26	4.0	1.43	7.20	137	3.21	2.42	2.02	102
	66	88.7	58.0	85.99	0.65	16	57.9	34.64	8.41	3.5	1.51	5.13	136	3.71	2.44	1.89	104
	67	69.6	25.4	47.91	0.18	16	59.4	36.46	5.86	4.0	0.80	7.15	135	3.34	2.38	1.64	102
	68	69.5	31.7	47.85	0.02	15	60.2	36.54	7.58	4.9	1.36	4.90	134	3.96	2.42	2.08	101
	69	62.2	25.4	31.92	0.75	16	59.8	35.55	7.37	4.1	1.18	6.45	134	3.50	2.41	1.90	102
	70	59.6	25.5	40.73	bllq	11	66.9	40.62	6.14	3.8	1.14	5.14	132	3.61	2.59	1.84	101
HD	71	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
	72	76.0	43.4	55.01	0.20	20	64.7	38.43	8.50	2.8	1.69	5.77	137	3.45	2.39	1.58	103
	73	73.4	27.7	39.68	bllq	18	63.2	38.40	7.42	3.5	1.08	6.31	136	3.34	2.39	2.00	102
	74	76.6	31.3	62.80	0.69	28	59.8	35.43	6.50	3.5	1.24	7.35	138	3.24	2.35	2.04	101
	75	72.9	28.4	58.85	0.55	18	62.0	36.53	6.25	5.0	1.50	7.28	135	3.67	2.35	1.68	101
	76	80.8	36.2	50.62	0.47	22	63.9	39.27	6.58	2.9	1.55	5.29	135	3.18	2.38	1.44	103
	77	70.7	23.1	70.13	1.44	15	59.8	33.95	4.86	2.6	0.98	8.62	135	3.37	2.33	1.20	102
	78	63.6	26.8	34.34	0.67	11	56.6	33.44	7.35	2.6	1.32	6.36	135	3.65	2.35	1.99	103
	79	84.2	35.5	63.21	0.49	22	63.8	38.06	6.90	4.9	1.09	5.36	133	3.24	2.42	1.69	100
	80	61.1	22.2	33.70	1.13	9	61.2	36.19	5.37	3.4	1.70	8.86	134	3.50	2.45	1.49	100

n.a. = no data available; bllq = below lower level of quantification (GGT < 0 U/L)

Individual Urinalysis - Males

Group	Animal No.	Colour/ appearance	Ery	UBG	BIL	Protein	Nitrite	Ket	Glucose	pH	Specific Gravity	Leuc
	Units	-	cells/µL	mg/dL	mg/dL	mg/dL	-	mg/dL	mg/dL	-	-	cells/µL
C	1	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	2	colourless	ca.50	norm.	neg.	neg.	neg.	neg.	neg.	8	1.005	ca. 25
	3	yellowish	ca.10	norm.	neg.	30	neg.	neg.	neg.	7	1.005	ca. 25
	4	yellowish	ca. 50	norm.	neg.	neg.	neg.	neg.	neg.	8	1.000	ca. 25
	5	yellowish	ca. 50	norm.	1	30	neg.	neg.	neg.	6	1.020	ca. 75
	6	yellowish	ca.10	norm.	neg.	30	neg.	neg.	neg.	8	1.005	ca. 25
	7	yellowish	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	8	yellowish	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	9	yellowish	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	10	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	7	1.005	ca. 25
LD	11	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	neg.
	12	colourless	neg.	norm.	neg.	30	neg.	neg.	neg.	8	1.005	ca. 25
	13	yellowish	ca.10	norm.	1	neg.	neg.	25	neg.	7	1.020	ca. 25
	14	yellowish	neg.	norm.	2	30	neg.	25	neg.	5	1.025	neg.
	15	yellow	neg.	norm.	2	100	neg.	25	neg.	6	1.020	ca. 25
	16	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.000	neg.
	17	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	8	1.005	ca. 25
	18	yellowish	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	19	yellowish	ca.10	norm.	1	30	neg.	neg.	neg.	7	1.005	ca. 25
	20	colourless	ca. 50	norm.	neg.	30	neg.	neg.	neg.	7	1.015	ca. 25

neg. = negative; norm. = normal

Individual Urinalysis – Males (Continued)

Group	Animal No.	Colour/ appearance	Ery	UBG	BIL	Protein	Nitrite	Ket	Glucose	pH	Specific Gravity	Leuc
	Units	-	cells/µL	mg/dL	mg/dL	mg/dL	-	mg/dL	mg/dL	-	-	cells/µL
MD	21	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	22	colourless	neg.	norm.	neg.	100	neg.	neg.	neg.	8	1.015	ca. 25
	23	colourless	ca. 50	norm.	1	30	neg.	neg.	neg.	7	1.000	ca. 25
	24	colourless	ca. 10	norm.	neg.	30	neg.	neg.	neg.	7	1.005	neg.
	25	yellowish	ca. 10	norm.	neg.	30	neg.	neg.	neg.	7	1.005	ca. 25
	26	colourless	ca. 10	norm.	neg.	neg.	neg.	neg.	neg.	8	1.000	ca. 25
	27	colourless	ca. 10	norm.	neg.	neg.	neg.	neg.	neg.	8	1.000	ca. 25
	28	yellowish	neg.	norm.	neg.	30	neg.	neg.	neg.	6	1.015	ca. 25
	29	yellowish	ca. 10	norm.	neg.	30	neg.	neg.	neg.	7	1.015	ca. 25
	30	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	6	1.025	ca. 25
HD	31	colourless	ca. 10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	32	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	8	1.005	ca. 25
	33	colourless	ca. 10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.015	ca. 25
	34	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	7	1.020	ca. 25
	35	yellowish	ca. 10	norm.	1	100	neg.	neg.	neg.	6	1.025	ca. 75
	36	yellowish	neg.	norm.	neg.	30	neg.	neg.	neg.	7	1.015	ca. 25
	37	colourless	ca. 50	norm.	neg.	neg.	neg.	neg.	neg.	8	1.005	ca. 25
	38	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	8	1.005	ca. 25
	39	yellowish	ca. 10	norm.	1	30	neg.	neg.	neg.	7	1.005	ca. 25
	40	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	7	1.015	ca. 25

neg. = negative; norm. = normal

Individual Urinalysis - Females

Group	Animal No.	Colour/ appearance	Ery	UBG	BIL	Protein	Nitrite	Ket	Glucose	pH	Specific Gravity	Leuc
	Units	-	cells/µL	mg/dL	mg/dL	mg/dL	-	mg/dL	mg/dL	-	-	cells/µL
C	41	yellowish	ca. 250	norm.	neg.	30	neg.	neg.	neg.	8	1.000	ca. 25
	42	yellowish	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	6	1.015	neg.
	43	yellowish	ca. 50	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	44	colourless	ca. 50	norm.	neg.	neg.	neg.	neg.	neg.	8	1.000	ca. 25
	45	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.015	neg.
	46	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	8	1.000	neg.
	47	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	8	1.005	neg.
	48	yellowish	ca.10	norm.	1	30	neg.	neg.	neg.	6	1.005	ca. 25
	49	yellowish	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.015	neg.
	50	yellowish	neg.	norm.	neg.	30	neg.	neg.	neg.	6	1.020	neg.
LD	51	yellowish	ca. 250	norm.	neg.	30	neg.	neg.	neg.	7	1.005	ca. 25
	52	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.000	neg.
	53	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	6	1.030	neg.
	54	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
	55	yellowish	ca.10	norm.	neg.	30	neg.	neg.	neg.	6	1.015	ca. 25
	56	yellowish	neg.	norm.	neg.	30	neg.	neg.	neg.	7	1.015	neg.
	57	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.000	ca. 25
	58	yellowish	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	6	1.015	ca. 25
	59	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	6	1.005	neg.
	60	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25

n.a. = no data available; neg. = negative; norm. = normal

Individual Urinalysis – Females (Continued)

Group	Animal No.	Colour/ appearance	Ery	UBG	BIL	Protein	Nitrite	Ket	Glucose	pH	Specific Gravity	Leuc
	Units	-	cells/µL	mg/dL	mg/dL	mg/dL	-	mg/dL	mg/dL	-	-	cells/µL
MD	61	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	ca. 25
	62	yellowish	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	neg.
	63	yellowish	neg.	norm.	1	neg.	neg.	neg.	neg.	6	1.020	neg.
	64	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	neg.
	65	yellowish	neg.	norm.	neg.	neg.	neg.	neg.	neg.	6	1.005	neg.
	66	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	6	1.020	neg.
	67	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	6	1.005	neg.
	68	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	5	1.025	neg.
	69	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	6	1.025	ca. 25
	70	yellowish	neg.	norm.	1	30	neg.	neg.	neg.	5	1.030	neg.
HD	71	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
	72	colourless	ca.10	norm.	neg.	30	neg.	neg.	neg.	7	1.005	ca. 25
	73	colourless	neg.	norm.	neg.	neg.	neg.	neg.	neg.	8	1.000	ca. 25
	74	yellowish	neg.	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	neg.
	75	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.000	neg.
	76	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.000	neg.
	77	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	8	1.000	neg.
	78	yellowish	neg.	norm.	neg.	neg.	neg.	neg.	neg.	6	1.020	neg.
	79	colourless	ca.50	norm.	neg.	neg.	neg.	neg.	neg.	7	1.005	neg.
	80	colourless	ca.10	norm.	neg.	neg.	neg.	neg.	neg.	7	1.015	ca. 25

n.a. = no data available; neg. = negative; norm. = normal

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex		M	M	M
	Dose Group	C / M	LD / M	MD / M	HD / M
BRAIN	BRAIN				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
SPINAL CORD	SPINAL CORD				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
SCIATIC NERVES	SCIATIC NERVES				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
HEART	HEART				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
AORTA	AORTA				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
TRACHEA	TRACHEA				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
LUNG	LUNG				
	Abnormal color				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Abnormal surface				
	dark				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
TONGUE	TONGUE				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
ESOPHAGUS	ESOPHAGUS				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
STOMACH	STOMACH				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Cannibalized				

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	M	M	M	M
	Dose Group	C / M	LD / M	MD / M	HD / M
STO	*Total affected /examined:*	*0/10*	*0/10*	*0/10*	*0/10*
DUODENUM	DUODENUM				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Cannibalized				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
JEJUNUM	JEJUNUM				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Cannibalized				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
ILEUM	ILEUM				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Cannibalized				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
CECUM	CECUM				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
COLON	COLON				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
RECTUM	RECTUM				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
LIVER	LIVER				
	Abnormal surface				
	marbled				
	pale				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
PANCREAS	PANCREAS				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
KID	KIDNEYS				

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	M	M	M	M
	Dose Group	C / M	LD / M	MD / M	HD / M
KIDNEY	*Total affected /examined:*	*0/10*	*0/10*	*0/10*	*0/10*
URETERS	URETERS				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
URINARY BLADDER	URINARY BLADDER				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
TESTES	TESTES				
	Small				
	right			023	
	Total affected /examined:	*0/10*	*0/10*	*1/10*	*0/10*
EPIDIDYMIDES	EPIDIDYMIDES				
	Abnormal color				
	yellow	006			
	Total affected /examined:	*1/10*	*0/10*	*0/10*	*0/10*
	Abnormal position				
	right	006			
	Total affected /examined:	*1/10*	*0/10*	*0/10*	*0/10*
PITUITARY GLAND	PITUITARY GLAND				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
THYROID GLAND	THYROID GLAND				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
THYROID/PARATHYROID	THYROID/PARATHYROID				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
PARATHYROID	PARATHYROID GLANDS				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
ADRENAL GLANDS	ADRENAL GLANDS				
	Enlarged				
	both sides				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Autolytic				

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	M	M	M	M
	Dose Group	C / M	LD / M	MD / M	HD / M
AD	*Total affected /examined:*	*0/10*	*0/10*	*0/10*	*0/10*
SPLEEN	SPLEEN				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
THYMUS	THYMUS				
	Abnormal color				
	red				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
MESENT. LYMPH	MESENT. LYMPH NODE				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
MANDIB. LYMPH	MANDIB.LYMPH NODES				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
SALIVARY	SALIVARY GLANDS				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
HARDERIAN	HARDERIAN GLANDS				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
MAMMARY GLAND	MAMMARY GLAND				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
SKIN/SUBCUTIS	SKIN/SUBCUTIS				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
SKELETAL	SKELETAL MUSCLE				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
EYES	EYES				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*
FEMURS	FEMURS				
	Autolytic				

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	M	M	M	M
	Dose Group	C / M	LD / M	MD / M	HD / M
FEM	*Total affected /examined:*	*0/10*	*0/10*	*0/10*	*0/10*
STERNUM	STERNUM				
	Autolytic				
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*0/10*

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	F	F	F	F
	Dose Group	C / F	LD / F	MD / F	HD / F
BRAIN	BRAIN				
	Autolytic		054		071
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*1/10*
SPINAL CORD	SPINAL CORD				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
SCIATIC NERVES	SCIATIC NERVES				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
HEART	HEART				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
AORTA	AORTA				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
TRACHEA	TRACHEA				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
LUNG	LUNG				
	Abnormal color				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Abnormal surface				
	dark		054		
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*0/10*
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
TONGUE	TONGUE				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
ESOPHAGUS	ESOPHAGUS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
STOMACH	STOMACH				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Cannibalized		054		

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	F	F	F	F
	Dose Group	C / F	LD / F	MD / F	HD / F
STO	*Total affected /examined:*	*0/10*	*1/10*	*0/10*	*0/10*
DUODENUM	DUODENUM				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Cannibalized		054		
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*0/10*
JEJUNUM	JEJUNUM				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Cannibalized		054		
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*0/10*
ILEUM	ILEUM				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Cannibalized		054		
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*0/10*
CECUM	CECUM				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
COLON	COLON				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
RECTUM	RECTUM				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
LIVER	LIVER				
	Abnormal surface				
	marbled				077
	pale				077
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
PANCREAS	PANCREAS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
KID	KIDNEYS				

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	F	F	F	F
	Dose Group	C / F	LD / F	MD / F	HD / F
KIDNEYS	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
URETERS	URETERS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
URINARY BLADDER	URINARY BLADDER				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
OVARIES	OVARIES				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Cannibalized		054		
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*0/10*
OVIDUCTS	OVIDUCTS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Cannibalized		054		
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*0/10*
UTERUS	UTERUS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Cannibalized		054		
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*0/10*
	fluid filled	042, 043, 044	059, 060	063	073, 074, 076
	Total affected /examined:	*3/10*	*2/10*	*1/10*	*3/10*
CERVIX	CERVIX				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
VAGINA	VAGINA				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
PITUITARY GLAND	PITUITARY GLAND				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
THYROID	THYROID GLAND				
	Autolytic				071

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	F	F	F	F
	Dose Group	C / F	LD / F	MD / F	HD / F
THY	*Total affected /examined:*	*0/10*	*0/10*	*0/10*	*1/10*
THYROID/PARATHYROID	THYROID/PARATHYROID				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
PARATHYROID	PARATHYROID GLANDS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
ADRENAL GLANDS	ADRENAL GLANDS				
	Enlarged				
	both sides				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
SPLEEN	SPLEEN				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
THYMUS	THYMUS				
	Abnormal color				
	red				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
MESENT. LYMPH	MESENT. LYMPH NODE				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
MANDIB. LYMPH	MANDIB.LYMPH NODES				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
SALIVARY	SALIVARY GLANDS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
HARDERIAN	HARDERIAN GLANDS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
MAMMARY	MAMMARY GLAND				
	Autolytic				071

Necropsy Incidences by Animal Numbers
Status at Necropsy: K0, incl. Decedents

	Sex	F	F	F	F
	Dose Group	C / F	LD / F	MD / F	HD / F
MA	*Total affected /examined:*	*0/10*	*0/10*	*0/10*	*1/10*
SKIN/SUBCUTIS	SKIN/SUBCUTIS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
SKELETAL	SKELETAL MUSCLE				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
EYES	EYES				
	Autolytic		054		071
	Total affected /examined:	*0/10*	*1/10*	*0/10*	*1/10*
FEMURS	FEMURS				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*
STERNUM	STERNUM				
	Autolytic				071
	Total affected /examined:	*0/10*	*0/10*	*0/10*	*1/10*

Codes and Symbols

Abbreviation	Description
K0	Final Necropsy

Dose Groups

Dose Group	Description
C / M	Control, males:
C / F	Control, females:
LD / M	Treated, males:
LD / F	Treated, females:
MD / M	Treated, males:
MD / F	Treated, females:
HD / M	Treated, males:
HD / F	Treated, females:

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: C / M, Control
Sex: Male

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Testes [g]	Kidneys [g]	Prostate Whole [g]	Pituitary Gland [g]
001	395.0000	0.9379	0.3755	3.4876	2.3164	1.0402	0.0107
002	417.0000	0.8232	0.2894	4.5543	2.3720	2.6421	0.0098
003	342.0000	0.6252	0.2859	3.9580	2.1829	2.6166	0.0107
004	373.0000	0.8082	0.4162	3.5105	2.4715	2.2426	0.0073
005	399.0000	0.6668	0.2698	3.7472	2.3687	3.1181	0.0088
006	368.0000	0.7000	0.2980	3.5254	2.5825	2.4564	0.0088
007	349.0000	0.7652	0.2971	3.7149	2.3257	2.1019	0.0126
008	396.0000	0.8004	0.2745	4.5585	2.8719	3.6100	0.0174
009	359.0000	0.7686	0.3355	3.5648	2.4743	2.7742	0.0140
010	380.0000	0.5940	0.3800	3.5295	2.1188	2.3475	0.0058
NO. WGTS	10	10	10	10	10	10	10
Mean	377.8000	0.7490	0.3222	3.8151	2.4085	2.4950	0.0106
SD	24.0407	0.1035	0.0515	0.4166	0.2125	0.6753	0.0034

Animal Number	Thyroid/parathyroid [g]	Adrenal Glands [g]	Heart [g]	Brain [g]	Epididymides [g]	Liver [g]
001	0.0386	0.0575	0.9403	2.2416	1.3015	9.1549
002	0.0301	0.0706	1.1041	2.1626	1.6292	10.2955
003	0.0345	0.0591	0.8714	2.0831	1.5399	7.8499
004	0.0253	0.0541	0.9656	2.1758	1.4266	9.1055
005	0.0246	0.0525	0.9601	2.1405	1.5690	9.5168
006	0.0588	0.0526	1.0801	2.1663	1.4379	9.3444
007	0.0302	0.0516	0.9800	2.1426	1.6353	9.1175
008	0.0249	0.0635	1.1960	2.6826	1.9475	10.3355
009	0.0122	0.0523	0.9054	2.3477	1.3098	7.9684
010	0.0337	0.0578	0.7962	2.2089	1.1383	8.0594
NO. WGTS	10	10	10	10	10	10
Mean	0.0313	0.0572	0.9799	2.2352	1.4935	9.0748
SD	0.0121	0.0061	0.1180	0.1725	0.2253	0.8890

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: C / F, Control
Sex: Female

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Ovaries [g]	Kidneys [g]	Pituitary Gland [g]	Thyroid/parathyroid [g]
041	219.0000	0.5486	0.5156	0.1656	1.4596	0.0136	0.0296
042	226.0000	0.7175	0.3902	0.1162	1.7066	0.0158	0.0340
043	222.0000	0.6664	0.3718	0.1175	1.5470	0.0119	0.0289
044	233.0000	0.4270	0.3570	0.1510	1.6748	0.0145	0.0294
045	215.0000	0.4880	0.3237	0.1698	1.5282	0.0124	0.0243
046	224.0000	0.6484	0.3758	0.1433	1.6046	0.0134	0.0342
047	215.0000	0.5245	0.3499	0.0958	1.3942	0.0120	0.0287
048	233.0000	0.6521	0.4024	0.1260	1.8144	0.0178	0.0320
049	201.0000	0.4102	0.3506	0.1172	1.5247	0.0127	0.0186
050	222.0000	0.5952	0.2878	0.1384	1.6446	0.0164	0.0138
NO. WGTS	10	10	10	10	10	10	10
Mean	221.0000	0.5678	0.3725	0.1341	1.5899	0.0141	0.0274
SD	9.4281	0.1053	0.0601	0.0237	0.1246	0.0020	0.0066

Animal Number	Adrenal Glands [g]	Uterus [g]	Heart [g]	Brain [g]	Liver [g]
041	0.0845	0.4525	0.6393	1.9040	5.3977
042	0.0720	1.4190	0.6569	2.0155	5.8879
043	0.0673	1.3464	0.6863	1.9187	6.1311
044	0.0820	1.5055	0.6328	2.0221	6.2588
045	0.0758	0.7650	0.7071	1.9142	5.8547
046	0.0868	0.6721	0.6641	1.9917	6.7777
047	0.0813	0.5601	0.6874	1.9736	5.4322
048	0.0960	0.6451	0.6628	2.0475	7.2495
049	0.0751	0.6249	0.5782	1.9306	5.4637
050	0.0934	0.9089	0.7213	2.1084	6.2297
NO. WGTS	10	10	10	10	10
Mean	0.0814	0.8900	0.6636	1.9826	6.0683
SD	0.0092	0.3889	0.0411	0.0671	0.6021

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: LD / M, Treated
Sex: Male

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Testes [g]	Kidneys [g]	Prostate Whole [g]	Pituitary Gland [g]
011	360.0000	0.8258	0.4365	4.2015	2.1557	2.5484	0.0109
012	348.0000	0.7641	0.4618	3.5687	2.1992	2.7587	0.0110
013	363.0000	0.6468	0.3940	3.3504	2.2845	2.5438	0.0078
014	394.0000	0.6439	0.2479	3.9608	2.2570	2.7010	0.0146
015	385.0000	0.8817	0.2787	4.2672	2.4599	2.6265	0.0113
016	338.0000	0.7382	0.2675	3.5878	2.2117	2.4677	0.0120
017	395.0000	0.8163	0.3395	3.9166	2.1959	3.0856	0.0149
018	376.0000	0.8504	0.4258	3.6796	2.4065	3.2367	0.0137
019	373.0000	0.7153	0.3686	3.4735	2.4063	3.4151	0.0101
020	408.0000	0.7430	0.3576	3.7997	2.6429	2.8035	0.0110
NO. WGTS	10	10	10	10	10	10	10
Mean	374.0000	0.7626	0.3578	3.7806	2.3220	2.8187	0.0117
SD	22.1410	0.0813	0.0745	0.3050	0.1537	0.3211	0.0022

Animal Number	Thyroid/parathyroid [g]	Adrenal Glands [g]	Heart [g]	Brain [g]	Epididymides [g]	Liver [g]
011	0.0326	0.0595	0.9502	2.0758	1.6885	8.4385
012	0.0347	0.0459	0.8016	2.2303	1.4623	8.3992
013	0.0241	0.0533	0.8528	2.1183	1.2075	7.6291
014	0.0422	0.0674	0.9718	2.3094	1.3718	8.9559
015	0.0372	0.0507	0.9724	2.2772	1.6336	7.9913
016	0.0398	0.0526	0.8845	2.2318	1.3384	8.3473
017	0.0280	0.0613	1.1055	2.0900	1.5526	9.0767
018	0.0317	0.0290	1.0550	2.3477	1.3651	10.0319
019	0.0241	0.0697	1.0527	2.1005	1.6657	8.5555
020	0.0325	0.0633	0.9945	2.3528	1.5927	9.7636
NO. WGTS	10	10	10	10	10	10
Mean	0.0327	0.0553	0.9641	2.2134	1.4878	8.7189
SD	0.0061	0.0119	0.0957	0.1092	0.1628	0.7500

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: LD / F, Treated
Sex: Female

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Ovaries [g]	Kidneys [g]	Pituitary Gland [g]	Thyroid/parathyroid [g]
051	217.0000	0.4702	0.3927	0.1339	1.3776	0.0126	0.0229
052	213.0000	0.5542	0.2673	0.1393	1.3845	0.0156	0.0287
053	222.0000	0.5097	0.3881	0.1576	1.6491	0.0129	0.0273
054	194.0000	-	-	-	-	-	-
055	200.0000	0.5565	0.3156	0.1390	1.4843	0.0041	0.0294
056	218.0000	0.6006	0.2448	0.1516	1.5975	0.0122	0.0277
057	239.0000	0.6388	0.2957	0.1420	1.8151	0.0111	0.0213
058	215.0000	0.5591	0.3151	0.1740	1.6978	0.0128	0.0281
059	224.0000	0.5596	0.2839	0.0877	1.5668	0.0149	0.0257
060	233.0000	0.6844	0.2751	0.1514	1.6353	0.0147	0.0325
NO. WGTS	10	9	9	9	9	9	9
Mean	217.5000	0.5703	0.3087	0.1418	1.5787	0.0123	0.0271
SD	13.5421	0.0642	0.0514	0.0237	0.1440	0.0034	0.0034

Animal Number	Adrenal Glands [g]	Uterus [g]	Heart [g]	Brain [g]	Liver [g]
051	0.0752	0.5626	0.6631	2.0102	5.0171
052	0.0854	0.7855	0.6585	1.8943	5.9195
053	0.0671	0.7508	0.6718	2.0965	5.3871
054	-	-	-	-	-
055	0.0827	1.4572	0.5841	1.9346	5.1303
056	0.0756	0.5475	0.6670	2.0528	5.6360
057	0.0882	0.6016	0.6622	2.2374	7.4312
058	0.0909	0.5534	0.6104	1.9925	5.9616
059	0.0908	1.4955	0.7309	1.8686	6.3704
060	0.0830	1.1508	0.6457	1.9569	6.1475
NO. WGTS	9	9	9	9	9
Mean	0.0821	0.8783	0.6549	2.0049	5.8890
SD	0.0080	0.3883	0.0410	0.1135	0.7361

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: MD / M, Treated
Sex: Male

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Testes [g]	Kidneys [g]	Prostate Whole [g]	Pituitary Gland [g]
021	360.0000	0.6774	0.3404	3.5378	2.2146	2.3300	0.0085
022	320.0000	0.6770	0.2754	3.6052	2.2343	2.4435	0.0071
023	411.0000	0.7475	0.2360	3.2394	2.4758	2.5099	0.0112
024	370.0000	0.7489	0.3760	3.3934	2.4477	2.6889	0.0085
025	408.0000	0.8470	0.4836	3.9599	2.3498	2.6413	0.0081
026	366.0000	0.7994	0.3630	4.1769	2.2401	3.1780	0.0138
027	391.0000	0.7691	0.3197	3.6223	2.4047	2.7358	0.0074
028	399.0000	0.8574	0.3627	4.1543	2.3806	3.6397	0.0116
029	363.0000	0.8609	0.2977	4.0777	2.5228	2.5010	0.0095
030	380.0000	0.6150	0.3886	3.7869	2.5843	2.7884	0.0153
NO. WGTS	10	10	10	10	10	10	10
Mean	376.8000	0.7600	0.3443	3.7554	2.3855	2.7457	0.0101
SD	27.3041	0.0843	0.0686	0.3280	0.1271	0.3918	0.0028

Animal Number	Thyroid/parathyroid [g]	Adrenal Glands [g]	Heart [g]	Brain [g]	Epididymides [g]	Liver [g]
021	0.0372	0.0663	0.8180	2.2445	1.3774	8.0657
022	0.0330	0.0485	0.7798	2.1965	1.3830	6.7195
023	0.0372	0.0702	1.1363	2.1049	1.4486	9.0144
024	0.0385	0.0567	0.8412	2.2847	1.3227	8.2736
025	0.0267	0.0698	1.0168	2.1187	1.3505	9.2655
026	0.0346	0.0540	1.0776	2.1726	1.6410	8.8714
027	0.0322	0.0617	1.0737	2.3254	1.2892	9.6121
028	0.0419	0.0660	1.2044	2.3057	1.6189	9.0159
029	0.0450	0.0569	0.9507	1.9321	1.3873	8.8888
030	0.0489	0.0566	1.0071	2.2548	1.2834	10.1385
NO. WGTS	10	10	10	10	10	10
Mean	0.0375	0.0607	0.9906	2.1940	1.4102	8.7865
SD	0.0065	0.0073	0.1416	0.1187	0.1259	0.9379

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: MD / F, Treated
Sex: Female

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Ovaries [g]	Kidneys [g]	Pituitary Gland [g]	Thyroid/parathyroid [g]
061	218.0000	0.4153	0.3594	0.1447	1.2656	0.0149	0.0255
062	215.0000	0.5961	0.3163	0.1705	1.6610	0.0139	0.0271
063	228.0000	0.5570	0.2820	0.1497	1.6621	0.0136	0.0289
064	218.0000	0.4955	0.2155	0.1437	1.5199	0.0123	0.0165
065	214.0000	0.5487	0.2640	0.1498	1.9470	0.0129	0.0196
066	218.0000	0.4767	0.2919	0.1414	1.4181	0.0109	0.0249
067	220.0000	0.5725	0.2576	0.1562	1.6684	0.0151	0.0240
068	214.0000	0.4840	0.4289	0.1126	1.4867	0.0130	0.0240
069	229.0000	0.7699	0.3113	0.1977	1.5810	0.0208	0.0295
070	209.0000	0.3978	0.3199	0.1453	1.5155	0.0119	0.0168
NO. WGTS	10	10	10	10	10	10	10
Mean	218.3000	0.5314	0.3047	0.1512	1.5725	0.0139	0.0237
SD	6.2013	0.1062	0.0590	0.0218	0.1816	0.0027	0.0046

Animal Number	Adrenal Glands [g]	Uterus [g]	Heart [g]	Brain [g]	Liver [g]
061	0.0826	0.5452	0.5818	2.0088	5.2532
062	0.0954	0.8838	0.6643	1.9135	6.6034
063	0.0826	1.8602	0.6341	1.9254	5.9003
064	0.0686	0.8779	0.6690	2.0130	6.0820
065	0.0831	0.5538	0.7042	1.9690	5.9847
066	0.0681	0.5247	0.6103	1.8890	5.3935
067	0.0769	0.8260	0.6607	1.9820	5.9243
068	0.0667	0.5979	0.6566	1.9277	5.1245
069	0.0883	0.6985	0.6594	1.9969	6.1804
070	0.0786	0.8412	0.7268	1.9503	5.5200
NO. WGTS	10	10	10	10	10
Mean	0.0791	0.8209	0.6567	1.9576	5.7966
SD	0.0093	0.3927	0.0417	0.0429	0.4629

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: HD / M, Treated
Sex: Male

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Testes [g]	Kidneys [g]	Prostate Whole [g]	Pituitary Gland [g]
031	406.0000	0.8097	0.2956	3.7716	2.2797	3.0075	0.0088
032	362.0000	0.7905	0.3967	3.7580	2.1137	1.8257	0.0107
033	400.0000	0.6443	0.3824	3.6285	2.4190	2.2812	0.0098
034	367.0000	0.6676	0.3280	4.0859	2.5065	2.8924	0.0134
035	395.0000	0.6911	0.4002	3.8599	2.5268	2.7700	0.0106
036	375.0000	0.7843	0.2895	3.7714	2.5260	3.1409	0.0107
037	331.0000	0.6236	0.2537	3.3981	2.2682	2.7648	0.0084
038	367.0000	0.7257	0.2694	3.7654	2.5182	2.3013	0.0156
039	425.0000	0.9530	0.3444	4.2318	2.7644	3.1281	0.0111
040	344.0000	0.7781	0.3488	4.4090	2.3429	2.8693	0.0106
NO. WGTS	10	10	10	10	10	10	10
Mean	377.2000	0.7468	0.3309	3.8680	2.4265	2.6981	0.0110
SD	29.1197	0.0979	0.0527	0.2967	0.1827	0.4276	0.0021

Animal Number	Thyroid/parathyroid [g]	Adrenal Glands [g]	Heart [g]	Brain [g]	Epididymides [g]	Liver [g]
031	0.0265	0.0709	1.0743	2.0560	1.5620	8.7991
032	0.0370	0.0689	0.9182	2.3649	1.3735	8.0838
033	0.0466	0.0614	0.9439	2.2839	1.4012	8.6403
034	0.0254	0.0525	0.9594	2.1697	1.6568	8.5784
035	0.0465	0.0617	0.9078	2.2163	1.4169	9.0129
036	0.0320	0.0594	1.0594	2.1722	1.6155	9.8475
037	0.0502	0.0619	0.9281	2.2964	1.3188	8.2900
038	0.0239	0.0610	0.9350	2.3205	1.3212	9.4111
039	0.0335	0.0804	1.2468	2.1948	1.8816	13.1035
040	0.0222	0.0618	1.1305	2.2561	1.8334	9.2336
NO. WGTS	10	10	10	10	10	10
Mean	0.0344	0.0640	1.0103	2.2331	1.5381	9.3000
SD	0.0103	0.0076	0.1132	0.0900	0.2059	1.4365

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Table of Individual Body and Organ Weights
Status at Necropsy: K0, incl. Decedents
Dose Group: HD / F, Treated
Sex: Female

Animal Number	Final Body Weight [g]	Spleen [g]	Thymus [g]	Ovaries [g]	Kidneys [g]	Pituitary Gland [g]	Thyroid/parathyroid [g]
071	238.0000	-	-	-	-	-	-
072	195.0000	0.5069	0.3021	0.1215	1.3675	0.0124	0.0249
073	208.0000	0.4674	0.3177	0.1358	1.4413	0.0154	0.0277
074	216.0000	0.6235	0.2950	0.1550	1.5653	0.0132	0.0265
075	241.0000	0.6291	0.3078	0.1635	1.7685	0.0141	0.0292
076	217.0000	0.4421	0.3928	0.1763	1.4039	0.0108	0.0250
077	206.0000	0.5642	0.2144	0.1164	1.4653	0.0132	0.0184
078	225.0000	0.6674	0.2640	0.1710	1.7121	0.0134	0.0245
079	223.0000	0.5479	0.3121	0.1464	1.4493	0.0196	0.0233
080	240.0000	0.5294	0.3133	0.1833	1.7938	0.0144	0.0221
NO. WGTS	10	9	9	9	9	9	9
Mean	220.9000	0.5531	0.3021	0.1521	1.5519	0.0141	0.0246
SD	15.5667	0.0761	0.0473	0.0239	0.1649	0.0025	0.0032

Animal Number	Adrenal Glands [g]	Uterus [g]	Heart [g]	Brain [g]	Liver [g]
071	-	-	-	-	-
072	0.0717	0.6224	0.6526	1.8959	5.8698
073	0.0816	0.8300	0.6970	2.0218	5.6708
074	0.0814	1.7639	0.6336	1.9615	6.0442
075	0.0817	0.5477	0.7222	1.9724	6.6427
076	0.0909	2.3758	0.6941	2.0299	6.1008
077	0.0768	0.5712	0.6068	1.9851	5.4133
078	0.0767	0.5649	0.6836	1.9750	6.1672
079	0.0722	0.7609	0.6698	1.9203	5.9272
080	0.0707	0.5203	0.7614	1.9265	6.9971
NO. WGTS	9	9	9	9	9
Mean	0.0782	0.9508	0.6801	1.9654	6.0926
SD	0.0065	0.6606	0.0465	0.0451	0.4802

NO. WGTS = Number of weights recorded
SD = Standard Deviation
underlined = Organ weights excluded from statistics

Codes and Symbols

Abbreviation	Description
-	No weight(s) recorded / value not calculated
K0	Final Necropsy

Dose Groups

Dose Group	
C / M	Control, males:
C / F	Control, females:
LD / M	Treated, males:
LD / F	Treated, females:
MD / M	Treated, males:
MD / F	Treated, females:
HD / M	Treated, males:
HD / F	Treated, females:

HISTOPATHOLOGY PHASE REPORT

Glucose oxidase produced with *Trichoderma reesei*

Histopathology Phase to:

90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*

Subtitle:

Histopathology Examinations

Study Director:	Dr. Philip Allingham **BSL BIOSERVICE** **Scientific Laboratories Munich GmbH** Behringstrasse 6/8 82152 Planegg / Germany
Principal Investigator:	Dr. Y. Okazaki
Test Site:	**AnaPath GmbH** Buchsweg 56 4625 Oberbuchsiten / Switzerland
Sponsor:	**AB Enzymes GmbH** Feldbergstr. 78 64293 Darmstadt / Germany

Study Identification:	Eurofins Munich / BSL Munich Study Number **154307** AnaPath Phase Number **11661C**
Version:	FINAL
Completion Date:	07-JUL-2016

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Individual Tables

[1] Animal organ finding table

GLP CERTIFICATE

The Swiss GLP Monitoring Authorities

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Home Affairs DHA
Federal Office of Public Health FOPH

Federal Department of the Environment, Transport, Energy and Communications DETEC
Federal Office for the Environment FOEN

swissmedic
Swiss Agency for Therapeutic Products

Statement of GLP Compliance

According to Article 14 paragraph 3 Ordinance on Good Laboratory Practice [OGLP, SR 813.112.1]

The notification authority for chemicals confirms that the following test facility was inspected with respect to the compliance with the Swiss Ordinance on Good Laboratory Practice, adopted on 18th May 2005 [OGLP, SR 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted on 26th November 1997 by decision of the OECD Council [C(97)186/Final].

Unequivocal name and address of the test facility:	Area of expertise according to article 3 paragraph 1 letter d OGLP:
AnaPath GmbH Buchsweg 56 4625 Oberbuchsiten AnaPath GmbH / AnaPath Services Hammerstrasse 49 4410 Liestal	9. other studies (Histopathology)

Inspection authority: Swissmedic (Swiss Agency for Therapeutic Products)

Date of inspection: 04 – 05 September 2014

Date of decision: 05 January 2015

Based on the above mentioned decision it can be confirmed that the above mentioned test facility is able to conduct studies according to the aforementioned area of expertise in compliance with the principles of GLP. The above mentioned test facility is listed in the register and GLP list according to the Article 14 OGLP and is inspected on a regular basis according to Article 6 paragraph 2 OGLP.

Swiss Federal Office of Public Health
Consumer protection directorate
Notification authority for chemicals
(b) (6)

FEDERAL OFFICE OF PUBLIC HEALTH

Bern, 09 February 2015, The Head, Dr. Pierre Favre.

The notification authority for chemicals is the coordination and decision authority for the good laboratory practice (GLP) for the FOEN, the FOPH and Swissmedic.
Swiss Federal Office of Public Health, Consumer protection directorate, Notification authority for chemicals, CH-3003 Bern
www.glp.admin.ch, Phone: +41 (0)31 322 73 05, Fax: +41 (0)31 324 90 34

GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE

This histopathology phase has been performed in compliance with the:

Swiss Ordinance relating to Good Laboratory Practice, adopted May 18th 2005 [SR 813.112.1] (Status as of December 1st, 2012). This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted November 26th 1997 by decision of the OECD Council [C (97) 186/Final].

There were no circumstances that may have affected the quality or integrity of the data.

Principal Investigator
Histopathology Phase: Dr. Yoshimasa Okazaki

(b) (6)

.....

Date: 07-Jul.-2016

QUALITY ASSURANCE STATEMENT

AnaPath GmbH. Buchsweg 56, 4625 Oberbuchsiten / Switzerland.

The general facilities and activities are inspected periodically and the results are reported to the responsible person and the management.

Procedures were periodically inspected. The study plan (related to the phase) including amendments and this phase report were audited by the quality assurance. The dates are given below:

Dates and Types of QA Inspections	Dates of Report to	
	Principal Investigator (PI) and Test Site Management	Study Director (SD), Lead QA and Test Facility Management
02.12.2015 - Study plan	02.12.2015	02.12.2015
22.03.2016 - Process based (histopathology)*	22.03.2016	---
19.04.2016 - Phase report (draft)	19.04.2016	19.04.2016
11.07.2016 - Phase report	---	---

*In case of Process Based inspection the inspection result was reported to one of the AnaPath PIs not necessarily to the PI of this Phase.

This statement also confirms that this histopathology phase report reflects the raw data.

Quality Assurance:
AnaPath GmbH

Cristina Zeugin

(b) (6)

Date: 11 Jul 2016

DEVIATION TO THE STUDY PLAN

In order to cope with changes of the circumstance related to the study schedule management, the change of the study pathologist (Principal Investigator of Histoevaluation) was decided internally at the test site:
- Initially assigned study pathologist/Principal investigator: Dr. Klaus Weber;
- Newly assigned study pathologist/Principal investigator: Dr. Yoshimasa Okazaki.

Study director/Test Facility was informed of this PI-change by e-mail communication dated on 27 March 2016 and 29 March 2016.
With Test Facility's permission by e-mail communications between Test Facility and Test Site, the new PI, in place of the former PI, began the pathology examination in order to execute the study without delay, before the amendment to the study plan is issued.

This process is recorded and reported as a deviation to the study plan.
However, this has no impact on the outcome of the study, since the experienced pathologist was newly assigned.
The pathology phase report was created by the new PI.

ARCHIVING

Original raw data generated at AnaPath GmbH, paraffin blocks and tissue slides as well as all fixed tissues will be returned to the Study Director for archiving after finalization of the study phase report.
The original phase report generated at AnaPath GmbH will be sent to the Study Director for archiving after finalization of the study phase report.

Copies of pathology evaluation raw data and an electronic version of the phase report as well as copies of histotechnique raw data will be retained at AnaPath GmbH for at least 15 years.

1 SUMMARY

The purpose of this study was to establish the effects of repeated oral administration of the test item to rats over a certain period of 90 days. The results of the study are believed to provide information on the possible health hazards which could arise from repeated exposure over a certain period of time. As a part of this study, histopathology examination was performed.

Eighty (80) rats were assigned to 4 groups each containing 10 males and 10 females, including 3 dose groups of the test item (100, 300, and 1000 mg/kg bw/day) and one vehicle control (sterile water) group. The animals were treated with the test item formulation or vehicle on 7 days per week for a period of 90 days. All animals were necropsied and examined *post mortem*, and histological examinations were performed on organs and tissues as described under “Materials and Methods”.

Under the conditions of this study, the test item, Glucose oxidase produced with *Trichoderma reesei*, produced no histomorphologic evidence of toxicological properties in any organs and tissues examined.

In this study two females died prematurely before the end of the treatment period. The cause of animals’ death was considered an accidental influx of the dosing solution into the respiratory tract or an accidental tissue injury related to dosing procedure in the respiratory tract. Either were not test item-related deaths.

All findings recorded in survivors were within the range of normal background lesions which may be recorded in animals of this strain and age, or were incidental lesions that were not related to treatment with the test item.

From the result of histopathology, the histomorphological no-observed effect level (NOEL) and the no-observed-adverse effect level (NOAEL) were established at 1000 mg/kg bw/day in both sexes under the condition of this study.

2 MATERIALS AND METHODS

2.1 Allocation

Allocation and Dose Levels mg/kg body weight/day	Group 1 Control* 0	Group 2 Low 100	Group 3 Medium 300	Group 4 High 1000
Males	1 - 10	11 - 20	21 - 30	31 - 40
Females	41 - 50	51 - 60	61 - 70	71 - 80

*, Control animals were treated with the vehicle, sterile water (aqua ad injectionem), alone..

2.2 Necropsy and Histopathology

Necropsies and the tissue-collection for histopathology were performed at the Test Facility, BSL BIOSERVICE Scientific Laboratories Munich GmbH, Planegg / Germany. Briefly, one day after the last administration, all surviving animals were sacrificed using anesthesia (ketamine/xylazin) and were subjected to a detailed gross necropsy. All animals found dead were subjected to a gross necropsy as well. After necropsy, organs and tissues listed in Table 1 were collected and fixed with 4% neutral-buffered formaldehyde except eyes, testes and epididymides which were fixed in modified Davidson's fixative for approximately 24 hours before preserving them in 70% ethanol.

Collected and preserved tissue samples were shipped to the Test Site AnaPath GmbH, AnaPath Services, Liestal / Switzerland where histotechnique was performed. The samples were processed, embedded in paraffin, cut at approximate thickness of 4 micrometers, and resulting sections were stained with hematoxylin and eosin (H&E). After the quality check under the microscope, sections were delivered to the study pathologist (AnaPath GmbH, Oberbuchsiten / Switzerland).

Sections from the organs and tissues listed in Table 1 were processed and examined by light microscopy for animals of groups 1 and 4 sacrificed at the end of treatment period and animals found dead. All gross lesions from all groups were processed and examined as well.

Table 1 Preserved and Examined Organs/Tissues

Tissues / Organs	Preserved at Necropsy	Examined Histopatho-logically
Adrenal glands	X	X
All gross lesions	X	X

Tissues / Organs	**Preserved at Necropsy**	**Examined Histopatho-logically**
Aorta	X	X
Brain - including sections of medulla/pons, cerebellar and cerebral cortex	X	X
Cecum	X	X
Colon	X	X
Duodenum	X	X
Epididymides	X	X
Eyes with optic nerve and Harderian gland	X	X
Femur with knee joint	X	-
Heart	X	X
Ileum (including Peyer's patches)	X	X
Jejunum	X	X
Kidneys	X	X
Liver	X	X
Lungs	X	X
Lymph nodes (mandibular)	X	-
Lymph nodes (mesenteric and axillary)	X	X
Mammary gland area	X	X
Esophagus	X	X
Ovaries	X	X
Oviducts	X	-
Pancreas	X	X
Pituitary	X	X
Prostate and seminal vesicles with coagulating glands	X	X
Rectum	X	X
Salivary glands (sublingual, submandibular)	X	X
Sciatic nerve	X	X
Skeletal muscle	X	X
Skin	X	X
Spinal cord (cervical, thoracic and lumbar segments)	X	X

Tissues / Organs	**Preserved at Necropsy**	**Examined Histopatho-logically**
Spleen	X	X
Sternum (with bone marrow)	X	X
Stomach	X	X
Testes	X	X
Thymus	X	X
Thyroid gland including parathyroid glands	X	X
Tongue	X	-
Trachea	X	X
Ureters	X	-
Urinary bladder	X	X
Uterus with Cervix and Vagina	X	X

Preservation or Examination was: X, Performed; -, Not performed.

Because test item-related changes were not observed in the high dose group, further histo-processing and histopathological examination for the low- and medium-dose groups were not conducted in this study.

2.3 Data Compilation

The animal data and necropsy findings were transferred manually into the PathData System (PDS), Version 6.2d2. The microscopic findings were recorded during histopathology examination by the pathologist and directly entered into the PDS. The slides of this study were evaluated during March and April 2016.

Histological changes were described, wherever possible, according to distribution, severity and morphologic character. Severity scores were assigned as given under “Explanation of Codes and Symbols”.

All microscopic findings are listed in the “Table of Individual Microscopic Findings (AOFT)”, along with an explanation of the codes and symbols used. Computer-generated incidence tables derived from these data are given under “Number of Animals with Microscopic Findings by Organ/Group/Sex” and are also presented as the complete narrative of both the macroscopic and microscopic findings under “Text of Gross and Microscopic Findings”. Additionally, attempts were made to correlate macroscopic with microscopic findings.

The phase number in the table generated by PDS was expressed as “11661” instead of the complete phase number “11661C”, due to the limitation of the number of characters that can be entered in the PDS.

The test facility study identification number in the table generated by PDS was expressed as “Eurofins/BSL Study 154307” instead of the complete study identification number “Eurofins Munich / BSL Munich Study Number 154307”, due to the limitation of the number of characters that can be entered in the PDS.

The name of the test item in the table generated by PDS was expressed as “Glucose oxidase (food enzyme)” which is a chemical name, instead of the complete name of the test item “Glucose oxidase produced with *Trichoderma reesei*”, due to the limitation of the number of characters that can be entered in the PDS.

3 RESULTS

3.1 Mortality

Female No. 54 of group 2 (Low dose group) and female No. 71 of group 4 (High dose group) were found dead on Test Day 27 and Test Day 82, respectively.

The remainder of animals survived the scheduled study period.

3.2 Macroscopic Findings

There were no gross lesions that could be attributed to treatment with the test item.

3.2.1 Decedents

In both of female No. 54 (group 2) and female No. 71 (group 4), autolysis was advancing. In addition, some organs and tissues including stomach, duodenum, jejunum, ileum, ovary, oviduct and uterus were partially or completely cannibalized in female No. 54.

In female No. 54, abnormal surface looking dark was recorded in the lung. This was deemed to correlate microscopically with inflammation in the pleural surface.

In female No. 71, abnormal color of lung, red discoloration (Abnormal color, red) of thymus, and bilateral enlargement (Enlarged) of adrenal glands were recorded, which were deemed to correlate microscopically with aspiration pneumonia of lung, congestion of thymus, and bilateral cortical diffuse hypertrophy of adrenal glands, respectively.

As being mentioned in the section “3.3 Microscopic Findings”, the cause of animals’ death was considered an accidental influx of the dosing solution into the respiratory tract or an accidental tissue injury related to dosing procedure in the respiratory tract. Either were not test item-related deaths.

3.2.2 Survivors

Abnormal color (yellow) of the epididymis was recorded in one animal of group 1 (male No. 6). This was deemed to correlate microscopically with sperm granuloma which was identified in one side. However, no histologic abnormalities were identified in another side. In the epididymis of this animal, abnormal position (right side) was also recorded, but no histologic abnormality was detected.

Small testis was recorded in one side (right) of one male of group 3 (male No. 23), which correlated microscopically with unilateral moderate tubular degeneration/atrophy. No treatment-related macroscopic and microscopic testicular abnormalities were observed in any males of

group 4, and therefore, tubular degeneration/atrophy recorded in male No. 23 was considered not to be related to treatment with the test item.

Bilateral renal pelvic dilation was recorded in one female of group 4 (female No. 74). This is the lesion which is frequently found in animals of this strain and age and this was recorded only in one animal of group 4, and therefore, this was considered a spontaneous change.

Abnormal surface showing marbled and pale appearances was recorded in the liver of one female of group 4 (female No. 77), but no histologic abnormality was observed in the liver of this animal.

Fluid distention (Fluid filled) in uterus was recorded in 3 females (Nos. 42, 43, and 44) of group 1, 2 females (Nos. 59 and 60) of group 2, one female (No. 63) of group 3, and 3 females (Nos. 73, 74, and 76) of group 4, which correlated microscopically with cornual dilation associated with estrous cycle. There were no dose-response relationship in the incidence, and this finding was deemed to be a normal, physiological change corresponding to estrous cycle.

In the remainder of animals, there were no macroscopic abnormalities.

3.3 Microscopic Findings

There were no histomorphologic changes that could be attributed to treatment with the test item.

3.3.1 Decedents

In female No. 54 of group 2, marked mucosal necrosis with inflammatory cell infiltrate and hemorrhage was recorded in the trachea. Slight inflammation in the pleural surface of the lung and the presence of food residue in the surrounding fatty tissue of the thymus were also observed. These findings indicate that accidental tissue injuries happened in the trachea during the dosing procedure and probably esophageal-gastric contents including food residue flowed out to the thoracic cavity. These events were considered a cause of animal's death.

In female No. 71 of group 4, marked aspiration pneumonia was observed. This was considered to be due to accidental influx of the dosing solution into the lung, which is deemed to be a cause of animal’s death.
In this animal, thymic atrophy/involution and adrenocortical diffuse hypertrophy were also recorded, at a slight severity. These were deemed to be histomorphologic changes as a response to a stressful condition.
Congestion recorded in thymus and adrenal glands were considered to be non-specific postmortem change which is commonly found in dead animals.

The remainder of findings recorded in decedents was within the range of normal background lesions which may be recorded in animals of this strain and age.

3.3.2 Survivors

All findings recorded in survivors were within the range of normal background lesions which may be recorded in animals of this strain and age, or were incidental lesions that were not related to treatment with the test item.

4 DISCUSSION AND CONCLUSION

Under the conditions of this study, the test item, Glucose oxidase produced with *Trichoderma reesei*, produced no histomorphologic evidence of toxicological properties in any organs and tissues examined.

In this study two females died prematurely before the end of the treatment period. The cause of animals' death was considered an accidental influx of the dosing solution into the respiratory tract or an accidental tissue injury related to dosing procedure in the respiratory tract. Either were not test item-related deaths.

All findings recorded in survivors were within the range of normal background lesions which may be recorded in animals of this strain and age, or were incidental lesions that were not related to treatment with the test item.

From the result of histopathology, the histomorphological no-observed effect level (NOEL) and the no-observed-adverse effect level (NOAEL) were established at 1000 mg/kg bw/day in both sexes under the condition of this study.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS

DOSE GROUP:	01		02		03		04	
SEX :	M	F	M	F	M	F	M	F
NO.ANIMALS:	10	10	10	10	10	10	10	10
GENERAL OBSERVATIONS :	—	—	—	1	—	—	—	1
— Autolysis, Advanced :	—	—	—	1	—	—	—	1
— Cannibalized :	—	—	—	1	—	—	—	—
HEART :	10	10	—	1	—	—	10	10
— Mononuclear Foci :	2	1	—	—	—	—	2	2
— Myocar.Degener./Nec.:	—	—	—	—	—	—	1	—
AORTA :	10	10	—	1	—	—	10	10
TRACHEA :	10	10	—	1	—	—	10	10
— Mucosal Necrosis :	—	—	—	1	—	—	—	—
— Inflammatory Foci :	2	2	—	—	—	—	2	1
— Glandular Dilation :	—	1	—	—	—	—	1	—
LUNGS :	10	10	—	1	—	—	10	10
— Alveolar Macrophages:	4	2	—	—	—	—	4	—
— Perivascular Inflam.:	2	—	—	1	—	—	—	—
— Alveolitis :	—	—	—	—	—	—	—	1
— Aspiration Pneumonia:	—	—	—	—	—	—	—	1
— Inflamm.,Pleural S. :	—	—	—	1	—	—	—	—
— Osseous Metaplasia :	—	1	—	—	—	—	1	—
ESOPHAGUS :	10	10	—	1	—	—	10	10
— Mononuclear Foci :	—	1	—	—	—	—	2	—
STOMACH :	10	10	—	1	—	—	10	10
— Incr.Inflam.C.Infil.:	5	3	—	—	—	—	3	1
— Vacuolation,Squam.E.:	3	3	—	—	—	—	2	—
— Gld.Stomach Erosion :	—	1	—	—	—	—	1	1
DUODENUM :	10	10	—	1	—	—	10	10
JEJUNUM :	10	10	—	—	—	—	10	10
ILEUM :	10	10	—	—	—	—	10	10

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS

DOSE GROUP:	01		02		03		04	
SEX :	M	F	M	F	M	F	M	F
NO.ANIMALS:	10	10	10	10	10	10	10	10
CECUM :	10	10	—	—	—	—	10	10
— Granuloma :	—	—	—	—	—	—	—	1
COLON :	10	10	—	—	—	—	10	10
RECTUM :	9	10	—	1	—	—	10	10
LIVER :	10	10	—	1	—	—	10	10
— Inflammatory Foci :	9	8	—	—	—	—	10	8
— Hemopoietic Foci :	—	1	—	—	—	—	—	—
— Fibrosis :	—	1	—	—	—	—	—	—
PANCREAS :	8	10	—	1	—	—	10	10
SAL.G.,SUBMANDIBULAR :	10	10	—	1	—	—	10	10
SAL.G.,SUBLINGUAL :	10	10	—	1	—	—	10	10
— Hypoplasia :	—	—	—	—	—	—	1	—
BONE MARROW, STERNUM :	10	10	—	1	—	—	10	10
SPLEEN :	10	10	—	1	—	—	10	10
— Extramed.Hemopoiesis:	10	10	—	1	—	—	9	10
— Hemosiderin Deposits:	10	9	—	1	—	—	10	10
THYMUS :	10	10	—	1	—	—	10	10
— Atrophy/Involution :	2	2	—	—	—	—	3	4
— Cyst(s) :	2	6	—	—	—	—	1	5
— Congestion :	—	—	—	—	—	—	—	1
— Fd.Residue,Surr.Tis.:	—	—	—	1	—	—	—	—
AXILLARY LYMPH NODES :	10	10	—	1	—	—	10	10
MESENT. LYMPH NODE :	10	10	—	—	—	—	10	10
— Mast Cells Increased:	2	1	—	—	—	—	1	3
PEYER'S PATCHES :	9	10	—	—	—	—	10	10

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS

DOSE GROUP:	01		02		03		04	
SEX :	M	F	M	F	M	F	M	F
NO.ANIMALS:	10	10	10	10	10	10	10	10
KIDNEYS :	10	10	—	1	—	—	10	10
— Hyaline Droplets :	7	—	—	—	—	—	8	—
— Tubular Basophilia :	5	2	—	—	—	—	5	1
— Tubular Cast(s) :	—	1	—	—	—	—	1	1
— Mononuclear Foci :	5	1	—	—	—	—	3	3
— Mineral.,Corticomed.:	—	5	—	—	—	—	—	2
— Cyst(s) :	—	—	—	—	—	—	—	1
— Infarct :	—	—	—	—	—	—	—	1
— Pelvic Dilation :	1	—	—	—	—	—	1	1
URINARY BLADDER :	10	10	—	1	—	—	10	10
— Mononuclear Foci :	1	—	—	—	—	—	2	—
TESTES :	10	—	—	—	1	—	10	—
— Tub.Degener./Atrophy:	—	—	—	—	1	—	—	—
— Sertoli C.Vacuolat. :	1	—	—	—	—	—	—	—
— Hypoplastic Tubule :	—	—	—	—	—	—	1	—
EPIDIDYMIDES :	10	—	—	—	—	—	10	—
— Mononuclear Foci :	5	—	—	—	—	—	5	—
— Sperm Granuloma :	2	—	—	—	—	—	—	—
PROSTATE GLAND :	10	—	—	—	—	—	10	—
— Mononuclear Foci :	1	—	—	—	—	—	2	—
COAGULATING GLANDS :	9	—	—	—	—	—	10	—
SEMINAL VESICLES :	10	—	—	—	—	—	10	—
OVARIES :	—	10	—	1	—	—	—	10
UTERUS :	—	10	—	3	—	1	—	10
— Cornual Dilation :	—	4	—	2	—	1	—	3
CERVIX :	—	10	—	1	—	—	—	10

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS

DOSE GROUP:	01		02		03		04	
SEX :	M	F	M	F	M	F	M	F
NO.ANIMALS:	10	10	10	10	10	10	10	10
VAGINA :	—	10	—	1	—	—	—	10
— Cycle:Proestrus :	—	3	—	1	—	—	—	2
— Cycle:Estrus :	—	2	—	—	—	—	—	3
— Cycle:Metestrus :	—	1	—	—	—	—	—	1
— Cycle:Diestrus :	—	4	—	—	—	—	—	4
PITUITARY GLAND :	10	10	—	1	—	—	10	10
— Cyst(s) :	1	—	—	—	—	—	—	—
ADRENAL GLANDS :	—	—	—	—	—	—	—	1
— Congestion :	—	—	—	—	—	—	—	1
ADRENAL CORTICES :	10	10	—	1	—	—	10	10
— Vacuolation,Z.Fasc. :	2	—	—	—	—	—	1	—
— Diffuse Hypertrophy :	—	—	—	—	—	—	—	1
ADRENAL MEDULLAS :	10	10	—	1	—	—	10	10
THYROID GLAND :	10	10	—	1	—	—	10	10
— Mononuclear Foci :	1	—	—	—	—	—	—	—
— Ectopic Thymus :	—	2	—	—	—	—	—	—
— Ductal Remnants :	—	1	—	1	—	—	3	—
PARATHYROID GLANDS :	10	10	—	1	—	—	9	10
BRAIN, CEREBRUM :	10	10	—	1	—	—	10	10
BRAIN, CEREBELLUM :	10	10	—	1	—	—	10	10
BRAIN, PONS/MEDULLA :	10	10	—	1	—	—	10	10
SPINAL CORD, CERVIC. :	10	10	—	1	—	—	10	10
SPINAL CORD, THORAC. :	10	10	—	1	—	—	10	10
SPINAL CORD, LUMBAR :	10	10	—	1	—	—	10	10

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS

DOSE GROUP:	01		02		03		04	
SEX :	M	F	M	F	M	F	M	F
NO.ANIMALS:	10	10	10	10	10	10	10	10
SCIATIC NERVES :	9	10	—	1	—	—	9	8
EYES :	10	10	—	1	—	—	10	10
— Retinal Degener./At.:	—	2	—	—	—	—	—	—
OPTIC NERVES :	10	9	—	1	—	—	10	10
HARDERIAN GLANDS :	10	10	—	1	—	—	10	10
— Porphyrin Deposits :	6	6	—	—	—	—	8	7
SKIN/SUBCUTIS :	10	10	—	1	—	—	9	10
— Mononuclear Foci :	1	—	—	—	—	—	1	1
— Folliculitis/Perif. :	—	1	—	—	—	—	—	—
MAMMARY GLAND AREA :	10	10	—	1	—	—	9	10
SKELETAL MUSCLE :	10	10	—	1	—	—	10	10
— Inflammation :	—	1	—	—	—	—	—	—
— Mononuclear Foci :	—	1	—	—	—	—	1	1
BONE, STERNUM :	10	10	—	1	—	—	10	10

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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CORRELATION TABLE: NECROPSY — MICROSCOPY DOSE GROUP 01, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 6
EPIDIDYMIDES	
— 01: Discoloration/Abnormal color, yellow.	— Sperm granuloma, unilateral, grade 1.
— 02: Abnormal position, one side (right).	— No corresponding finding.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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CORRELATION TABLE: NECROPSY — MICROSCOPY DOSE GROUP 01, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 42
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change).
	ANIMAL NO: 43
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change).
	ANIMAL NO: 44
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change).

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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CORRELATION TABLE: NECROPSY — MICROSCOPY DOSE GROUP 02, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 54
GENERAL OBSERVATIONS	
— 01: Autolysis, Advanced.	— Autolysis, advanced.
— 02: Cannibalized, partial or whole: stomach, duodenum, jejunum, ileum, ovary, oviduct, uterus.	— Cannibalized.
LUNGS	
— 01: Abnormal surface, dark.	— Inflammation, pleural surface, focal, grade 2.
	ANIMAL NO: 59
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change), proestrus.
	ANIMAL NO: 60
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change), estrus.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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CORRELATION TABLE: NECROPSY — MICROSCOPY DOSE GROUP 03, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 23
TESTES	
— 01: Small/Reduced in size, one side (right).	— Tubular degeneration/atrophy, unilateral, grade 3.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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CORRELATION TABLE: NECROPSY — MICROSCOPY DOSE GROUP 03, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 63
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change), proestrus.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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CORRELATION TABLE: NECROPSY — MICROSCOPY DOSE GROUP 04, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 71
GENERAL OBSERVATIONS	
— 01: Autolysis, Advanced.	— Autolysis, advanced.
LUNGS	
— 01: Discoloration/Abnormal color.	— Aspiration pneumonia, grade 4.
THYMUS	
— 01: Discoloration/Abnormal color, red.	— Congestion, grade 2.
ADRENAL GLANDS	
— 01: Enlarged/Big size, both sides.	— SEE UNDER: ADRENAL CORTICES.
ADRENAL CORTICES	
Finding 01 in ADRENAL GLANDS	— Diffuse hypertrophy, bilateral, grade 2.
	ANIMAL NO: 73
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change).
	ANIMAL NO: 74
KIDNEYS	
— 01: Pelvic dilation, both sides.	— Pelvic dilation, bilateral, grade 2.
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change).

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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CORRELATION TABLE: NECROPSY — MICROSCOPY DOSE GROUP 04, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 76
UTERUS	
— 01: Fluid filled.	— Cornual dilation (cyclic change).
	ANIMAL NO: 77
LIVER	
— 01: Abnormal surface, marbled, pale.	— Nothing abnormal discovered.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
F = Female animal
K0 = Terminal sacrifice group
+ = Intercurrent death/sacrificed moribund
+1 = Found dead

CODES AND SYMBOLS USED AT ORGAN LEVEL:

G = Gross observation checked off histologically
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
— = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
GRADE 3 = Moderate / moderate number / moderate size
GRADE 4 = Marked / many / large
P = Finding present, severity not scored
(= Finding unilateral in paired organs
* = Comment in text of individual animal data

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
HEART	—	—	—	—	—	+	—	—	+	—
— Mononuclear Foci	.	.	.	.	.	1.	.	.	1.	.
AORTA	—	—	—	—	—	—	—	—	—	—
TRACHEA	—	—	—	—	—	—	—	+	—	+
— Inflammatory Foci	.	.	.	.	.	.	.	1.	.	1.
LUNGS	+	—	—	—	+	—	+	+	+	+
— Alveolar Macrophages	1.	.	.	.	1.	.	.	1.	.	1.
— Perivascular Inflam.	.	.	.	.	.	.	1.	.	1.	.
ESOPHAGUS	—	—	—	—	—	—	—	—	—	—
STOMACH	—	+	+	—	+	—	—	+	—	+
— Incr.Inflam.C.Infil.	.	1*	1.	.	1.	.	.	1.	.	1*
— Vacuolation,Squam.E.	.	.	.	.	1.	.	.	1.	.	1.
DUODENUM	—	—	—	—	—	—	—	—	—	—
JEJUNUM	—	—	—	—	—	—	—	—	—	—
ILEUM	—	—	—	—	—	—	—	—	—	—
CECUM	—	—	—	—	—	—	—	—	—	—
COLON	—	—	—	—	—	—	—	—	—	—
RECTUM	0	—	—	—	—	—	—	—	—	—
LIVER	+	+	+	+	+	+	+	—	+	+
— Inflammatory Foci	1.	1.	1.	1.	1.	1.	1.	.	1.	1.
PANCREAS	—	—	—	—	—	0	—	—	0	—
SAL.G.,SUBMANDIBULAR	—	—	—	—	—	—	—	—	—	—
SAL.G.,SUBLINGUAL	—	—	—	—	—	—	—	(—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
BONE MARROW, STERNUM	—	—	—	—	—	—	—	—	—	—
SPLEEN	+	+	+	+	+	+	+	+	+	+
— Extramed.Hemopoiesis	2.	1.	1.	1.	1.	1.	1.	1.	1.	1.
— Hemosiderin Deposits	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
THYMUS	—	—	—	+	+	—	—	+	+	—
— Atrophy/Involution	.	.	.	.	1.	.	.	1.	.	.
— Cyst(s)	.	.	.	P.	.	.	.	.	P.	.
AXILLARY LYMPH NODES	—	—	—	—	—	(—	—	—	—	—
MESENT. LYMPH NODE	—	—	—	—	+	—	—	+	—	—
— Mast Cells Increased	.	.	.	.	1.	.	.	1.	.	.
PEYER'S PATCHES	—	—	—	—	—	—	—	—	0	—
KIDNEYS	+	+	+	+	+	+	+	+	+	+
— Hyaline Droplets	1.	1.	1.	1.	1.	1.	.	.	1.	.
— Tubular Basophilia	.	(1.	.	.	.	.	(1.	1.	(1.	(1.
— Mononuclear Foci	.	.	.	1.	.	.	1.	1.	1.	(1.
— Pelvic Dilation	.	.	.	.	.	.	.	.	(1.	.
URINARY BLADDER	—	—	—	—	—	—	—	—	+	—
— Mononuclear Foci	.	.	.	.	.	.	.	.	1.	.
TESTES	—	—	—	—	—	—	+	—	—	—
— Sertoli C.Vacuolat.	.	.	.	.	.	.	(1.	.	.	.
EPIDIDYMIDES	—	+	—	—	+	+G	+	+	+	—
— Mononuclear Foci	.	(1.	.	.	1.	.	(1.	1.	(1.	.
— Sperm Granuloma	.	.	.	.	.	(1.	.	.	(1.	.
PROSTATE GLAND	—	—	—	—	—	—	+	—	—	—
— Mononuclear Foci	.	.	.	.	.	.	1.	.	.	.
COAGULATING GLANDS	—	—	—	—	—	—	—	0	—	—
SEMINAL VESICLES	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PITUITARY GLAND	—	—	+	—	—	—	—	—	—	—
— Cyst(s)	.	.	P.	.	.	.	.	.	.	.
ADRENAL CORTICES	—	—	—	+	—	+	—	—	—	—
— Vacuolation,Z.Fasc.	.	.	.	1.	.	1.	.	.	.	.
ADRENAL MEDULLAS	—	—	—	—	—	—	—	—	—	—
THYROID GLAND	—	—	—	—	—	—	—	+	(—	—
— Mononuclear Foci	.	.	.	.	.	.	.	(1.	.	.
PARATHYROID GLANDS	—	—	—	—	—	—	—	—	(—	—
BRAIN, CEREBRUM	—	—	—	—	—	—	—	—	—	—
BRAIN, CEREBELLUM	—	—	—	—	—	—	—	—	—	—
BRAIN, PONS/MEDULLA	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, CERVIC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, THORAC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, LUMBAR	—	—	—	—	—	—	—	—	—	—
SCIATIC NERVES	0	—	—	—	—	—	—	—	—	—
EYES	—	—	—	—	—	—	—	—	—	—
OPTIC NERVES	—	—	—	—	(—	—	(—	(—	—	—
HARDERIAN GLANDS	+	+	+	+	+	—	—	+	—	—
— Porphyrin Deposits	1.	1.	1.	(1.	1.	.	.	1.	.	.
SKIN/SUBCUTIS	—	—	—	—	+	—	—	—	—	—
— Mononuclear Foci	.	.	.	.	1.	.	.	.	.	.
MAMMARY GLAND AREA	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
SKELETAL MUSCLE	—	—	—	—	—	—	—	—	—	—
BONE, STERNUM	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	41 FK0	42 FK0	43 FK0	44 FK0	45 FK0	46 FK0	47 FK0	48 FK0	49 FK0	50 FK0
HEART	—	+	—	—	—	—	—	—	—	—
— Mononuclear Foci	.	1.	.	.	.	.	.	.	.	.
AORTA	—	—	—	—	—	—	—	—	—	—
TRACHEA	+	—	—	—	—	—	—	—	—	+
— Inflammatory Foci	1.	.	.	.	.	.	.	.	.	1.
— Glandular Dilation	1.	.	.	.	.	.	.	.	.	.
LUNGS	—	—	—	+	—	—	+	—	—	+
— Alveolar Macrophages	.	.	.	.	.	.	1.	.	.	1.
— Osseous Metaplasia	.	.	.	P.	.	.	.	.	.	.
ESOPHAGUS	—	—	—	—	—	—	—	—	—	+
— Mononuclear Foci	.	.	.	.	.	.	.	.	.	1.
STOMACH	+	—	—	—	—	—	—	—	+	+
— Incr.Inflam.C.Infil.	1.	.	.	.	.	.	.	.	1.	1*
— Vacuolation,Squam.E.	1.	.	.	.	.	.	.	.	1.	1.
— Gld.Stomach Erosion	.	.	.	.	.	.	.	.	1.	.
DUODENUM	—	—	—	—	—	—	—	—	—	—
JEJUNUM	—	—	—	—	—	—	—	—	—	—
ILEUM	—	—	—	—	—	—	—	—	—	—
CECUM	—	—	—	—	—	—	—	—	—	—
COLON	—	—	—	—	—	—	—	—	—	—
RECTUM	—	—	—	—	—	—	—	—	—	—
LIVER	+	+	—	+	—	+	+	+	+	+
— Inflammatory Foci	1.	1.	.	1.	.	1.	1.	1.	1.	1.
— Hemopoietic Foci	1.	.	.	.	.	.	.	.	.	.
— Fibrosis	.	.	.	1.	.	.	.	.	.	.
PANCREAS	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90–Day, Oral (Gavage) *DATE* : 07–JUL–16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	41 FK0	42 FK0	43 FK0	44 FK0	45 FK0	46 FK0	47 FK0	48 FK0	49 FK0	50 FK0
SAL.G.,SUBMANDIBULAR	–	–	–	–	–	–	–	–	–	–
SAL.G.,SUBLINGUAL	–	–	–	–	–	–	–	–	–	–
BONE MARROW, STERNUM	–	–	–	–	–	–	–	–	–	–
SPLEEN	+	+	+	+	+	+	+	+	+	+
– Extramed.Hemopoiesis	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
– Hemosiderin Deposits	1.	2.	1.	1.	.	1.	2.	1.	1.	2.
THYMUS	+	+	–	+	+	+	+	+	–	+
– Atrophy/Involution	.	.	.	.	.	.	.	1.	.	1.
– Cyst(s)	P.	P.	.	P.	P.	P.	P.	.	.	.
AXILLARY LYMPH NODES	–	–	–	–	–	–	–	–	–	–
MESENT. LYMPH NODE	–	–	–	–	+	–	–	–	–	–
– Mast Cells Increased	.	.	.	.	1.	.	.	.	.	.
PEYER'S PATCHES	–	–	–	–	–	–	–	–	–	–
KIDNEYS	+	+	+	+	–	–	+	–	+	+
– Tubular Basophilia	.	.	.	(1.	.	.	.	.	.	(1.
– Tubular Cast(s)	.	.	.	(1.	.	.	.	.	.	.
– Mononuclear Foci	.	.	.	.	.	.	(1.	.	.	.
– Mineral.,Corticomed.	(1.	1.	1.	2.	.	.	.	.	(1.	.
URINARY BLADDER	–	–	–	–	–	–	–	–	–	–
OVARIES	–	–	–	–	–	–	–	–	–	–
UTERUS	–	+G	+G	+G	+	–	–	–	–	–
– Cornual Dilation	.	P.	P.	P.	P.	.	.	.	.	.
CERVIX	–	–	–	–	–	–	–	–	–	–

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	41	42	43	44	45	46	47	48	49	50
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
VAGINA	+	+	+	+	+	+	+	+	+	+
— Cycle:Proestrus	.	.	P.	P.	.	.	.	.	.	P.
— Cycle:Estrus	.	P.	.	.	P.	.	.	.	.	.
— Cycle:Metestrus	P.	.	.	.	.	.	.	.	.	.
— Cycle:Diestrus	.	.	.	.	.	P.	P.	P.	P.	.
PITUITARY GLAND	—	—	—	—	—	—	—	—	—	—
ADRENAL CORTICES	—	—	—	—	—	—	—	—	—	—
ADRENAL MEDULLAS	—	—	—	—	—	—	—	—	—	—
THYROID GLAND	—	—	+	—	—	—	—	+	—	—
— Ectopic Thymus	.	.	(P.	.	.	.	.	(P.	.	.
— Ductal Remnants	.	.	(P.	.	.	.	.	.	.	.
PARATHYROID GLANDS	—	(—	(—	—	—	—	—	(—	—	(—
BRAIN, CEREBRUM	—	—	—	—	—	—	—	—	—	—
BRAIN, CEREBELLUM	—	—	—	—	—	—	—	—	—	—
BRAIN, PONS/MEDULLA	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, CERVIC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, THORAC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, LUMBAR	—	—	—	—	—	—	—	—	—	—
SCIATIC NERVES	—	—	—	—	—	—	—	—	—	—
EYES	—	—	—	—	—	—	+	+	—	—
— Retinal Degener./At.	.	.	.	.	.	.	(1.	(1.	.	.
OPTIC NERVES	—	0	(—	—	—	(—	—	—	—	—
HARDERIAN GLANDS	+	—	+	—	—	+	+	+	—	+
— Porphyrin Deposits	1.	.	1.	.	.	(1.	(1.	(1.	.	1.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER :	41 FK0	42 FK0	43 FK0	44 FK0	45 FK0	46 FK0	47 FK0	48 FK0	49 FK0	50 FK0
SKIN/SUBCUTIS	—	—	—	—	—	—	—	—	—	+
— Folliculitis/Perif.	.	.	.	.	.	.	.	.	.	1.
MAMMARY GLAND AREA	—	—	—	—	—	—	—	—	—	—
SKELETAL MUSCLE	—	—	—	—	—	—	+	—	—	+
— Inflammation	.	.	.	.	.	.	1.	.	.	.
— Mononuclear Foci	.	.	.	.	.	.	.	.	.	1.
BONE, STERNUM	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90–Day, Oral (Gavage) *DATE* : 07–JUL–16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day

ANIMAL NUMBER :	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0+	FK0	FK0	FK0	FK0	FK0	FK0
GENERAL OBSERVATIONS	'	'	'	+G	'	'	'	'	'	'
– Autolysis, Advanced				P.						
– Cannibalized				P.						
HEART	'	'	'	–	'	'	'	'	'	'
AORTA	'	'	'	–	'	'	'	'	'	'
TRACHEA	'	'	'	+	'	'	'	'	'	'
– Mucosal Necrosis				4*						
LUNGS	'	'	'	+G	'	'	'	'	'	'
– Perivascular Inflam.				1.						
– Inflamm.,Pleural S.				2.						
ESOPHAGUS	'	'	'	–	'	'	'	'	'	'
STOMACH	'	'	'	–	'	'	'	'	'	'
DUODENUM	'	'	'	–	'	'	'	'	'	'
JEJUNUM	'	'	'	0	'	'	'	'	'	'
ILEUM	'	'	'	0	'	'	'	'	'	'
CECUM	'	'	'	0	'	'	'	'	'	'
COLON	'	'	'	0	'	'	'	'	'	'
RECTUM	'	'	'	–	'	'	'	'	'	'
LIVER	'	'	'	–	'	'	'	'	'	'
PANCREAS	'	'	'	–	'	'	'	'	'	'
SAL.G.,SUBMANDIBULAR	'	'	'	–	'	'	'	'	'	'
SAL.G.,SUBLINGUAL	'	'	'	–	'	'	'	'	'	'

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day

ANIMAL NUMBER :	51 FK0	52 FK0	53 FK0	54 FK0+	55 FK0	56 FK0	57 FK0	58 FK0	59 FK0	60 FK0
BONE MARROW, STERNUM	'	'	'	—	'	'	'	'	'	'
SPLEEN	'	'	'	+	'	'	'	'	'	'
— Extramed.Hemopoiesis				1.						
— Hemosiderin Deposits				1.						
THYMUS	'	'	'	+	'	'	'	'	'	'
— Fd.Residue,Surr.Tis.				P.						
AXILLARY LYMPH NODES	'	'	'	—	'	'	'	'	'	'
MESENT. LYMPH NODE	'	'	'	0	'	'	'	'	'	'
PEYER'S PATCHES	'	'	'	0	'	'	'	'	'	'
KIDNEYS	'	'	'	—	'	'	'	'	'	'
URINARY BLADDER	'	'	'	—	'	'	'	'	'	'
OVARIES	'	'	'	—	'	'	'	'	'	'
UTERUS	'	'	'	—	'	'	'	'	+G	+G
— Cornual Dilation				.					P.	P.
CERVIX	'	'	'	—	'	'	'	'	'	'
VAGINA	'	'	'	+	'	'	'	'	'	'
— Cycle:Proestrus				P.						
PITUITARY GLAND	'	'	'	—	'	'	'	'	'	'
ADRENAL CORTICES	'	'	'	—	'	'	'	'	'	'
ADRENAL MEDULLAS	'	'	'	—	'	'	'	'	'	'
THYROID GLAND	'	'	'	+	'	'	'	'	'	'
— Ductal Remnants				(P.						
PARATHYROID GLANDS	'	'	'	—	'	'	'	'	'	'

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day

ANIMAL NUMBER :	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0+	FK0	FK0	FK0	FK0	FK0	FK0
BRAIN, CEREBRUM	'	'	'	—	'	'	'	'	'	'
BRAIN, CEREBELLUM	'	'	'	—	'	'	'	'	'	'
BRAIN, PONS/MEDULLA	'	'	'	—	'	'	'	'	'	'
SPINAL CORD, CERVIC.	'	'	'	—	'	'	'	'	'	'
SPINAL CORD, THORAC.	'	'	'	—	'	'	'	'	'	'
SPINAL CORD, LUMBAR	'	'	'	—	'	'	'	'	'	'
SCIATIC NERVES	'	'	'	—	'	'	'	'	'	'
EYES	'	'	'	—	'	'	'	'	'	'
OPTIC NERVES	'	'	'	(—	'	'	'	'	'	'
HARDERIAN GLANDS	'	'	'	—	'	'	'	'	'	'
SKIN/SUBCUTIS	'	'	'	—	'	'	'	'	'	'
MAMMARY GLAND AREA	'	'	'	—	'	'	'	'	'	'
SKELETAL MUSCLE	'	'	'	—	'	'	'	'	'	'
BONE, STERNUM	'	'	'	—	'	'	'	'	'	'

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day

ANIMAL NUMBER :	21 MK0	22 MK0	23 MK0	24 MK0	25 MK0	26 MK0	27 MK0	28 MK0	29 MK0	30 MK0
TESTES	'	'	(+G	'	'	'	'	'	'	'
— Tub.Degener./Atrophy			(3*							

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day

ANIMAL NUMBER :	61	62	63	64	65	66	67	68	69	70
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
UTERUS	'	'	+G	'	'	'	'	'	'	'
— Cornual Dilation			P.							

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	31 MK0	32 MK0	33 MK0	34 MK0	35 MK0	36 MK0	37 MK0	38 MK0	39 MK0	40 MK0
HEART	+	—	—	—	—	—	—	+	+	—
— Mononuclear Foci	1.	.	.	.	.	.	.	.	1.	.
— Myocar.Degener./Nec.	.	.	.	.	.	.	.	1.	.	.
AORTA	—	—	—	—	—	—	—	—	—	—
TRACHEA	—	—	+	—	—	+	—	—	—	+
— Inflammatory Foci	.	.	1.	.	.	.	.	.	.	1.
— Glandular Dilation	.	.	.	.	.	1.	.	.	.	.
LUNGS	—	+	—	—	+	+	—	+	—	—
— Alveolar Macrophages	.	1.	.	.	1.	1.	.	1.	.	.
— Osseous Metaplasia	.	.	.	.	P.	.	.	.	.	.
ESOPHAGUS	—	—	—	—	+	—	—	—	—	+
— Mononuclear Foci	.	.	.	.	1.	.	.	.	.	1.
STOMACH	—	—	—	+	—	+	—	+	—	+
— Incr.Inflam.C.Infil.	.	.	.	1.	.	.	.	1*	.	1*
— Vacuolation,Squam.E.	.	.	.	1.	.	.	.	1.	.	.
— Gld.Stomach Erosion	.	.	.	.	.	1.	.	.	.	.
DUODENUM	—	—	—	—	—	—	—	—	—	—
JEJUNUM	—	—	—	—	—	—	—	—	—	—
ILEUM	—	—	—	—	—	—	—	—	—	—
CECUM	—	—	—	—	—	—	—	—	—	—
COLON	—	—	—	—	—	—	—	—	—	—
RECTUM	—	—	—	—	—	—	—	—	—	—
LIVER	+	+	+	+	+	+	+	+	+	+
— Inflammatory Foci	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
PANCREAS	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	31	32	33	34	35	36	37	38	39	40
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
SAL.G.,SUBMANDIBULAR	—	—	—	—	—	—	—	—	—	—
SAL.G.,SUBLINGUAL	—	—	(—	(—	—	—	—	—	—	+
— Hypoplasia	.	.	.	.	.	.	.	.	.	P.
BONE MARROW, STERNUM	—	—	—	—	—	—	—	—	—	—
SPLEEN	+	+	+	+	+	+	+	+	+	+
— Extramed.Hemopoiesis	1.	1.	1.	1.	.	1.	1.	1.	1.	1.
— Hemosiderin Deposits	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
THYMUS	+	+	—	+	—	—	—	—	—	+
— Atrophy/Involution	1.	.	.	1.	.	.	.	.	.	1.
— Cyst(s)	.	P.	.	.	.	.	.	.	.	.
AXILLARY LYMPH NODES	—	—	—	—	—	—	—	—	—	—
MESENT. LYMPH NODE	—	—	—	—	—	—	—	—	+	—
— Mast Cells Increased	.	.	.	.	.	.	.	.	1.	.
PEYER'S PATCHES	—	—	—	—	—	—	—	—	—	—
KIDNEYS	+	+	+	+	+	+	+	+	+	+
— Hyaline Droplets	1.	.	1.	1.	1.	1.	.	1.	1.	1.
— Tubular Basophilia	.	1.	.	.	(1.	(1.	(1.	.	.	(1.
— Tubular Cast(s)	.	.	(1.	.	.	.	.	.	.	.
— Mononuclear Foci	.	.	.	.	.	.	.	(1.	1.	(1.
— Pelvic Dilation	(1.	.	.	.	.	.	.	.	.	.
URINARY BLADDER	—	—	—	+	—	+	—	—	—	—
— Mononuclear Foci	.	.	.	1.	.	2.	.	.	.	.
TESTES	—	—	—	—	—	+	—	—	—	—
— Hypoplastic Tubule	.	.	.	.	.	(1.	.	.	.	.
EPIDIDYMIDES	—	+	+	—	—	+	—	+	+	—
— Mononuclear Foci	.	(1.	(1.	.	.	(1.	.	1.	(1.	.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	31 MK0	32 MK0	33 MK0	34 MK0	35 MK0	36 MK0	37 MK0	38 MK0	39 MK0	40 MK0
PROSTATE GLAND	—	—	—	—	—	+	—	—	+	—
— Mononuclear Foci	.	.	.	.	.	1.	.	.	1.	.
COAGULATING GLANDS	—	—	—	—	—	—	—	—	—	—
SEMINAL VESICLES	—	—	—	—	—	—	—	—	—	—
PITUITARY GLAND	—	—	—	—	—	—	—	—	—	—
ADRENAL CORTICES	—	+	—	—	—	—	—	—	—	—
— Vacuolation,Z.Fasc.	.	1.	.	.	.	.	.	.	.	.
ADRENAL MEDULLAS	—	—	—	—	—	—	—	—	(—	—
THYROID GLAND	—	—	+	—	—	—	—	—	+	+
— Ductal Remnants	.	.	(P.	.	.	.	.	.	(P.	(P.
PARATHYROID GLANDS	(—	—	—	—	—	—	—	—	0	(—
BRAIN, CEREBRUM	—	—	—	—	—	—	—	—	—	—
BRAIN, CEREBELLUM	—	—	—	—	—	—	—	—	—	—
BRAIN, PONS/MEDULLA	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, CERVIC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, THORAC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, LUMBAR	—	—	—	—	—	—	—	—	—	—
SCIATIC NERVES	—	—	0	—	—	—	—	—	—	—
EYES	—	—	—	—	—	—	—	—	—	—
OPTIC NERVES	—	—	—	—	(—	—	—	—	(—	—
HARDERIAN GLANDS	+	+	—	+	+	+	—	+	+	+
— Porphyrin Deposits	(1.	(1.	.	1.	(1.	1.	.	1.	1.	1.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	31 MK0	32 MK0	33 MK0	34 MK0	35 MK0	36 MK0	37 MK0	38 MK0	39 MK0	40 MK0
SKIN/SUBCUTIS	—	+	—	—	—	—	0	—	—	—
— Mononuclear Foci	.	1.	.	.	.	.	.	.	.	.
MAMMARY GLAND AREA	—	—	—	—	—	—	0	—	—	—
SKELETAL MUSCLE	—	—	—	—	—	—	—	—	+	—
— Mononuclear Foci	.	.	.	.	.	.	.	.	1.	.
BONE, STERNUM	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	71	72	73	74	75	76	77	78	79	80
	FK0+	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
GENERAL OBSERVATIONS	+G	'	'	'	'	'	'	'	'	'
— Autolysis, Advanced	P.									
HEART	+	—	—	—	—	—	—	+	—	—
— Mononuclear Foci	1.	.	.	.	.	.	.	1.	.	.
AORTA	—	—	—	—	—	—	—	—	—	—
TRACHEA	—	—	—	—	+	—	—	—	—	—
— Inflammatory Foci	.	.	.	.	1.	.	.	.	.	.
LUNGS	+G	—	—	—	—	—	—	—	—	+
— Alveolitis	.	.	.	.	.	.	.	.	.	1.
— Aspiration Pneumonia	4.	.	.	.	.	.	.	.	.	.
ESOPHAGUS	—	—	—	—	—	—	—	—	—	—
STOMACH	—	—	—	—	+	—	—	+	—	—
— Incr.Inflam.C.Infil.	.	.	.	.	1*	.	.	.	.	.
— Gld.Stomach Erosion	.	.	.	.	.	.	.	1.	.	.
DUODENUM	—	—	—	—	—	—	—	—	—	—
JEJUNUM	—	—	—	—	—	—	—	—	—	—
ILEUM	—	—	—	—	—	—	—	—	—	—
CECUM	—	—	—	—	—	—	—	—	—	+
— Granuloma	.	.	.	.	.	.	.	.	.	1.
COLON	—	—	—	—	—	—	—	—	—	—
RECTUM	—	—	—	—	—	—	—	—	—	—
LIVER	+	+	—	+	+	+	—G	+	+	+
— Inflammatory Foci	1.	1.	.	1.	1.	1.	.	1.	1.	1.
PANCREAS	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	71 FK0+	72 FK0	73 FK0	74 FK0	75 FK0	76 FK0	77 FK0	78 FK0	79 FK0	80 FK0
SAL.G.,SUBMANDIBULAR	—	—	—	—	—	—	—	—	—	—
SAL.G.,SUBLINGUAL	—	—	—	—	—	—	—	—	—	—
BONE MARROW, STERNUM	—	—	—	—	—	—	—	—	—	—
SPLEEN	+	+	+	+	+	+	+	+	+	+
— Extramed.Hemopoiesis	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
— Hemosiderin Deposits	1.	1.	1.	1.	1.	2.	1.	1.	2.	2.
THYMUS	+G	+	+	—	+	+	+	+	+	—
— Atrophy/Involution	2.	1.	.	.	.	.	1.	.	1.	.
— Cyst(s)	.	.	P.	.	P.	P.	P.	P.	.	.
— Congestion	2.	.	.	.	.	.	.	.	.	.
AXILLARY LYMPH NODES	—	—	—	—	—	—	—	—	—	—
MESENT. LYMPH NODE	—	+	+	—	—	—	—	—	—	+
— Mast Cells Increased	.	1.	1.	.	.	.	.	.	.	1.
PEYER'S PATCHES	—	—	—	—	—	—	—	—	—	—
KIDNEYS	—	—	—	+G	+	+	+	—	—	+
— Tubular Basophilia	.	.	.	(1.	.	.	.	.	.	.
— Tubular Cast(s)	.	.	.	.	(1.	.	.	.	.	.
— Mononuclear Foci	.	.	.	(1.	(1.	.	.	.	.	(1.
— Mineral.,Corticomed.	.	.	.	.	.	(1.	(1.	.	.	.
— Cyst(s)	.	.	.	.	.	(P.	.	.	.	.
— Infarct	.	.	.	.	.	.	(1.	.	.	.
— Pelvic Dilation	.	.	.	2.	.	.	.	.	.	.
URINARY BLADDER	—	—	—	—	—	—	—	—	—	—
OVARIES	—	—	—	—	—	—	—	—	—	—
UTERUS	—	—	+G	+G	—	+G	—	—	—	—
— Cornual Dilation	.	.	P.	P.	.	P.	.	.	.	.
CERVIX	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	71 FK0+	72 FK0	73 FK0	74 FK0	75 FK0	76 FK0	77 FK0	78 FK0	79 FK0	80 FK0
VAGINA	+	+	+	+	+	+	+	+	+	+
— Cycle:Proestrus	P.	.	.	P.	.	.	.	.	.	.
— Cycle:Estrus	.	.	P.	.	.	P.	.	.	P.	.
— Cycle:Metestrus	.	P.	.	.	.	.	.	.	.	.
— Cycle:Diestrus	.	.	.	.	P.	.	P.	P.	.	P.
PITUITARY GLAND	—	—	—	—	—	—	—	—	—	—
ADRENAL GLANDS	+G	'	'	'	'	'	'	'	'	'
— Congestion	2.									
ADRENAL CORTICES	+	—	—	—	—	—	—	—	—	—
— Diffuse Hypertrophy	2.	.	.	.	.	.	.	.	.	.
ADRENAL MEDULLAS	—	—	—	—	—	—	—	—	—	—
THYROID GLAND	—	—	—	—	—	(—	—	—	—	—
PARATHYROID GLANDS	—	—	—	—	(—	(—	(—	(—	—	(—
BRAIN, CEREBRUM	—	—	—	—	—	—	—	—	—	—
BRAIN, CEREBELLUM	—	—	—	—	—	—	—	—	—	—
BRAIN, PONS/MEDULLA	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, CERVIC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, THORAC.	—	—	—	—	—	—	—	—	—	—
SPINAL CORD, LUMBAR	—	—	—	—	—	—	—	—	—	—
SCIATIC NERVES	0	—	—	—	—	—	—	—	—	0
EYES	—	—	—	—	—	—	—	—	—	—
OPTIC NERVES	(—	—	—	(—	—	(—	(—	(—	(—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER :	71 FK0+	72 FK0	73 FK0	74 FK0	75 FK0	76 FK0	77 FK0	78 FK0	79 FK0	80 FK0
HARDERIAN GLANDS	+	—	—	—	+	+	+	+	+	+
— Porphyrin Deposits	1.	.	.	.	(1.	(1.	(1.	(1.	(1.	(1.
SKIN/SUBCUTIS	—	—	—	—	+	—	—	—	—	—
— Mononuclear Foci	.	.	.	.	1.	.	.	.	.	.
MAMMARY GLAND AREA	—	—	—	—	—	—	—	—	—	—
SKELETAL MUSCLE	+	—	—	—	—	—	—	—	—	—
— Mononuclear Foci	1.	.	.	.	.	.	.	.	.	.
BONE, STERNUM	—	—	—	—	—	—	—	—	—	—

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90–Day, Oral (Gavage) *DATE* : 07–JUL–16
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ANIMAL HEADING DATA
DOSE GROUP : 01, Control, 0 mg/kg bw/day

ANIMAL NUMBER	SEX M/F	DEFINED STATE OF NECROPSY	FINAL STATE OF NECROPSY	TEST DAYS	FIRST DAY UNDER TEST	LAST DAY UNDER TEST	DATE OF NECROPSY
1	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
2	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
3	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
4	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
5	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
6	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
7	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
8	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
9	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
10	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
41	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
42	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
43	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
44	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
45	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
46	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
47	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
48	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
49	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
50	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 1

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
RECTUM:
Tissue not present for histologic examination
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 2
—Hemosiderin deposits, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
SCIATIC NERVES:
Tissue not present for histologic examination
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 2

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
and glandular stomach.
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Tubular basophilia, focal/multifocal, unilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 3

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
PITUITARY GLAND:
—Cyst(s), anterior lobe
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 4

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1
ADRENAL CORTICES:
—Vacuolation (fatty change), zona fasciculata, diffuse, bilateral, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 5

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
—Vacuolation, squamous epithelium, limiting ridge, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Atrophy/involution, grade 1
MESENTERIC LYMPH NODE:
—Mast cells increased, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
SKIN/SUBCUTIS:
—Mononuclear cell focus/foci, dermis, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
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TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 6

* NECROPSY FINDINGS

EPIDIDYMIDES:
01: Discoloration/Abnormal color, yellow.
02: Abnormal position, one side (right).
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

HEART:
—Mononuclear cell focus/foci, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
PANCREAS:
Tissue not present for histologic examination
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
AXILLARY LYMPH NODES:
Only one of paired organs examined/present
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
EPIDIDYMIDES:
No microscopic finding corresponding to necropsy observation no. 02.
—Sperm granuloma, unilateral, grade 1
This finding corresponds to necropsy observation no: 01.
ADRENAL CORTICES:
—Vacuolation (fatty change), zona fasciculata, diffuse, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 7

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:
—Perivascular inflammation, focal/multifocal, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Tubular basophilia, focal/multifocal, unilateral, grade 1
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1
TESTES:
—Sertoli cell vacuolation, focal/multifocal, unilateral,
grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
PROSTATE GLAND:
—Mononuclear cell focus/foci, grade 1
OPTIC NERVES:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 8

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Inflammatory cell focus/foci, submucosa, grade 1
LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
—Vacuolation, squamous epithelium, limiting ridge, grade 1
SALIVARY GLAND, SUBLINGUAL:
Only one of paired organs examined/present
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Atrophy/involution, grade 1
MESENTERIC LYMPH NODE:
—Mast cells increased, grade 1
KIDNEYS:
—Tubular basophilia, focal/multifocal, bilateral, grade 1
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1
COAGULATING GLANDS (ANTERIOR PROSTATE):
Tissue not present for histologic examination
THYROID GLAND (BOTH LOBES):
—Mononuclear cell focus/foci, unilateral, grade 1
OPTIC NERVES:
Only one of paired organs examined/present

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

CONT./FF. ANIMAL NO. : 8

HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 9

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART:
—Mononuclear cell focus/foci, grade 1
LUNGS:
—Perivascular inflammation, focal/multifocal, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
PANCREAS:
Tissue not present for histologic examination
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
PEYER'S PATCHES:
Tissue not present for histologic examination
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Tubular basophilia, focal/multifocal, unilateral, grade 1
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

CONT./FF. ANIMAL NO. : 9

—Pelvic dilation, unilateral, grade 1
URINARY BLADDER:
—Mononuclear cell focus/foci, lamina propria, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
—Sperm granuloma, unilateral, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 10

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Inflammatory cell focus/foci, submucosa, grade 1
LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge,
grade 1
and glandular stomach.
—Vacuolation, squamous epithelium, limiting ridge, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day MALE

CONT./FF. ANIMAL NO. : 10

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Tubular basophilia, focal/multifocal, unilateral, grade 1
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 41

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Inflammatory cell focus/foci, grade 1
—Glandular dilation, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
—Vacuolation, squamous epithelium, limiting ridge, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
—Hemopoietic cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
KIDNEYS:
—Mineralization, corticomedullary, focal/multifocal, unilateral, grade 1
VAGINA:
—Metestrus phase of the estrous cycle
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 42

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

HEART:
—Mononuclear cell focus/foci, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 2
THYMUS:
—Cyst(s)
KIDNEYS:
—Mineralization, corticomedullary, focal/multifocal, bilateral, grade 1
UTERUS:
—Cornual dilation (cyclic change)
This finding corresponds to necropsy observation no: 01.
VAGINA:
—Estrus phase of the estrous cycle
PARATHYROID GLANDS:
Only one of paired organs examined/present
OPTIC NERVES:
Tissue not present for histologic examination
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 43

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Mineralization, corticomedullary, focal/multifocal, bilateral, grade 1
UTERUS:
—Cornual dilation (cyclic change)
This finding corresponds to necropsy observation no: 01.
VAGINA:
—Proestrus phase of the estrous cycle
THYROID GLAND (BOTH LOBES):
—Ectopic thymus, unilateral
—Ductal remnants, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 44

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNGS:
—Osseous metaplasia, focal
LIVER:
—Inflammatory cell focus/foci, grade 1
—Fibrosis, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
KIDNEYS:
—Tubular basophilia, focal/multifocal, unilateral, grade 1
—Tubular cast(s), hyaline, focal, unilateral, grade 1
—Mineralization, corticomedullary, focal/multifocal, bilateral, grade 2
UTERUS:
—Cornual dilation (cyclic change)
This finding corresponds to necropsy observation no: 01.
VAGINA:
—Proestrus phase of the estrous cycle
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 45

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

SPLEEN:
—Extramedullary hemopoiesis, grade 1
THYMUS:
—Cyst(s)
MESENTERIC LYMPH NODE:
—Mast cells increased, grade 1
UTERUS:
—Cornual dilation (cyclic change)
VAGINA:
—Estrus phase of the estrous cycle
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 46

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 46

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
VAGINA:
—Diestrus phase of the estrous cycle
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 47

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 47

SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 2
THYMUS:
—Cyst(s)
KIDNEYS:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
VAGINA:
—Diestrus phase of the estrous cycle
EYES:
—Retinal degeneration/atrophy, focal, unilateral, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
SKELETAL MUSCLE:
—Inflammation, focal, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 48

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 48

THYMUS:
—Atrophy/involution, grade 1
VAGINA:
—Diestrus phase of the estrous cycle
THYROID GLAND (BOTH LOBES):
—Ectopic thymus, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
EYES:
—Retinal degeneration/atrophy, focal, unilateral, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 49

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
—Vacuolation, squamous epithelium, limiting ridge, grade 1
—Glandular stomach erosion, focal, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 49

SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Mineralization, corticomedullary, focal/multifocal, unilateral, grade 1
VAGINA:
—Diestrus phase of the estrous cycle
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 50

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Inflammatory cell focus/foci, grade 1
LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
ESOPHAGUS:
—Mononuclear cell focus/foci, muscle layer, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
and glandular stomach.
—Vacuolation, squamous epithelium, limiting ridge, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control, 0 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 50

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 2
THYMUS:
—Atrophy/involution, grade 1
KIDNEYS:
—Tubular basophilia, focal/multifocal, unilateral, grade 1
VAGINA:
—Proestrus phase of the estrous cycle
PARATHYROID GLANDS:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
SKIN/SUBCUTIS:
—Folliculitis/perifolliculitis, focal, grade 1
SKELETAL MUSCLE:
—Mononuclear cell focus/foci, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90–Day, Oral (Gavage) *DATE* : 07–JUL–16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

ANIMAL HEADING DATA
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day

ANIMAL NUMBER	SEX M/F	DEFINED STATE OF NECROPSY	AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST DAY UNDER TEST	LAST DAY UNDER TEST	DATE OF NECROPSY
11	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
12	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
13	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
14	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
15	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
16	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
17	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
18	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
19	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
20	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
51	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
52	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
53	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
54	F	K0	+1	27	19–NOV–15	15–DEC–15	15–DEC–15
55	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
56	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
57	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
58	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
59	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
60	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 11

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 12

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 13

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 14

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 15

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 16

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 17

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 18

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 19

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 20

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 51

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 52

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 53

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 27 * ANIMAL NO. : 54

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
01: Autolysis, Advanced.
02: Cannibalized, partial or whole: stomach, duodenum, jejunum, ileum, ovary, oviduct, uterus.
LUNGS:
01: Abnormal surface, dark.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:
—Autolysis, advanced
This finding corresponds to necropsy observation no: 01.
—Cannibalized
This finding corresponds to necropsy observation no: 02.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 54

TRACHEA:
—Mucosal necrosis, with inflammatory cell infiltrate, grade 4
and hemorrhage.
LUNGS:
—Perivascular inflammation, focal/multifocal, grade 1
—Inflammation, pleural surface, focal, grade 2
This finding corresponds to necropsy observation no: 01.
JEJUNUM:
Tissue not present for histologic examination
ILEUM:
Tissue not present for histologic examination
CECUM:
Tissue not present for histologic examination
COLON:
Tissue not present for histologic examination
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Food residue, in surrounding fatty tissue
MESENTERIC LYMPH NODE:
Tissue not present for histologic examination
PEYER'S PATCHES:
Tissue not present for histologic examination
VAGINA:
—Proestrus phase of the estrous cycle
THYROID GLAND (BOTH LOBES):
—Ductal remnants, unilateral
OPTIC NERVES:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 55

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 56

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 57

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 58

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, Low dose, 100 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 59

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

UTERUS:
—Cornual dilation (cyclic change), proestrus
This finding corresponds to necropsy observation no: 01.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 60

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

UTERUS:
—Cornual dilation (cyclic change), estrus
This finding corresponds to necropsy observation no: 01.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90–Day, Oral (Gavage) *DATE* : 07–JUL–16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

ANIMAL HEADING DATA
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day

ANIMAL NUMBER	SEX M/F	DEFINED STATE OF NECROPSY	AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST DAY UNDER TEST	AND LAST DAY UNDER TEST	DATE OF NECROPSY
21	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
22	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
23	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
24	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
25	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
26	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
27	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
28	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
29	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
30	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
61	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
62	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
63	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
64	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
65	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
66	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
67	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
68	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
69	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
70	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 21

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 22

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 23

* NECROPSY FINDINGS

TESTES:
01: Small/Reduced in size, one side (right).
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTES:
Only one of paired organs examined/present
—Tubular degeneration/atrophy, unilateral, grade 3
with multinuclear giant cells.
This finding corresponds to necropsy observation no: 01.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 24

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 25

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 26

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 27

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 28

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 29

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 30

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 61

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 62

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 63

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

UTERUS:
—Cornual dilation (cyclic change), proestrus
This finding corresponds to necropsy observation no: 01.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 64

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 65

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 66

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 67

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 68

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, Medium dose, 300 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 69

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 70

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90–Day, Oral (Gavage) *DATE* : 07–JUL–16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

ANIMAL HEADING DATA
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day

ANIMAL NUMBER	SEX M/F	DEFINED STATE OF NECROPSY	FINAL STATE OF NECROPSY	TEST DAYS	FIRST DAY UNDER TEST	LAST DAY UNDER TEST	DATE OF NECROPSY
31	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
32	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
33	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
34	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
35	M	K0	K0	90	17–NOV–15	14–FEB–16	15–FEB–16
36	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
37	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
38	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
39	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
40	M	K0	K0	90	18–NOV–15	15–FEB–16	16–FEB–16
71	F	K0	+1	82	19–NOV–15	08–FEB–16	08–FEB–16
72	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
73	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
74	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
75	F	K0	K0	90	19–NOV–15	16–FEB–16	17–FEB–16
76	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
77	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
78	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
79	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16
80	F	K0	K0	90	20–NOV–15	17–FEB–16	18–FEB–16

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 31

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* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART:
—Mononuclear cell focus/foci, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Atrophy/involution, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Pelvic dilation, unilateral, grade 1
PARATHYROID GLANDS:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 32

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
KIDNEYS:
—Tubular basophilia, focal/multifocal, bilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
ADRENAL CORTICES:
—Vacuolation (fatty change), zona fasciculata, diffuse, bilateral, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
SKIN/SUBCUTIS:
—Mononuclear cell focus/foci, dermis, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 33

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Inflammatory cell focus/foci, submucosa, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SALIVARY GLAND, SUBLINGUAL:
Only one of paired organs examined/present
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Tubular cast(s), hyaline, focal, unilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
THYROID GLAND (BOTH LOBES):
—Ductal remnants, unilateral
SCIATIC NERVES:
Tissue not present for histologic examination
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 34

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
—Vacuolation, squamous epithelium, limiting ridge, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SALIVARY GLAND, SUBLINGUAL:
Only one of paired organs examined/present
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Atrophy/involution, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
URINARY BLADDER:
—Mononuclear cell focus/foci, lamina propria, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 35

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
—Osseous metaplasia, focal
ESOPHAGUS:
—Mononuclear cell focus/foci, muscle layer, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Hemosiderin deposits, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Tubular basophilia, focal/multifocal, unilateral, grade 1
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 36

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Glandular dilation, grade 1
LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
STOMACH:
—Glandular stomach erosion, focal, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Tubular basophilia, focal/multifocal, unilateral, grade 1
URINARY BLADDER:
—Mononuclear cell focus/foci, lamina propria, grade 2
TESTES:
—Hypoplastic tubule(s), focal, unilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
PROSTATE GLAND:
—Mononuclear cell focus/foci, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 37

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Tubular basophilia, focal/multifocal, unilateral, grade 1
SKIN/SUBCUTIS:
Tissue not present for histologic examination
MAMMARY GLAND AREA:
Tissue not present for histologic examination
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 38

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

CONT./FF. ANIMAL NO. : 38

* MICROSCOPIC FINDINGS

HEART:
—Myocardial degeneration/necrosis, focal, grade 1
LUNGS:
—Alveolar macrophages, foamy, focal/multifocal, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
and glandular stomach.
—Vacuolation, squamous epithelium, limiting ridge, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 39

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART:
—Mononuclear cell focus/foci, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
MESENTERIC LYMPH NODE:
—Mast cells increased, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Mononuclear cell focus/foci, interstitium, bilateral, grade 1
EPIDIDYMIDES:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
PROSTATE GLAND:
—Mononuclear cell focus/foci, grade 1
ADRENAL MEDULLAS:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
—Ductal remnants, unilateral
PARATHYROID GLANDS:
Tissue not present for histologic examination
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
SKELETAL MUSCLE:
—Mononuclear cell focus/foci, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

CONT./FF. ANIMAL NO. : 39

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 40

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Inflammatory cell focus/foci, submucosa, grade 1
ESOPHAGUS:
—Mononuclear cell focus/foci, muscle layer, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
and glandular stomach.
LIVER:
—Inflammatory cell focus/foci, grade 1
SALIVARY GLAND, SUBLINGUAL:
—Hypoplasia, bilateral
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Atrophy/involution, grade 1
KIDNEYS:
—Hyaline droplets, proximal tubules, bilateral, grade 1
—Tubular basophilia, focal/multifocal, unilateral, grade 1
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day MALE

CONT./FF. ANIMAL NO. : 40

THYROID GLAND (BOTH LOBES):
—Ductal remnants, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 82 * ANIMAL NO. : 71

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
01: Autolysis, Advanced.
LUNGS:
01: Discoloration/Abnormal color.
THYMUS:
01: Discoloration/Abnormal color, red.
ADRENAL GLANDS:
01: Enlarged/Big size, both sides.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:
—Autolysis, advanced
This finding corresponds to necropsy observation no: 01.
HEART:
—Mononuclear cell focus/foci, grade 1
LUNGS:
—Aspiration pneumonia, grade 4
This finding corresponds to necropsy observation no: 01.
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Atrophy/involution, grade 2
—Congestion, grade 2
This finding corresponds to necropsy observation no: 01.
VAGINA:
—Proestrus phase of the estrous cycle

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 71

ADRENAL GLANDS:
For diagnosis of necropsy observation no. 01 see under:
ADRENAL CORTICES.
—Congestion, bilateral, grade 2
ADRENAL CORTICES:
—Diffuse hypertrophy, bilateral, grade 2
This finding corresponds to necropsy observation no.: 01
in the ADRENAL GLANDS.
SCIATIC NERVES:
Tissue not present for histologic examination
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, bilateral, grade 1
SKELETAL MUSCLE:
—Mononuclear cell focus/foci, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 72

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 72

THYMUS:
—Atrophy/involution, grade 1
MESENTERIC LYMPH NODE:
—Mast cells increased, grade 1
VAGINA:
—Metestrus phase of the estrous cycle
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 73

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
MESENTERIC LYMPH NODE:
—Mast cells increased, grade 1
UTERUS:
—Cornual dilation (cyclic change)
This finding corresponds to necropsy observation no: 01.
VAGINA:
—Estrus phase of the estrous cycle

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 73

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 74

* NECROPSY FINDINGS

KIDNEYS:
01: Pelvic dilation, both sides.
UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
KIDNEYS:
—Tubular basophilia, focal/multifocal, unilateral, grade 1
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
—Pelvic dilation, bilateral, grade 2
This finding corresponds to necropsy observation no: 01.
UTERUS:
—Cornual dilation (cyclic change)
This finding corresponds to necropsy observation no: 01.
VAGINA:
—Proestrus phase of the estrous cycle

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 74

OPTIC NERVES:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 75

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
—Inflammatory cell focus/foci, grade 1
STOMACH:
—Increased inflammatory cell infiltrate, limiting ridge, grade 1
and glandular stomach.
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
KIDNEYS:
—Tubular cast(s), hyaline, focal, unilateral, grade 1
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
VAGINA:
—Diestrus phase of the estrous cycle

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 75

PARATHYROID GLANDS:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
SKIN/SUBCUTIS:
—Mononuclear cell focus/foci, dermis, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 76

* NECROPSY FINDINGS

UTERUS:
01: Fluid filled.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 2
THYMUS:
—Cyst(s)
KIDNEYS:
—Mineralization, corticomedullary, focal/multifocal, unilateral, grade 1
—Cyst(s), unilateral

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 76

UTERUS:
—Cornual dilation (cyclic change)
This finding corresponds to necropsy observation no: 01.
VAGINA:
—Estrus phase of the estrous cycle
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 77

* NECROPSY FINDINGS

LIVER:
01: Abnormal surface, marbled, pale.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
Nothing abnormal discovered corresponding to necropsy obser—
vation no.01.
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 77

THYMUS:
—Atrophy/involution, grade 1
—Cyst(s)
KIDNEYS:
—Mineralization, corticomedullary, focal/multifocal, unilateral, grade 1
—Infarct, focal, unilateral, grade 1
VAGINA:
—Diestrus phase of the estrous cycle
PARATHYROID GLANDS:
Only one of paired organs examined/present
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 78

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART:
—Mononuclear cell focus/foci, grade 1
STOMACH:
—Glandular stomach erosion, focal, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 78

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 1
THYMUS:
—Cyst(s)
VAGINA:
—Diestrus phase of the estrous cycle
PARATHYROID GLANDS:
Only one of paired organs examined/present
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 79

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 2

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 79

THYMUS:
—Atrophy/involution, grade 1
VAGINA:
—Estrus phase of the estrous cycle
OPTIC NERVES:
Only one of paired organs examined/present
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 90 * ANIMAL NO. : 80

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:
—Alveolitis, focal, grade 1
CECUM:
—Granuloma, submucosa, focal, grade 1
LIVER:
—Inflammatory cell focus/foci, grade 1
SPLEEN:
—Extramedullary hemopoiesis, grade 1
—Hemosiderin deposits, grade 2
MESENTERIC LYMPH NODE:
—Mast cells increased, grade 1

TEST ITEM : Glucose oxidase (food enzyme) *PATHOL. NO.:* 11661 OKY
TEST SYSTEM : RAT, 90—Day, Oral (Gavage) *DATE* : 07—JUL—16
SPONSOR : AB Enzymes GmbH *PathData©System V6.2d2*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, High dose, 1000 mg/kg bw/day FEMALE

CONT./FF. ANIMAL NO. : 80

KIDNEYS:
—Mononuclear cell focus/foci, interstitium, unilateral, grade 1
VAGINA:
—Diestrus phase of the estrous cycle
PARATHYROID GLANDS:
Only one of paired organs examined/present
SCIATIC NERVES:
Tissue not present for histologic examination
HARDERIAN GLANDS:
—Porphyrin deposits, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

Analytical Phase Report
to
BSL BIOSERVICE Study No. 154307
ibacon project 106931100

90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*

(GLP compliant study)

Authors: **Dr. Volker Wydra**
Gundula Mollandin

Analytical Phase Completion Date: July 04, 2016

Sponsor

AB Enzymes GmbH
Feldbergstr. 78
64293 Darmstadt
Germany

Test Facility

BSL BIOSERVICE
Scientific Laboratories Munich GmbH
Behringstraße 6/8
82152 Planegg
Germany

Study No. 154307

Test Site

Ibacon GmbH
Arheilger Weg 17
64380 Rossdorf
Germany

Project 106931100

Copy of GLP-Certificate

HESSEN

Gute Laborpraxis/Good Laboratory Practice

GLP-Bescheinigung/Statement of GLP Compliance
(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EEC at:

☒ Prüfeinrichtung/Test facility ☐ Prüfstandort/Test site

Institut für Biologische Analytik und Consulting IBACON GmbH
Arheilger Weg 17
64380 Rossdorf

(Unverwechselbare Bezeichnung und Adresse/Unequivocal name and adress)

Prüfungen nach Kategorien/Areas of Expertise
(gemäß/according chemVwV-GLP Nr. 5.3/OECD guidance)

1 Prüfungen zur Bestimmung der physikalisch-chemischen Eigenschaften und Gehaltsbestimmungen
4 Ökotoxikologische Prüfungen zur Bestimmung der Auswirkungen auf aquatische und terrestrische Organismen
5 Prüfungen zum Verhalten im Boden, im Wasser und in der Luft, Prüfungen zur Bioakkumulation und zur Metabolisierung
6 Prüfungen zur Bestimmung von Rückständen

1Physical and chemical properties and determination of content
4 Environmental toxicity studies on aquatic and terrestrial organisms
5 Behaviour in water soil and air, Bioaccumulation and metabolism
6 Residues

19.03., 24. – 26.06., 22.07.2013
Datum der Inspektion/Date of Inspection
(Tag Monat Jahr/day month year)

Die genannte Prüfeinrichtung befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP- Grundsätze durchgeführt werden können.

Based on the inspection report it can be confirmed, that this test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

(b) (6)

Th. Zimmermann, Referent, Wiesbaden, den **24. September 2013**
(Name und Funktion der verantwortlichen Person/
Name and function of responsible person)

Hess. Ministerium für Umwelt, Energie, Landwirtschaft und Verbraucherschutz,
Mainzer Straße 80 D65189 Wiesbaden
(Name und Adresse der GLP-Überwachungsbehörde/Name and address of the GLP Monitoring Authority

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List of Figures

1. Summary (Analytical Phase)

Title: 90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*

Purpose: The purpose of the analytical phase of the study was the determination of Glucose oxidase in specimens received from BSL BIOSERVICE, Scientific Laboratories GmbH, Behringstr. 6/8, 82152 Planegg, Germany after application of the test item in a 90-Day Repeated Dose Oral Toxicity Study in Wistar Rats.

The analytical measurements of the samples were performed using Total Organic Carbon determination (TOC method). The analytical method was validated in the present study.

Analytical Method: Dose verification was performed by quantification of the test item using Total Organic Carbon determination (TOC-method).

Fortification Levels: 0.03 and 0.07 mg/mL

Results:

Mean Recovery Rate of the Test Item in the Fortification Samples:	0.03 mg/mL:	97% of nominal (n = 5; RSD = 1%)
	0.07 mg/mL:	99% of nominal (n = 5; RSD = 1%)
Mean Recovery Rate of the Test Item in the Test Specimens:	20 mg/mL:	98% of nominal (n = 10; RSD = 2%)
	60 mg/mL:	96% of nominal (n = 3; RSD = 3%)
	200 mg/mL:	95% of nominal (n = 10; RSD = 6%)
Control Samples:	There was no trace of test item in the control samples.	

2. Survey of the Study on the Test Site (Analytical Phase)

2.1. General Information on the Test Site (Analytical Phase)

Test Site for the Analytical Phase:
ibacon GmbH
Arheilger Weg 17
64380 Rossdorf
Germany

Principal Investigator:
(Analytics)
Dr. Volker Wydra
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Head of Quality Assurance Unit:
(Test Site)
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Address: see Test Site

2.2. Schedule

Start of the Analytical Phase:	February 25, 2016
End of the Analytical Phase:	March 22, 2016
Analytical Phase Completion Date:	July 04, 2016

2.3. Good Laboratory Practice

This analytical phase of this study was performed in compliance with the most recent edition of:

- The OECD Principles of Good Laboratory Practice
- German Chemicals Act (ChemG), Annex 1
- Directive 2004/10/EC
- OECD Consensus Document No. 13

These requirements are accepted by regulatory authorities throughout the European Community, the United States of America (FDA and EPA) and Japan (MHLW, MAFF and METI) on the basis of intergovernmental agreements.

The analytical phase of this study was assessed in compliance with the analytical phase plan to the study plan BSL 154307 and the ibacon Standard Operating Procedures. The analytical phase and procedures were periodically inspected by the Test Site Quality Assurance Unit (QAU) and the dates and the phases of the inspections are included in the final analytical phase report. The data contained within the final analytical phase report were audited in comparison to the raw data. A quality assurance statement, signed by the Test Site QAU, is included in the final analytical phase report.

2.4. Information on Archival Storage (Analytical Phase)

2.4.1 Documents

ibacon GmbH, Arheilger Weg 17, D-64380 Rossdorf, will archive the following documents under GLP-conditions:

- one copy of the Study Plan
- one copy of any amendment to the Study Plan regarding the analytical phase
- certified copies of the raw data of the analytical phase
- one certified copy of the analytical phase report

The premises for storing the documents and materials are settled according to the principles of Good Laboratory Practice in the organization of the Test Site.

The original raw data will be sent to the Study Director.

2.4.1 Materials

ibacon GmbH, Arheilger Weg 17, D-64380 Rossdorf, will archive the following materials under GLP conditions:

- A sample of the test item will be archived for a period of time specified in the German GLP-regulations.
- Remaining specimens will be disposed of after authorisation of the Study Director and not before the finalisation of the study (date of Final Report).

2.5. Signatures

Principal Investigator: Dr. Volker Wydra

(Test Site)

(b) (6)

date: July 04, 2016

Head of Test Site: Dr. Melanie Lichtenberger

(b) (6)

date: July 04, 2016

3. Quality Assurance Unit Statement

Test Site:	ibacon GmbH Arheilger Weg 17 64380 Rossdorf Germany
ibacon Project:	106931100
Title of the Study:	90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Prinicipal Investigator (Analytics):	Dr. Volker Wydra

Study based Inspections

Phases inspected	Dates of QAU Inspections	Dates of Reports to the Prinicipal Investigator (Analytics) and to Test Site Management
Analytical Phase Plan	February 15, 2016	February 15, 2016
Experimental Phase		
Sample Preparation, Processing, Measurements	February 25, 2016	February 25, 2016
Analytical Phase Draft Report	April 12 - 15, 2016	April 15, 2016
	June 30, 2016	June 30, 2016
Analytical Phase Report	JUL 04 2016	JUL 04 2016

This statement confirms that the final analytical phase report accurately reflects the raw data.

Quality Assurance Unit:

Biologist
Christiane Rutschmann-Fröhlich

(b) (6)

date: July 04, 2016

4. Statement of Compliance

ibacon Project:	106931100
Title of the Study:	90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*
Test Item:	Glucose oxidase produced with *Trichoderma reesei*
Prinicipal Investigator (Analytics):	Dr. Volker Wydra

GLP-Regulations:

- The OECD Principles of Good Laboratory Practice
- German Chemicals Act (ChemG), Annex 1
- Directive 2004/10/EC
- OECD Consensus Document No. 13

These requirements are accepted by regulatory authorities throughout the European Community, the United States of America (FDA and EPA) and Japan (MHLW, MAFF and METI) on the basis of intergovernmental agreements.

Integrity of the Study:

This analytical phase, performed in the test site of ibacon, was conducted in compliance with the Good Laboratory Practice regulations. There were no circumstances that may have affected the quality or integrity of the study.

Prinicipal Investigator (Analytics): Dr. Volker Wydra

(b) (6)

date: July 04, 2016

5. Nature and Purpose of the Analytical Phase of the Study

5.1. Title

90-Day Repeated Dose Oral Toxicity Study in Wistar Rats with Glucose oxidase produced with *Trichoderma reesei*

5.2. Purpose

The purpose of the analytical phase of the study was the determination of Glucose oxidase in specimens received from BSL BIOSERVICE, Scientific Laboratories GmbH, Behringstr. 6/8, 82152 Planegg, Germany after application of the test item in a 90-Day Repeated Dose Oral Toxicity Study in Wistar Rats.

The analytical measurements of the samples were performed using Total Organic Carbon determination (TOC method). The analytical method was validated in the present study.

6. Material and Methods

6.1. Test Item

The test item and related data were provided by the Sponsor. The test item was used for fortification experiments (laboratory concurrent recovery specimens) and preparation of the calibration solutions.

Name:	Glucose oxidase produced with *Trichoderma reesei*
Batch Number:	P 140032 J
Physical Appearance / Colour:	Powder/Brownish
Expiry Date:	September 2016
Storage:	At room temperature (20 °C ± 5 °C) in the dark

6.2. Reference Item

The test item was used as reference item.

6.3. Test Water (Vehicle)

The vehicle and the information concerning the vehicle were provided by the Sponsor

Name:	Aqua ad injectionem
Batch No.:	503424
Physical State at Room Temperature:	Liquid
Colour:	Colourless
Minimum Shelf Life:	Februar 2018
Storage Conditions:	At room temperature (20 °C ± 5 °C) in the dark

6.4. Test System

The specimens from a 90-Day Repeated Dose Oral Toxicity Study in Wistar Rats were examined for the concentration of the test item in the specimens. The specimens and the information concerning the specimens were provided by BSL BIOSERVICE:

Test System:

Table 1. Specimens from BSL BIOSERVICE Study No. 154307

Week	Datum	Kürzel	C	LD Top	LD Middle	LD Bottom	MD	HD Top	HD Middle	HD Bottom	Code a + b
Week 1			X								1
				X							2
					X						3
						X					4
							X				5
								X			6
									X		7
										X	8
Week 6			X								9
				X							10
					X						11
						X					12
							X				13
								X			14
									X		15
										X	16

Week	Datum	Kürzel	C	LD Top	LD Middle	LD Bottom	MD	HD Top	HD Middle	HD Bottom	Code a + b
Week 12			X								17
				X							18
					X						19
						X					20
							X				21
								X			22
									X		23
										X	24

Origin:

The specimens were received from BSL BIOSERVICE Scientific Laboratories GmbH, Behringstr. 6/8, 82152 Planegg, Germany. The specimens were obtained from a 90-Day Repeated Dose Oral Toxicity Study in Wistar Rats (BSL BIOSERVICE Study No. 154307). Collecting, processing, storage and transportation of the specimens to ibacon were at the responsibility of BSL BIOSERVICE.

Storage:

All specimens were stored deep frozen at ≤ -20 °C. Remaining specimens will be disposed of after authorisation of the Study Director and not before the finalisation of the study (date of Final Report).

6.5. Description of the Analytical Method

The analytical method Total Organic Carbon determination (TOC) was validated according to GLP based on the criteria set forth by SANCO/3029. Method validation was done in concurrence with the analysis of the samples.

6.6. Sample Preparation

Sample Preparation Procedure:	For analysis the samples were taken out of the freezer and allowed to thaw at room temperature. The specimens were then shaken well and treated with ultrasound for 1 minute to obtain homogenous samples.
Number of Specimens:	Each specimen (of each the code a replicate) shown in Table 1 was analysed and two specimens (code 20 a and 24 a) randomly selected were analysed twice. Afterwards the second replicate (code 1 b) of the control sample taken in week 1 was analysed to confirm the result of the measurement of the first replicate (code 1 a).

6.7. Analytical Standard

The test item was used to prepare the stock solution and the standard solutions.

6.8. Fortified Samples

Approximately 20 mg of the test item were dissolved (1 minute ultrasonication and approx. 5 hours stirring) in 200 mL test water to obtain a stock solution of approximately 0.1 g test item/L. Two independent stock solutions were prepared. Appropriate amounts of these stock solutions were diluted with test water to obtain fortified samples at a level of 30 and 70 mg test item/L.

Exact values were documented in the raw data.

6.9. Analytical Method

Raw data of the validation of the analytical method will be archived under the project number 106931100.

Method for Determination:	Total Organic Carbon Determination (TOC)

6.10. Standard Solutions used for the Quantification

Stock Solution:	The test item was used to prepare a stock solution. 50.72 mg of the test item was dissolved in 500 mL test water (with 1 minute ultrasonication, 3.5 hours strirring) to obtain a stock solution of approximately 0.1 g test item /L.
Standard Solutions:	Appropriate amounts of the stock solution were diluted with test water to obtain standard solutions in the range from 2 to 80 mg test item /L. Exact data were documented in the raw data.

6.11. TOC conditions

TOC-Analyzer:	TOC-V CPH, Shimadzu
Autosampler:	ASI-V, Shimadzu
Carbon-Oxidation	680 °C combustion catalytic oxidation
Inorganic Carbon	Acidification with H_3PO_4 (25%)
Detector:	Infrared Gas Analyzer
Injection Volume:	50 µL
Carrier Gas:	Oxygen
Integration Software:	TOC-Control V Software

6.12. Validity Criteria

The analytical method for the determination should comply with the following criteria:

Linearity:	Regression coefficient of calibration curve should be at least 0.99.
Accuracy:	The mean recovery values of samples fortified with the analyte should be 70 - 110 %.
Precision:	The relative standard deviation of repeated analysis of five independent fortification samples should be ≤ 20 %.

6.13. Result Evaluation

Abbreviations:	TOC: total organic carbon TC: total carbon IC: inorganic carbon
Identification:	The identification of the test item cannot be established with TOC-analysis.
Determination of the TOC content:	As the IC content of the test item is negligible the nominal TOC-value of the test item samples is obtained as the TC content.
Quantification:	Samples were quantified by measuring the peak area with reference to the calibration curve. The latter was obtained by correlation of peak area of the standard solutions to their corresponding concentration. The correlation was performed using a linear regression function given by equation (1): $y = a * x + b$ (1) where y: peak area x: concentration of analyte a: slope b: y-axis intercept

Calculated Concentration:	The concentration of the analyte in a sample was calculated by equation (2): $c = x * d$ (2) where c: concentration of analyte in original sample x: concentration of analyte in the analysed sample (calculated in equation (1)) d: dilution factor
Recovery Rate:	The recovery rate (% of nominal) in a sample was calculated by equation (3): $\%\ \text{of nominal} = (c/c_{noma}) * 100\ \%$ (3) where c: concentration of analyte in original sample, cf. equation (2) c_{noma}: nominal concentration of analyte
Limit of Detection:	The limit of detection (LOD) is determined mathematically from the linear calibration curve according to DIN 32 645.
Limit of Quantification:	The Limit of Quantification (LOQ) was determined as the lowest fortification level at which an acceptable mean recovery (70 to 110% of nominal) with a relative standard deviation (RSD) < 20% was obtained.

6.14. Deviations to the Study Plan

Concerning:	Fortification Level
According to Study Plan:	At least two fortification levels will be tested. The fortification levels will cover the range of samples' analyte concentration ± at least 10 %, e.g.: 110 % of the highest concentration of the analyte in the test sample solution
Deviation to the Study Plan:	The concentration of the fortification level was not adjusted to the original concentration of the test samples but to the concentration of the test samples after sample preparation. Since the sample preparation comprised different dilutions with test water ("Aqua ad injectionem") the concentrations of the test samples before and after sample preparation were different.
Reason for the Deviation:	Technical reasons
Presumed Effect on the Study:	None, since the test water contains only negligible amounts of carbon, the dilutions did not influence the recoveries.

7. Results and Discussion

As the test item was used as analytical standard and the IC content of the test item is negligible, it was not appropriate to apply the inorganic carbon (IC) calibration curve (see Figure 2). Therefore the TOC-value of the test item samples is obtained as the total carbon (TC) content of the test item samples.

Limit of Detection:	2 mg Carbon/L (calculated according DIN 32 645)	
Limit of Quantification:	0.03 mg/mL (30 mg test item/L)	
Mean Recovery Rate of the Test Item in the Fortification Samples:	0.03 mg/mL:	97% of nominal (n = 5; RSD = 1%)
	0.07 mg/mL:	99% of nominal (n = 5; RSD = 1%)
Mean Recovery Rate of the Test Item in the Test Specimens:	20 mg/mL:	98% of nominal (n = 10; RSD = 2%)
	60 mg/mL:	96% of nominal (n = 3; RSD = 3%)
	200 mg/mL:	95% of nominal (n = 10; RSD = 6%)
Control Samples:	There was no trace of test item in the control samples. In the control sample taken in week 1 an elevated content of inorganic carbon was detected. This was confirmed by measurement of the corresponding second replicate (Code 1 b). For details see Table 1 and Table 2 in Appendix I (Tables and Figures).	

7.1. Validity Criteria of the Analytical Part

Linearity:	<u>Calibration Range:</u> 2 – 100 mg test item/L <u>Linearity of Response:</u> Correlation of peak area of different standard solutions with their corresponding concentrations, using a linear regression <u>Regression Coefficient:</u> r = 0.9999 <u>Total Carbon (TC) Calibration Curve:</u> y = 2.0339 * x + 3.3171 (see also Figure 1)
Accuracy and Precision:	<u>Mean Recovery Rates in the Fortified Samples:</u> 98% (n = 10, RSD 2%) The values found for the precision (RSD) and for the accuracy (mean recovery rate) are acceptable (for details see Table 2).
Conclusion:	The validity criteria for the analytical method have been met.

8. References

Chemicals Act (ChemG) of the Federal Republic of Germany, Annex 1, in the version published on 28 August 2013 (Federal Law Gazette I, p. 3498) last amended by Article 431 of the Ordinance of 31 August 2015 (Federal Law Gazette I, p. 1474)

DIN 32645, 1994-05 Chemical analysis - Decision limit, detection limit and determination limit under repeatability conditions - Terms, methods, evaluation

Directive 2004/10/EC of 11 February 2004 amending Council Directive 87/18/EEC, Official Journal of the European Union No. L 50: 44 - 59

OECD Principles of Good Laboratory Practice, adopted by Council on 26th November 1997 [C(97)186/Final], Environment Directorate, Organisation for Economic Co-operation and Development, ENV/MC/CHEM(98)17, Paris 1998

SANCO/3029/99 rev.4 11/07/00: Residues: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A; Section 4) and Annex III (part A; Section 5) of directive 91/414

The Application of the OECD Principles of GLP to the Organisation and Management of Multi-Site Studies, OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 13, Paris 2002

9. Distribution of the Analytical Phase Report

Sponsor: original analytical phase report

ibacon: one certified copy of the analytical phase report

Appendix I
(Tables and Figures)

Table 1. Results for the Determination of the Test Item in the Test Specimens

Sample Description Week	Concentration [mg/mL]		Code		Analysis No.	IC response [peak area]	TC response [peak area]	Concentration found [mg test item/L][1]	D.F.	Concentration calculated [mg test item/L][1]	Concentration nominal [mg test item/L]	% of nominal[1]
1	C	0	1	a	1	*53.50*	56.34	*n.a.*	1	-	0	n.a.
1	C	0	1	b	1	*49.74*	55.26	*n.a.*	1	-	0	n.a.
1	LD_{Top}	20	2	a	1	3.420	102.1	48.568	400	19427.063	20000	97
1	LD_{Middle}	20	3	a	1	2.731	100.3	47.683	400	19073.067	20000	95
1	LD_{Bottom}	20	4	a	1	1.744	101.9	48.469	400	19387.730	20000	97
1	MD	60	5	a	1	1.696	117.5	56.139	1000	56139.230	60000	94
1	HD_{Top}	200	6	a	1	1.493	93.57	44.374	4000	177495.171	200000	89
1	HD_{Middle}	200	7	a	1	1.750	94.53	44.846	4000	179383.148	200000	90
1	HD_{Bottom}	200	8	a	1	1.701	92.64	43.917	4000	175666.194	200000	88
6	C	0	9	a	1	1.298	7.205	1.912	1	<LOQ	0	n.a.
6	LD_{Top}	20	10	a	1	1.410	103.4	49.207	400	19682.726	20000	98
6	LD_{Middle}	20	11	a	1	1.642	101.2	48.125	400	19250.065	20000	96
6	LD_{Bottom}	20	12	a	1	1.442	106.6	50.780	400	20312.052	20000	102
6	MD	60	13	a	1	1.453	121.2	57.958	1000	57958.374	60000	97
6	HD_{Top}	200	14	a	1	1.466	105.6	50.288	4000	201153.877	200000	101
6	HD_{Middle}	200	15	a	1	1.418	104.8	49.895	4000	199580.563	200000	100
6	HD_{Bottom}	200	16	a	1	1.633	106.3	50.633	4000	202530.526	200000	101
12	C	0	17	a	1	1.554	8.311	2.455	1	<LOQ	0	n.a.
12	LD_{Top}	20	18	a	1	1.510	103.1	49.059	400	19623.727	20000	98
12	LD_{Middle}	20	19	a	1	1.493	102.6	48.813	400	19525.395	20000	98
12	LD_{Bottom}	20	20	a	1	1.111	100.6	47.830	400	19132.067	20000	96
12	LD_{Bottom}	20	20	a	2	1.396	103.1	49.059	400	19623.727	20000	98
12	MD	60	21	a	1	1.471	123.6	59.138	1000	59138.359	60000	99
12	HD_{Top}	200	22	a	1	1.197	103.6	49.305	4000	197220.592	200000	99
12	HD_{Middle}	200	23	a	1	1.521	103.1	49.059	4000	196237.271	200000	98
12	HD_{Bottom}	200	24	a	1	1.209	99.89	47.481	4000	189924.350	200000	95
12	HD_{Bottom}	200	24	a	2	1.068	94.81	44.983	4000	179933.808	200000	90

[1] The tabulated results represent rounded results calculated on the exact raw data

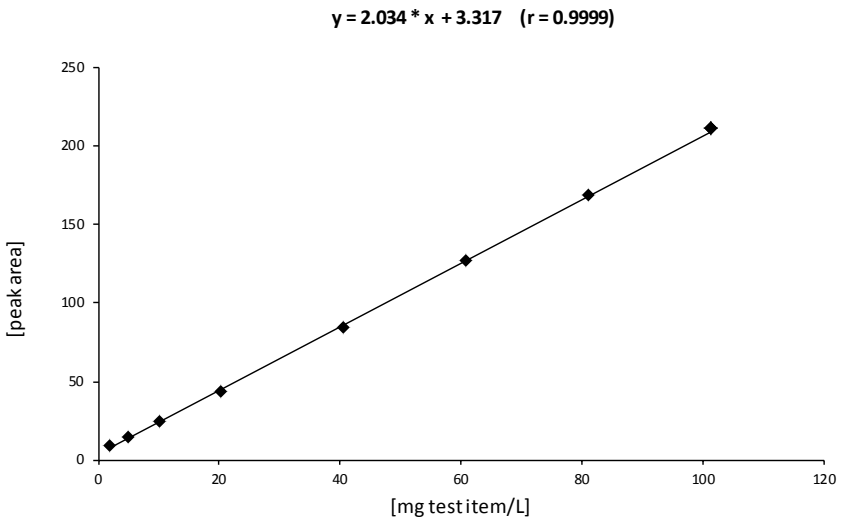
Italic values:The signal in the control sample taken in week 1 resulted from an inorganic contamination. Therefore, it can be clearly concluded that the TC-signal did not arise from contamination with test item.

n.a. not applicable

Table 2. Results for the Determination of the Test Item in the Fortified Samples

Sample Description	nominal [mg/mL]	IC response [peak area]	TC response [peak area]	Concentration found [mg test item/L][1]	D.F.	Concentration calculated [mg test item/L][1]	Concentration nominal [mg test item/L][1]	Recovery [%][1]
Analytical Blank Control	0	1.739	4.178	0.423	1	n.a.	0.000	n.a.
Analytical Blank Control	0	1.758	4.154	0.411	1	n.a.	0.000	n.a.
Fortified Sample	0.03	1.678	65.38	30.514	1	30.514	31.245	98
Fortified Sample	0.03	1.402	63.39	29.535	1	29.535	31.245	95
Fortified Sample	0.03	1.683	62.75	29.221	1	29.221	30.195	97
Fortified Sample	0.03	1.659	62.67	29.181	1	29.181	30.195	97
Fortified Sample	0.03	1.609	63.26	29.472	1	29.472	30.195	98
							mean value (n=5):	**97**
							RSD (n=5):	**1**
Fortified Sample	0.07	1.790	148.3	71.282	1	71.282	72.905	98
Fortified Sample	0.07	1.630	148.7	71.479	1	71.479	72.905	98
Fortified Sample	0.07	1.732	148.4	71.332	1	71.332	70.455	101
Fortified Sample	0.07	1.643	145.8	70.053	1	70.053	70.455	99
Fortified Sample	0.07	1.621	145.8	70.053	1	70.053	70.455	99
							mean value (n=5):	**99**
							RSD (n=5):	**1**
							overall mean value (n=10):	**98**
							RSD (n=10):	**2**

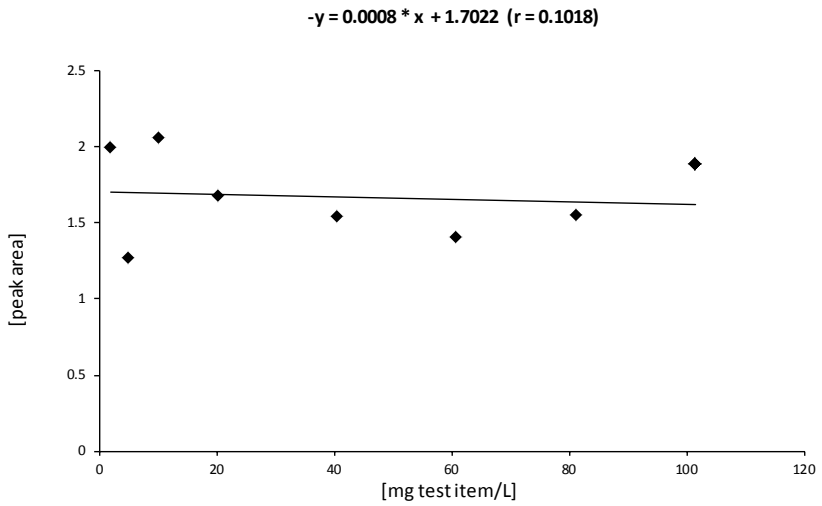
[1] The tabulated results represent rounded results calculated on the exact raw data



Data set

Concentration [mg test item/L]	Total Carbon [peak area]
2.029	9.045
5.072	14.310
10.144	23.910
20.288	43.340
40.576	84.070
60.864	126.700
81.152	168.600
101.440	210.600

Figure 1. Calibration Curve: Total Carbon Determination



Data set

Concentration [mg test item/L]	Inorganic Carbon [peak area]
2.029	1.994
5.072	1.271
10.144	2.057
20.288	1.675
40.576	1.539
60.864	1.404
81.152	1.545
101.440	1.885

Figure 2. Inorganic Carbon Determination: Not appropriate to apply the inorganic carbon (IC) calibration curve, since the test item used as analytical standard has negligible IC content

Appendix II
(Analysis report)

NOVALAB OY

ANALYSIS REPORT

Order: 1404846 1(2)
Date: 28.11.2014

ROAL Oy
Vilma Ikonen
Tykkimäentie 15
PL 57, 05201 Rajamäki

FINAS
Finnish Accreditation Service
T071 (EN ISO/IEC 17025)

Order name:	**Enzyme sample,P140032J, nutritional analysis**
Sample:	14MU0883 Glukoosi-oksidaasi, P140032J
Sampling time:	10.11.2014
Sample arrived:	11.11.2014
Analysis started:	13.11.2014

Analysis		Result	Method
Dry matter	%	94.9	Novalab 010*
Ash	%	3.5	Novalab 009*
Moisture	%	5.1	Novalab 010*
Protein	%	68.3	Novalab 001.A, kjeldahl*
Carbohydrate, calculated	%	23,1	
Energy value, calculated	kJ/100 g	1554	
Fat	%	<0.1	Novalab 076*

* Accredited method. Statement is not accredited. Results apply only samples analyzed.

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Finland

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Bank
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Karkkila
FI43 5297 2820 0007 16

Business ID 0733227-8
Location Karkkila
VAT reg.

NOVALAB OY

ANALYSIS REPORT

Order: 1404846 2(2)
Date: 28.11.2014

ROAL Oy
Vilma Ikonen
Tykkimäentie 15
PL 57, 05201 Rajamäki

FINAS
Finnish Accreditation Service
T071 (EN ISO/IEC 17025)

Novalab Oy
(b) (6)

Eeva Luoma
Head of Quality
The certificate has been signed electronically.

Add.details Methods:
Moisture: AOAC 2002 950.46 (39.1.02) modified
Protein: AOAC 2002 2001.11 (4.2.11) modified
Fat: NMKL 131:1989 modified
Ash: NMKL 173:2005 modified
Carbohydrate: By difference 100 % - (moisture+protein+fat+ash)%
Energy value: Calculated on the basis of contents of protein, fat and carbohydrate. Factors protein and carbohydrate 17 kJ/g, fat 37 kJ/g

Measurement uncertainty:
Moisture: ± 3 relative-%
Ash: ± 10 relative-%
Fat: under the limit of measurement
Protein: ± 5 relative-%
Carbonhydrates, calculated: ± 5 relative-%
Energy, calculated: ± 5 relative-%

Distribute vilma.ikonen@roal.fi

* Accredited method. Statement is not accredited. Results apply only samples analyzed.

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FI43 5297 2820 0007 16

Business ID 0733227-8
Location Karkkila
VAT reg.

Bonnette, Richard

Subject: FW: Submission for glucose oxidase from Trichoderma reesei
Attachments: UPS Delivery Notification, Tracking Number 1Z53R73E6850179662; COA 2017.pdf

---

From: Cryne, Candice [mailto:Candice.Cryne@abenzymes.com]
Sent: Wednesday, May 17, 2017 4:45 PM
To: Bonnette, Richard
Cc: Srinivasan, Jannavi
Subject: RE: Submission for glucose oxidase from Trichoderma reesei

Dear Richard and Jannavi,

I have resent the version consistent with the new regulations below. See attached for notification of acceptance by your mail room.

I just noticed that I sent an old COA, I have attached here the new COA that is listed as appendix #2. Could you please use this in the public dossier posted to the website, once it goes to the reviewers?

Many thanks, Candice

Analytical report
RF11400
17.02.2017

The Art of Enzymes
roal

Objective: **Chemical composition analysis of Glucose oxidase from *Trichoderma reesei* strain RF11400**

Sample: **1. Fermentation concentrate P160011I, LIMS ID 2016-635-1**
2. Fermentation concentrate 161130700, LIMS ID 2016-542-62

Table 1. Enzyme activity, presence of production strain and recombinant DNA and microbiological quality of the product

	P160011I	161130700
Glucose oxidase (GOX/g)	14100	13100
Presence of production strain (in 20 ml)	not detected	not detected
Recombinant DNA	not detected	not detected
Total viable count (cfu*/g)	<1000	<1000
Escherichia coli (in 25 g)	not detected	not detected
Salmonella (in 25 g)	not detected	not detected
Total coliforms (cfu*/g)	<1	<1
Lead (mg/kg)	<0,05	<0,05

GOX: Assay of glucose oxidase activity, Roal internal method B080
Production strain: Detection of production strain (Trichoderma, Aspergillus) M001, Roal internal
rDNA: Qualitative PCR for rDNA in food and feed enzymes, validated for the specific sequences
Total viable count: ISO 4833-1:2013
E. coli: SFS 4089:1998, mod.
Salmonella: NMKL 71:1999, mod.
Total coliforms: ISO 4832:2006, mod.
Lead: ISO 17294-2:2003
*cfu: colony forming units

Table 2. Nutritional analysis

	P160011I	161130700
Fat %	0,17	0,14
Protein %	15,8	11,7
Moisture %	78,6	82,8
Ash %	0,61	0,51
Carbohydrates %	4,82	4,85
Energy value (kJ/100 g)	357	287
TOS % Total organic solids [100-(moisture+ash)]	20,8	16,7

Fat: NMKL 131, Gravimetry
Protein: NMKL 6, Kjeldahl
Moisture: NMKL 23, Gravimetry
Ash: NMKL 173, Gravimetry
Carbohydrates: (EU) No 1169/2011, Calculation
Energy value: (EU) No 1169/2011, Calculation

Table 3. Mycotoxins (µg/kg)

	P160011I	161130700
T2-Toxin	<10	<10
HT-2-Toxin	<10	<10

T2- and HT-2Toxin: Internal Method LC-MS/MS

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