TATE & LYLE

Science \ Solutions \ Society

31 March 2023

Dr. Paulette Gaynor
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition (CFSAN)
Food and Drug Administration
5001 Campus Drive
College Park, MD
20740 USA

Dear Dr. Gaynor:

Re: GRAS Notice for Enzymatically Produced Steviol Glycosides

In accordance with 21 CFR §170 Subpart E consisting of §§ 170.203 through 170.285, Tate & Lyle [5450 Prairie Stone Parkway, Hoffman Estates, IL, 60192 USA], as the notifier, is submitting one hard copy and one electronic copy (on CD), of all data and information supporting the company's conclusion that enzymatically produced steviol glycosides are GRAS on the basis of scientific procedures, for use as general purpose sweeteners. These food uses of the enzymatically produced steviol glycosides are therefore not subject to the premarket approval requirements of the *Federal Food, Drug and Cosmetic Act*. Information setting forth the basis for Tate & Lyle's GRAS conclusions are enclosed for review by the Agency.

I certify that the enclosed electronic files were scanned for viruses prior to submission and are thus certified as being virus-free using Symantec Endpoint Protection 12.1.5.

Should you have any questions or concerns regarding this GRAS Notice, please do not hesitate to contact me at any point during the review process so that we may provide a response in a timely manner.

Sincerely,

Juan Cristián Santa María
Senior Director, Global Regulatory & Scientific Affairs
Tate & Lyle
JuanCristian.SantaMaria@tateandlyle.com

GRAS NOTICE FOR ENZYMATICALLY PRODUCED STEVIOL GLYCOSIDES

SUBMITTED TO:
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition (CFSAN)
Food and Drug Administration
5001 Campus Drive
College Park, MD
20740 USA

SUBMITTED BY:
Tate & Lyle
5450 Prairie Stone Parkway
Hoffman Estates, IL
USA, 60192

DATE:
30 March 2023

GRAS Notice for Enzymatically Produced Steviol Glycosides

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GRAS Notice for Enzymatically Produced Steviol Glycosides

Part 1. § 170.225 Signed Statements and Certification

In accordance with 21 CFR §170 Subpart E consisting of §§170.203 through 170.285, Tate & Lyle hereby informs the United States (U.S.) Food and Drug Administration (FDA) that the intended uses of enzymatically produced steviol glycosides, as manufactured by Tate & Lyle, as general purpose sweeteners as described in Section 1.3 below, are not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on Tate & Lyle's view that these notified uses of enzymatically produced steviol glycosides are Generally Recognized as Safe (GRAS). In addition, as a responsible official of Tate & Lyle, the undersigned hereby certifies that all data and information presented in this notice represents a complete and balanced submission that is representative of the generally available literature. Tate & Lyle considered all unfavorable as well as favorable information that is publicly available and/or known to Tate & Lyle and that is pertinent to the evaluation of the safety and GRAS status of enzymatically produced steviol glycosides as general purpose sweeteners, as described herein.

Signed,

March 30, 2023

Juan Cristián Santa María
Senior Director, Global Regulatory & Scientific Affairs
Tate & Lyle
JuanCristian.SantaMaria@tateandlyle.com

Date

1.1 Name and Address of Notifier

Tate & Lyle
5450 Prairie Stone Parkway
Hoffman Estates, IL
USA, 60192

1.2 Common Name of Notified Substance

Enzymatically produced steviol glycosides

1.3 Conditions of Use

Tate & Lyle's enzymatically produced steviol glycosides are intended for use as general purpose sweeteners in accordance with current good manufacturing practice (cGMP). The enzymatically produced steviol glycosides will be used under similar conditions of use as other high purity steviol glycoside compositions,

within the range of 200 to 300 times sweeter than sucrose, which is consistent with the sweetness profile of steviol glycosides in general (JECFA, 2021). Therefore, considering that steviol glycosides are characterized by a sweetness profile that is, for the most part, comparable to other high -intensity sweeteners, the food uses and use levels of Tate & Lyle's enzymatically produced steviol glycoside are expected to reflect those currently permitted for other high-intensity sweeteners in the U.S., and intakes of steviol glycosides (as steviol equivalents) will remain the same. Tate & Lyle's enzymatically produced steviol glycosides will serve as a substitutional source of steviol glycosides currently on the U.S. marketplace, and not expected to increase current dietary exposure to these compounds.

The ingredient is not intended for use in infant formula or infant food products, and the proposed food categories do not include food uses that are subject to the oversight by the U.S. Department of Agriculture (USDA) and the USDA Food Safety Inspection Service (FSIS).

1.4 Basis for GRAS

Pursuant to 21 CFR § 170.30 (a)(b) of the Code of Federal Regulations (CFR) (U.S. FDA, 2018b), Tate & Lyle has concluded that the intended uses of the enzymatically produced steviol glycosides as described herein are GRAS on the basis of scientific procedures.

1.5 Availability of Information

The data and information that serve as the basis for this GRAS Notification will be sent to the U.S. FDA upon request, or will be available for review and copying at reasonable times at the offices of:

Tate & Lyle
5450 Prairie Stone Parkway
Hoffman Estates, IL
USA, 60192

Should the FDA have any questions or additional information requests regarding this Notification, Tate & Lyle will supply these data and information upon request.

1.6 Freedom of Information Act, 5 U.S.C. 552

It is Tate & Lyle's view that all data and information presented in Parts 2 through 7 of this Notice do not contain any trade secret, commercial, or financial information that is privileged or confidential, and therefore, all data and information presented herein are not exempted from the Freedom of Information Act, 5 U.S.C. 552.

Part 2. § 170.230 Identity, Method of Manufacture, Specifications, and Physical or Technical Effect

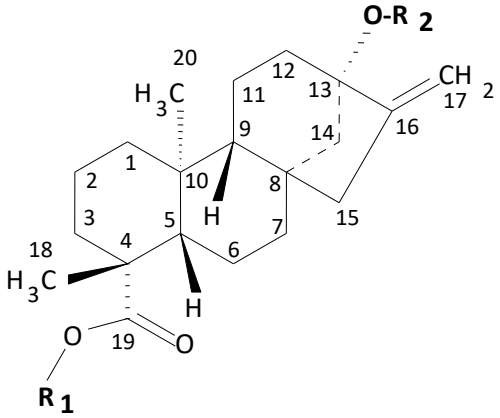
2.1 Identity

2.1.1 Description of the Enzymatically Produced Steviol Glycosides

Tate & Lyle's enzymatically produced steviol glycoside products are white to off-white powders that are very slightly to freely soluble in water. The enzymatically produced steviol glycosides are obtained through

enzymatic conversion of steviol glycosides and comply with JECFA's definition of enzyme-modified steviol glycosides (JECFA, 2021). The enzymatically produced steviol glycosides consist of compounds containing a steviol backbone conjugated to any number or combination of the principal sugar moieties (*i.e.,* glucose, xylose, rhamnose, fructose, deoxyglucose, galactose, and/or arabinose) at positions R_1 and R_2 (Figure 2.1.1-1), corresponding to any of the orientations occurring in the leaves of *S. rebaudiana* Bertoni. To date, over 60 different steviol glycosides have been identified within the leaves of *S. rebaudiana* Bertoni (JECFA, 2021). It is generally recognized that all steviol glycosides share the same metabolic fate owing to the fact that the sugar moieties are cleaved from the same steviol backbone structure (Purkayastha *et al.,* 2014, 2015, 2016). The steviol glycoside distribution of Tate & Lyle's enzymatically produced steviol glycosides are presented in Section 2.1.2. Tate & Lyle's enzymatically produced steviol glycosides have a sweetness intensity that fall within the range of 200 to 300 times sweeter than sucrose, consistent with the sweetness profile of steviol glycosides in general (JECFA, 2021), and similar to the sweetness intensity of high purity Rebaudioside M as described in GRN 780 (U.S. FDA, 2018).

Figure 2.1.1-1 Backbone Structure for Steviol Glycosides



R1 and R2 may be a single or multiple glycoside unit, including glucose, xylose, rhamnose, fructose, deoxyglucose, galactose, and/or arabinose

2.1.2 Information on the Identity of the Enzymatically Produced Steviol Glycosides

As discussed above, all steviol glycosides share a common steviol backbone structure and differ only with respect to the type and number of glycoside units (*i.e.,* glucose, xylose, rhamnose, fructose, deoxyglucose, galactose, and/or arabinose) at positions R_1 and R_2 (see Figure 2.1.1-1). Steviol glycosides may be considered "major" or "minor", depending on whether appropriate analytical reference standards are commercially available. "Minor" steviol glycosides can be referred to as steviol glycosides without a commercially available analytical standard. Nevertheless, these compounds have been demonstrated to share the same steviol backbone as the "major" steviol glycosides which undergo the same metabolic fate (Purkayastha and Kwok, 2020).

Tate & Lyle's enzymatically produced steviol glycosides are manufactured through enzymatic conversion of a stevia leaf extract containing ≥60% total steviol glycosides (see Section 2.2 for further details on the manufacturing process). Tate & Lyle measured the steviol glycoside distribution, including major and minor steviol glycosides, for 9 production batches of the company's enzymatically produced steviol glycosides using the HPLC method described by JECFA (2021) against commercially available standards. Minor steviol glycosides (*i.e*., steviol glycosides with no commercial reference standards available) were identified, confirmed, and quantified using the method described in JECFA (2021) in both the starting material (*i.e.,* leaf extract) and the final product based on the identical peak retention times and ion fragmentation using tandem mass spectrometry (MS/MS). The range, mean, and standard deviation of 9 production batches of the enzymatically produced steviol glycosides are summarized in Table 2.1.2-1 below. The HPLC chromatograms for select batches are provided in Appendix A. As shown in Table 2.1.2-1 below, the final products are highly purified and contain at least 95% total steviol glycosides, which is consistent with the purity criteria for steviol glycosides as established by JECFA (2021) and indicates that Tate & Lyle's production process consistently yields a highly purified final product.

Table 2.1.2-1 Steviol Glycoside Distribution of Tate & Lyle's Enzymatically Produced Steviol Glycosides

Steviol Glycoside (% dwb)	Range[a]	Mean	ndard Deviation
Rebaudioside A	0.03 to 13.91	7.78	6.33
Rebaudioside B	0.14 to 3.73	1.56	1.21
Rebaudioside C	0.84 to 1.06	0.92	0.10
Rebaudioside D	0.41 to 12.19	9.20	5.07
Rebaudioside E	0.44 to 0.69	0.53	0.11
Rebaudioside F	0.20 to 0.21	0.21	0.00
Rebaudioside I	0.28 to 5.62	2.07	2.20
Rebaudioside J	0.32 to 0.88	0.68	0.26
Rebaudioside M	54.02 to 98.11	81.59	18.46
Rebaudioside N	2.94 to 3.35	3.13	0.17
Rebaudioside O	1.15 to 2.10	1.49	0.43
Stevioside	0.04	0.04	0.00
Dulcoside A	ND	ND	N/A
Rubusoside	0.56 to 0.57	0.57	0.00
Steviolbioside	0.03 to 0.03	0.03	0.00
Total 'minor' steviol glycosides (as determined by LC-MS)[b]	3.68 to 7.44	5.87	1.54
Total Steviol Glycosides	**96.25 to 103.77**	**99.92**	**2.76**

dwb = dry weight basis; LC-MS = liquid chromatography – mass spectrometry; N/A = not available; ND = not detected.

[a] Values for 9 independent production batches of the enzymatically produced steviol glycosides produced from leaf extract containing ≥60% total steviol glycosides.

[b] "Minor" steviol glycosides include compounds for which commercial reference standards are not available.

2.2 Manufacturing Process of the Enzymatically Produced Steviol Glycosides

The manufacturing process of Tate & Lyle's enzymatically produced steviol glycosides complies with cGMP and the principles of Hazard Analysis and Critical Control Points (HACCP). A schematic of the production process is provided in Figure 2.2-1 and is described below. All raw materials, processing aids, and purification equipment used in manufacturing are food-grade and comply with appropriate Food Chemical Codex (FCC) monographs or equivalent international food or pharmacopeia standard (*e.g.,* JECFA, CODEX, United States Pharmacopeia [USP], European Pharmacopoeia) where applicable. The enzymes used in the manufacturing process for the enzymatic conversion of steviol glycosides, glycosyltransferases and sucrose synthases, are obtained from a genetically modified strain of *E. coli* K-12 W3110 that is considered a Biosafety Level 1 organism according to the National Institutes of Health and a non-pathogenic and non-toxigenic species. The enzymes and their sources are consistent with the enzymes described in the JECFA (2021) monograph for enzyme modified steviol glycosides and are considered safe for their intended use in the production of enzymatically produced steviol glycosides. The gene sequences encoding for the enzymes are synthesized *de novo* and optimized for expression in *E. coli*. The expression plasmids carrying each synthetic gene sequence were generated by standard recombinant DNA technology. The plasmid does not contain any DNA cloned from the source organism, and therefore do not contain extraneous unidentified DNA that can be transferred from the donor organism to the production strain.

The expression plasmids do not have any mobility or conjugative sequences, and therefore, it is unlikely that the antibiotic resistance gene[1] will be introduced to other bacteria or the environment. The plasmids have been fully sequenced and shown to not carry any sequences of concern. The enzymes are manufactured in an International Organization for Standardization (ISO) 9001-certified facility and in accordance with cGMP. Food-grade specifications have been established for the enzymes to ensure compliance with the purity requirements for enzyme preparations established by JECFA (2006a) and FCC (2021).

The production process broadly consists of 2 phases: stevia leaf extraction (starting material) and enzymatic conversion, followed by concentration and purification of the steviol glycosides. In the first phase, leaves of the *S. rebaudiana* Bertoni plant are subject to hot water extraction to obtain a stevia leaf extract comprising of a mixture of steviol glycosides, containing a minimum of 60% total steviol glycosides on a dry basis. The remainder of the leaf extract is comprised predominately of water and fibers. This extract/mixture may be purified by activated carbon and/or ion-exchange chromatography. The glycosyltransferase and sucrose synthase enzymes are added with sucrose and the required processing aids to initiate the enzymatic conversion process. The obtained distribution of steviol glycosides is influenced by the composition of the starting material, amount and ratio of enzymes added to the enzymatic conversion process, and duration of enzymatic conversion process. The enzymatic reaction is allowed to proceed until the desired distribution of steviol glycosides is obtained (see Table 2.1.2-1).

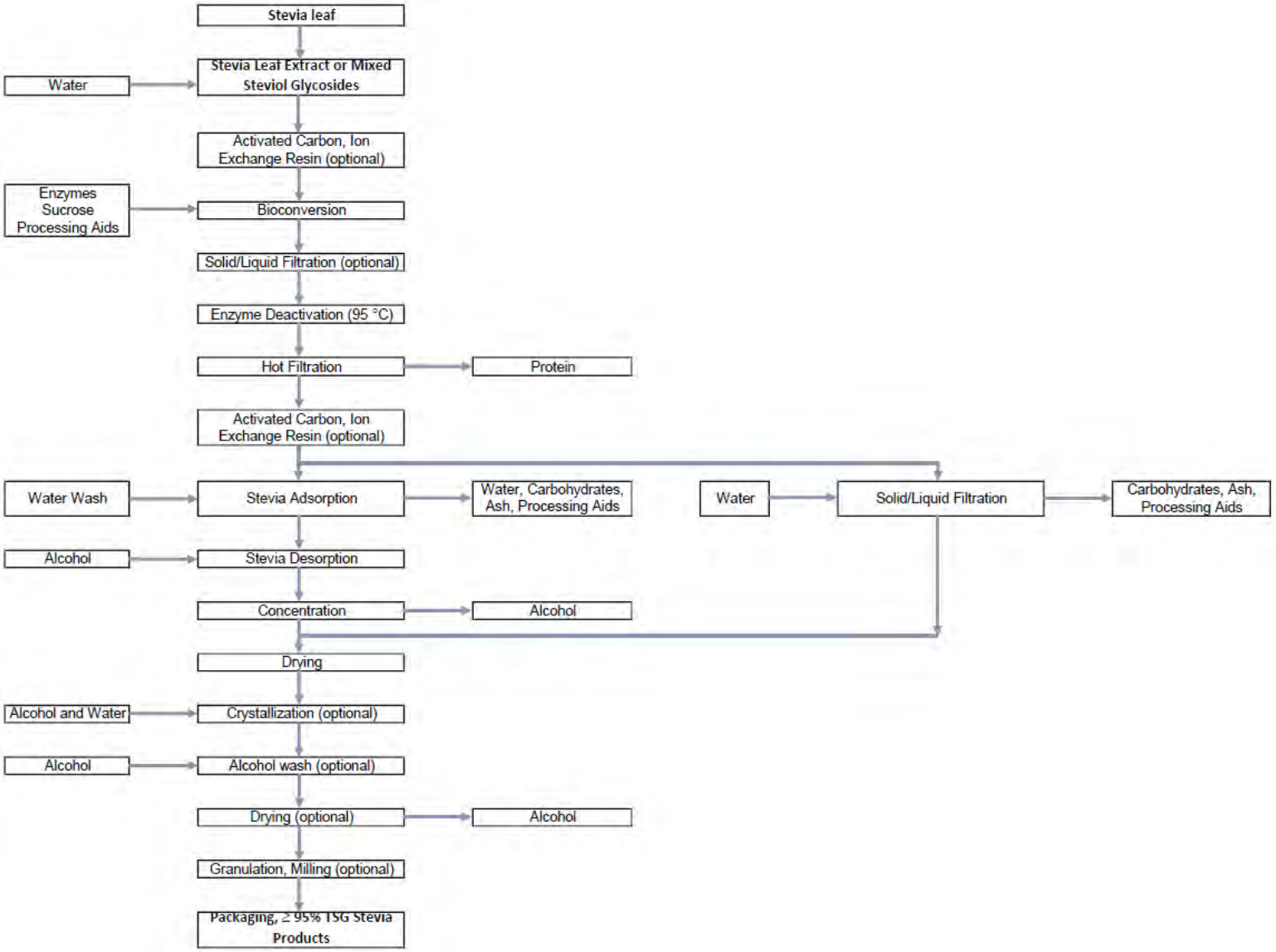
The second phase of the process denatures and removes the enzyme and other impurities (*e.g*., excess water, carbohydrates, ash, alcohol, non-steviol glycosides) using 1 of 2 alternate process streams. In both cases, the mixture is subject heat treatment step (95°C) and filtration to inactivate and remove the enzymes. Additional filtration steps and/or the use of ion exchange resins and adsorption and desorption of the steviol glycosides is used to remove impurities and concentrate the steviol glycoside product. This then undergoes drying with optional crystallization, alcohol washing, oven drying, and/or granulation steps to

[1] The chloramphenicol acetyltransferase gene used in pCK900 is originally from *E. coli* Tn9 and is naturally present in many wild-type host cells.

obtain the final product of a steviol glycoside mixture containing ≥95% total steviol glycosides in powder or granular form.

The production of Tate & Lyle's enzymatically produced steviol glycosides is consistent with the manufacturing process steps described for enzyme modified steviol glycosides by JECFA (2021), including the enzymes used in the production process. As highlighted in Annex 3 of the JECFA (2021) monograph for steviol glycosides, *"Enzyme modified steviol glycosides consist of a mixture of compounds containing a steviol backbone conjugated to any number or combination of the principal sugar moieties (glucose, rhamnose, xylose, fructose, arabinose, galactose and deoxyglucose) in any of the orientations occurring in the leaves of Stevia rebaudiana Bertoni"* whilst the manufacturing process typically "*maximizes the production of specific steviol glycosides that are not naturally present in high concentration in the leaf extract, primarily rebaudioside M and rebaudioside D with minor amounts of other steviol glycosides*" with the key specification requirement being that the end product contains at least 95% total steviol glycosides. As shown in Section 2.1.2, the production process described herein yields a final product that meets or exceeds the purity requirements for enzyme modified steviol glycosides as established by JECFA (2021) and is absent of chemical and microbiological impurities (see Section 2.3 for further details).

Figure 2.2-1 Schematic Overview of the Manufacturing Process for Tate & Lyle's Enzymatically Produced Steviol Glycosides



2.3 Product Specifications and Batch Analyses

2.3.1 Product Specifications

Tate & Lyle have established food-grade product specifications for the enzymatically modified steviol glycosides that are consistent with the purity requirements established by JECFA for enzyme-modified steviol glycosides (see Table 2.3.1-1). All analytical methods used to measure each specification parameter are internationally recognized methods (*e.g.,* USP, Association of Official Analytical Chemists [AOAC], or JECFA). Total steviol glycoside content is measured using the HPLC method described in the most recent JECFA specification monograph for steviol glycosides from *S. rebaudiana* Bertoni (JECFA, 2021).

Table 2.3.1-1 Product Specifications for Tate & Lyle's Enzymatically Produced Steviol Glycosides

Specification Parameter	Tate & Lyle's Enzymatically Produced Steviol Glycosides	JECFA Specifications for Enzyme-Modified Steviol Glycosides	Method of Analysis
Physical and Chemical Parameters			
Appearance	White to off-white powder	White to light-yellow powder	Visual inspection
Total steviol glycosides	≥95%	≥95% total steviol glycosides[a]	JECFA (2021)
Loss on drying	≤6%	≤6% (105°, 2 hours)	TN46540B (CRA MOIST.04)
pH (1% solution)	4.5 to 7.0	4.5 to 7.0	TN60730 (AOAC 981.12)
Residual ethanol	≤5,000 mg/kg	NMT 5,000 mg/kg	TN64080 (USP 32-NF 27)
Residual methanol	≤200 mg/kg	NMT 200 mg/kg	TN64081 (USP 32-NF 27)
Total ash	≤1%	≤1%	TN09560 (AOAC 900.02)
Lead	≤1 ppm	≤1 ppm	TN44290 (AOAC 993.14)
Arsenic	≤1 ppm	≤1 ppm	TN44292 (AOAC 993.14)
Cadmium	≤1 ppm	NS	TN44291 (AOAC 993.14)
Mercury	≤0.1 ppm	NS	TN44293 (AOAC 993.14)
Microbiological Parameters			
Total plate count	<1,000 CFU/g	<1,000 CFU/g	TN10560 (CRA Microbiological Methods I-A)
Mold	<100 CFU/g	<200 CFU/g	TN47010 (CRA Microbiological Methods II-A-1)
Yeast	<100 CFU/g	<200 CFU/g	TN97010 (CRA Microbiological Methods I-A)
Coliforms	<10 MPN/g	NS	TN10510 (CRA Microbiological Methods IV-B)
Escherichia coli	Not detected in 1 g	Negative in 1 g	TN10512 (CRA Microbiological Methods IV-B)
Salmonella spp.	Not detected in 25 g	Negative in 25 g	TN10547 (CRA Microbiological Methods V-A)

AOAC = Association of Official Analytical Chemists; CFU = colony-forming units; CRA = Corn Refiners Association; JECFA = Joint FAO/WHO Expert Committee on Food Additives; MPN = most probable number; NF = National Formulary; NMT = not more than; NS = not specified; ppm = parts-per-million; USP = United States Pharmacopeia.

[a] Where steviol glycosides "*consists of a mixture of compounds containing a steviol backbone conjugated to any number or combination of the principal sugar moieties in any of the orientations occurring in the leaves of Stevia rebaudiana Bertoni including, glucose, rhamnose, xylose, fructose, deoxyglucose, galactose, and arabinose*."

2.3.2 Batch Analysis

The results of analysis for 9 non-consecutive production batches of the enzymatically produced steviol glycosides produced from leaf extracts containing ≥60% total steviol glycosides are presented in Table 2.3.2-1. The range, mean, and standard deviation of the production batches are presented. The results demonstrate that the manufacturing process as described in Section 2.2 produces a consistent product that meets the established specifications (Table 2.3.2-1).

Table 2.3.2-1 Summary of the Batch Analysis for 9 Non-Consecutive Batches of Enzymatically Produced Steviol Glycosides

Specification Parameter	Specification Limit	Range[a]	Mean[a]	Standard Deviation
Total steviol glycosides (%)	≥95	96.25 to 103.77	99.92	2.76
Loss on drying (%)	≤6	3.44 to 5.86	4.39	0.85
pH (1% solution)	4.5 to 7.0	5.01 to 6.23	5.59	0.41
Residual ethanol (mg/kg)	≤5,000	105 to 3,200[b]	1,174	1,433
Residual methanol (mg/kg)	≤200	<100	N/A	N/A
Total ash (%)	≤1	0.05[c]	N/A	N/A
Lead (ppm)	≤1	0.007 to 0.027[d]	0.01	0.01
Arsenic (ppm)	≤1	0.0058[e]	N/A	N/A
Cadmium (ppm)	≤1	<0.005	<0.005	N/A
Mercury (ppm)	≤0.1	0.019 to 0.028[f]	0.02	0.00
Total plate count (CFU/g)	<1,000	40[g]	N/A	N/A
Mold (CFU/g)	<100	<10	<10	N/A
Yeast (CFU/g)	<100	<10	<10	N/A
Coliforms (MPN/g)	<10	<0.3	<0.3	N/A
Escherichia coli	Not detected in 1 g	ND	ND	N/A
Salmonella	Negative/25 g	Negative	Negative	N/A

CFU = colony-forming units; MPN = most probable number; ppm = parts-per-million.

[a] Values for 9 independent production batches of the enzymatically produced steviol glycosides produced from leaf extract containing ≥60% total steviol glycosides.

[b] Ethanol was present in 3 batches at levels of 105, 217, and 3,200 mg/kg. These values are within the established specification limit. Levels of residual ethanol were <100 in the remaining batches.

[c] Ash content was 0.05% in 1 batch and was <0.10 in the remaining batches. The ash content remained within the established specification limit.

[d] Levels of lead ranged between 0.007 to 0.027 mg/kg in 5 production batches and were <0.005 mg/kg in the remaining batches. The levels of lead remained within the established specification limit.

[e] Levels of arsenic was 0.0058 mg/kg in 1 production batch and were <0.01 mg/kg in the remaining batches. The levels of arsenic remained within the established specification limit.

[f] Levels of mercury were 0.019 to 0.028 mg/kg in 3 production batches and were <0.005 mg/kg in the remaining batches. The levels of mercury remained within the established specification limit.

[g] Total plate count was 40 CFU/g in 1 production batch and was <10 CFU/g in the remaining batches.

2.4 Additional Chemical Characterization

2.4.1 Residual Protein

Residual protein was analyzed in the same 9 production batches of the enzymatically produced steviol glycosides described in Section 2.3.2 using the bicinchoninic acid (BCA) assay. Samples were diluted in a ratio of 1:10 and analyzed at 1,000 mg/kg (0.1% w/w). Levels of residual protein ranged between 0.7 to 10.3 mg/kg (mean: 6.77 mg/kg; standard deviation 2.88 mg/kg) across the 9 production batches indicating that proteinaceous compounds, including enzymes, are present at negligible levels in the final product.

The BCA method is commonly used to demonstrate the absence of residual protein, and by extension, absence of the enzymes involved in the enzymatic conversion process, in steviol glycoside products produced through enzymatic conversion that have been notified to the FDA and received "no questions" (*e.g.,* GRNs 667, 780 and 1010). For the rebaudioside M product described in GRN 780, all results were below the detection limit of 5 ppm (U.S. FDA, 2018). In GRN 1010, the results for residual protein in rebaudioside M obtained from the enzymatic treatment of steviol glycosides ranged from approximately 4 to 19 mg/L (roughly equivalent to 4 to 19 ppm) (U.S. FDA, 2022). The residual protein levels in Tate & Lyle's enzymatically produced steviol glycosides are within range of the levels demonstrated for other steviol glycoside products with GRAS status (<5 ppm and 4 to 19 ppm as described in GRNs 780 and 1010, respectively).

Following the enzymatic conversion step, the steviol glycoside mixture undergoes heat treatment at up to 95°C for 30 minutes to heat denature and inactivate the enzymes, followed by ion-exchange filtration and several cycles of diafiltration to remove the inactivated enzymes. The enzymes used in the production of a high purity rebaudioside M produced by enzymatic conversion as described in GRN 780 are removed and inactivated in a similar manner including a heat treatment step, centrifugation, and ultrafiltration.

2.4.2 Residual Pesticides

Pesticide analysis was conducted for 4 representative batches of the enzymatically produced steviol glycosides The analytical results are presented in Appendix B. The levels of residual pesticides do not pose any safety concerns.

2.5 Stability of the Enzymatically Produced Steviol Glycosides

In the initial safety evaluations of steviol glycosides conducted by various global scientific and regulatory bodies, including JECFA, the European Food Safety Authority (EFSA), and Food Standards Australia New Zealand (FSANZ), the stability of steviol glycosides was reviewed and evaluated based on data submitted by the applicants, as well as data available in several published studies (Chang and Cook, 1983; Kroyer, 1999). The stability of a large number of steviol glycoside mixtures and preparations have also been reviewed by the U.S. Food and Drug Administration (FDA) through review of numerous GRAS notifications pertaining to steviol glycosides (see Section 6.2). In their evaluation of steviol glycosides, JECFA concluded that these compounds do not undergo browning or caramelization when heated and are stable at elevated temperatures under their conditions of use in foods (JECFA, 2007). Furthermore, it was noted that steviol glycosides (approximately 90 to 94% purity) are stable for at least 180 days when stored at temperatures up to 24°C and pH 2.0 to 4.0. At temperatures up to 80°C, steviol glycoside solutions in water showed 4 and 8% decomposition at pH 4.0 and 3.0, respectively, after 8 hours. At temperatures of 100°C, higher rates of decomposition were observed, with 10 and 40% decomposed at pH 4.0 and 3.0, respectively. These findings

suggest the stability of steviol glycosides to be pH- and temperature-dependent. JECFA ultimately concluded that steviol glycosides are thermally and hydrolytically stable for use in foods and acidic beverages under normal processing and storage conditions (JECFA, 2007).

To date, the U.S. FDA have reviewed numerous GRAS notifications pertaining to high-purity steviol glycosides that contain ≥95% total steviol glycosides and meet the purity requirements for steviol glycosides established by JECFA, including information on the shelf-life stability of these compounds, and have not identified any safety-related issue on the stability of steviol glycosides. A summary of GRAS notifications pertaining to high purity steviol glycoside mixtures and preparations is provided in Section 6.2. Considering that all steviol glycosides share the same steviol backbone structure, and therefore a similar metabolic fate (Purkayastha *et al.,* 2014, 2015, 2016), it is expected that these compounds will exhibit similar chemical stability to one another. On this basis, it is anticipated that the existing knowledge on the stability of steviol glycosides described in the publicly available scientific literature and GRAS notifications that received "no questions" from the FDA can be extended to support the shelf-life stability of Tate & Lyle's enzymatically produced steviol glycosides as described herein.

Part 3. §170.235 Dietary Exposure

The dietary consumption of steviol glycoside mixtures/preparations have been estimated using a post-market surveillance approach as outlined in a number of GRAS Notices for steviol glycosides submitted to the FDA (see Section 6.2 for a list of GRAS Notices for steviol glycosides). This approach uses the publicly available post-market surveillance data for other high-intensity sweeteners and assumes full/complete replacement of the currently approved high-intensity sweeteners with the new sweetener (Renwick, 2008). This results in a conservative estimate of the dietary exposure to a high-intensity sweetener that can be considered realistic as they reflect actual post-market intakes of high-intensity sweeteners. The average and high-end dietary intakes of rebaudioside A as sucrose equivalents was estimated in various population groups, such as non-diabetic and diabetic adults and children, and adjusted the values accordingly using the sweetness intensity of rebaudioside A relative to sucrose (Renwick, 2008). JECFA considered various intake models for the estimation of dietary exposure to steviol glycosides, including the intake analysis conducted by Renwick (2008) as part of their evaluation of the safety of steviol glycosides (JECFA, 2008). Although higher intake estimates than those presented by Renwick (2008) were identified using other methodologies, JECFA noted that such replacement estimates were highly conservative and that actual exposures to steviol glycosides (expressed as steviol equivalents) would be 20 to 30% of these values (1 to 2 mg/kg body weight/day, expressed as steviol equivalents). JECFA also noted that the post-market surveillance approach further confirmed the lower intake estimate range.

As discussed in Section 1.3, Tate & Lyle's enzymatically produced steviol glycosides have a sweetness intensity that falls within the range of other steviol glycoside mixtures (*i.e.,* 200 to 300 times sweeter than sucrose) as described within the JECFA Monograph for steviol glycosides and enzyme modified steviol glycosides (JECFA, 2021). The enzymatically produced steviol glycosides are intended for use as general-purpose sweeteners. Considering that a number of different steviol glycoside mixtures/preparations consisting of varying amounts of steviol glycosides (*e.g.,* rebaudiosides M, D, E) are currently on the U.S. marketplace, Tate & Lyle's enzymatically produced steviol glycosides will serve as a substitutional source of steviol glycosides in finished food products, or will be used in combination with such preparations at levels that are technologically feasible without adversely impacting the organoleptic properties of the final product. As a result, it is not expected that the introduction of Tate & Lyle's enzymatically produced steviol glycosides will increase the current consumption of steviol glycosides by the U.S. population as the introduction of these mixtures will not result in additional exposure to steviol glycosides (*i.e.,* the intakes of steviol glycosides (as steviol equivalents) will remain the same). Furthermore, considering the sweetening properties of steviol glycosides, it is not expected that the consumption of Tate & Lyle's enzymatically produced steviol glycosides will be additive to other steviol glycosides currently on the U.S. marketplace as there are self-limiting uses of these compounds (*i.e.,* higher amounts of steviol glycoside use would elicit adverse organoleptic properties in the final food, impacting consumer acceptance). Therefore, on the basis that Tate & Lyle's enzymatically produced steviol glycosides would be substitutional to existing steviol glycosides and the introduction of these products to the U.S. marketplace would not result in cumulative exposures, a dietary intake assessment of the enzymatically produced steviol glycosides was not considered necessary. The dietary intakes of Tate & Lyle's enzymatically produced steviol glycosides would be below the current acceptable daily intake (ADI) of 4 mg/kg body weight/day (as steviol) as established by JECFA (2016) and maintained in their 2018 and 2021 evaluations. The EFSA Panel on Food Additives and Nutrient Sources Added to Food (ANS Panel) also established an ADI of 4 mg/kg body weight/day for steviol glycosides (expressed as steviol equivalents) (EFSA, 2010, 2020).

Part 4. §170.240 Self-Limiting Levels of Use

The use of the enzymatically produced steviol glycosides is largely limited by the desired sweetness intended for a particular food or beverage product. Therefore, the use of the enzymatically produced steviol glycosides as a general-purpose sweetener in foods is self-limiting based on its organoleptic properties; higher amounts of steviol glycoside use would elicit adverse organoleptic properties in the final food, impacting consumer acceptance.

Part 5. §170.245 Experience Based on Common Use in Food Before 1958

Not applicable as the enzymatically produced steviol glycosides have not been used in food before 1958.

Part 6. §170.250 Narrative and Safety Information

6.1 Safety Narrative

The safety of steviol glycosides has been extensively reviewed by the FDA in a large number of GRAS Notices (see Section 6.2 for further details). To date, over 50 GRAS Notices describing the GRAS status of major individual steviol glycosides, including stevioside, rebaudiosides A, C, D, and X/M, mixtures of steviol glycosides, and glucosylated and enzyme-modified steviol glycosides, have been notified to the FDA. The FDA has consistently raised no questions on the GRAS status of various high purity steviol glycoside preparations, indicating that the Agency recognizes no safety concern with respect to the use of these compounds as general-purpose sweeteners. Likewise, the safety of steviol glycosides has been extensively reviewed by scientific bodies and regulatory agencies, including JECFA, European Commission's Scientific Committee on Food (SCF), EFSA, FSANZ, and Health Canada. The existing safety database on steviol glycosides includes an extensive evaluation of the metabolism and pharmacokinetics of steviol glycosides in rodents and humans, and a standard battery of toxicological tests, including acute toxicity, short- and long-term toxicity and carcinogenicity, reproductive and developmental toxicity, *in vitro* and *in vivo* mutagenicity and genotoxicity, as well as several human studies.

The safety of steviol glycosides have been largely supported through early studies on stevioside, the predominant steviol glycoside in *S. rebaudiana* leaves, and other steviol glycosides such as rebaudioside A and D, as well as recent metabolism and pharmacokinetic studies demonstrating the shared metabolic fate of steviol glycosides (Aze *et al.*, 1991; Toyoda *et al.*, 1997; Curry and Roberts, 2008; Curry *et al*., 2008; Nikiforov and Eapen, 2008; Williams and Burdock, 2009; Purkayastha *et al.,* 2016). The FDA, EFSA, FSANZ, Health Canada, and JECFA recognize that, due to the common metabolic fate of steviol glycosides, the safety opinion of any individual steviol glycoside (*e.g.,* rebaudioside M) may be extended to support the safety of all steviol glycosides. In 2021, JECFA adopted a safety framework for steviol glycosides that recognizes advancements in technologies used in the production of steviol glycosides, such as enzyme-modified steviol glycosides as described herein (JECFA, 2021). This framework describes a general manufacturing process for enzyme-modified steviol glycosides and purity specifications. It is anticipated that no safety concerns would be expected provided that steviol glycoside mixtures/preparations are manufactured consistent with one of the described technologies and meet the corresponding purity specifications. As discussed previously, Tate & Lyle's enzymatically produced steviol glycosides are manufactured with processing steps that generally comply with the process described for enzyme modified steviol glycosides [see Annex 3 of JECFA (2021)], and specifications have been established for these compounds that meet or exceed the JECFA purity specifications. The mixtures have been demonstrated to be absent of chemical impurities, such as heavy metals and residual solvents, and microbiological contaminants through 3 non-consecutive batches of each product. Therefore, it is not expected that the production process would yield any safety concern in the final product.

Considering that the existing safety database on steviol glycosides has been extensively reviewed by the FDA, the pertinent generally available data and information used to support the safety of steviol glycosides, including major individual steviol glycosides and other steviol glycoside mixtures/preparations, is incorporated by reference to information cited within prior GRAS notifications (see list of GRAS Notices reviewed by the FDA in Section 6.2). Updated searches of the scientific literature were conducted through October 2022 to identify new data and information relevant to the safety of steviol glycosides that have been published since the FDA's last review.[2] In the following sections, the common metabolic fate of steviol

[2] GRN 1010 was the most recent steviol glycoside GRAS Notice to receive a "no questions" letter from the FDA which summarized literature prior to November 2020.

glycosides is briefly discussed (Section 6.3), and a brief summary of the conclusions of the scientific and authoritative bodies is provided in Section 6.4. New studies identified in the scientific literature that have been published since GRN 1010 are outlined in Section 6.5.

6.2 Regulatory Status of Steviol Glycosides in the U.S.

A number of GRAS Notices for major individual steviol glycosides, including stevioside, rebaudiosides A, C, D, and X/M, mixtures of steviol glycosides, and glucosylated and enzyme-modified steviol glycosides have been reviewed by the U.S. Food and Drug Administration (FDA) (Table 6.2-1). The FDA has consistently raised "no questions" regarding the GRAS status of these steviol glycoside products for use as general-purpose sweeteners in various food and beverage products, suggesting that these products have a general recognition of safety. Of note, the FDA acknowledged that the Agency "filed, evaluated, and has not objected to more than 50 GRAS notices for the use of various high-purity steviol glycosides as sweeteners in food", suggesting that the Agency recognizes the safety of high-purity steviol glycosides when used as general purpose sweeteners (Perrier *et al.,* 2018). The FDA also noted that specifications for the notified substance should meet or exceed established specifications (e.g., JECFA). As discussed in Section 2.2 and 2.3, Tate & Lyle's enzymatically produced steviol glycosides are manufactured in a consistent manner as described by JECFA (2021) for enzyme modified steviol glycosides, and the final products meet or exceed the purity specifications for enzyme modified steviol glycosides and steviol glycosides in general as established by JECFA. Furthermore, considering that Tate & Lyle's enzymatically produced steviol glycosides will serve as a substitutional source of steviol glycosides currently on the U.S. marketplace, and that the introduction of the steviol glycoside mixtures would not result in any cumulative dietary exposure to steviol glycosides, it is not anticipated that the introduction of Tate & Lyle's enzymatically produced steviol glycosides would pose any safety concern in the U.S. population.

Table 6.2-1 Summary of GRAS Notices for Steviol Glycosides

Company	Substance	FDA Response	GRAS Notice No.
Whole Earth Sweetener Company LLC (subsidiary of Merisant)	Rebaudioside A purified from *Stevia rebaudiana* (Bertoni) Bertoni	No questions	252
Cargill, Inc.	Rebaudioside A purified from *Stevia rebaudiana* (Bertoni) Bertoni	No questions	253
McNeil Nutritionals	Purified steviol glycosides with rebaudioside A as the principal component	No questions	275
Blue California	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni	No questions	278
Sweet Green Fields, LLC	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni	No questions	282
Wisdom Natural Brands	Purified steviol glycosides with rebaudioside A and stevioside as the principal components	No questions	287
Sunwin USA, LLC and Wild Flavors	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni	No questions	303
Sunwin USA, LLC and Wild Flavors	Purified steviol glycosides with rebaudioside A and stevioside as the principal components	No questions	304
Pyure Brands, LLC	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni	No questions	318
PureCircle USA, Inc.	Purified steviol glycosides with rebaudioside A and stevioside as the principal components	No questions	323

Table 6.2-1 Summary of GRAS Notices for Steviol Glycosides

Company	Substance	FDA Response	GRAS Notice No.
GLG Life Tech, Ltd.	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni	No questions	329
NOW Foods	Enzyme modified steviol glycoside preparation (EMSGP)	No questions	337
GLG Life Tech, Ltd.	Stevioside purified from the leaves of Stevia rebaudiana (Bertoni) Bertoni (stevioside)	No questions	348
GLG Life Tech, Ltd.	Purified steviol glycosides with rebaudioside A and stevioside as the principal components	No questions	349
Guilin Layn Natural Ingredients, Corp.	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside A)	No questions	354
BrazTek International Inc.	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside A)	No questions	365
Sinochem Qingdao Co., Ltd.	Purified steviol glycosides with rebaudioside A and stevioside as the principal components	No questions	367
Zhucheng Haotian Pharm Co., Ltd.	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni	No questions	369
Toyo Sugar Refining Co., Ltd. and Nippon Paper Chemicals Co., Ltd.	Enzyme modified steviol glycosides	No questions	375
GLG Life Tech Corporation	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside A)	No questions	380
Chengdu Wagott Pharmaceutical	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside A)	No questions	388
Chengdu Wagott Pharmaceutical	Steviol glycosides with stevioside as the principal component	No questions	389
Daepyung Co., Ltd.	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside A)	No questions	393
Daepyung Co., Ltd.	Steviol glycosides with rebaudioside A and stevioside as the principal components	No questions	395
MiniStar International, Inc.	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside A)	No questions	418
Daepyung Co., Ltd.	Enzyme-modified steviol glycosides	No questions	448
Daepyung Co., Ltd.	Enzyme-modified steviol glycosides	No questions	452
PureCircle USA, Inc.	Rebaudioside D purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside D)	No questions	456
Almendra Limited	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni (rebaudioside A)	No questions	461
Qufu Xiangzhou Stevia Products Co., Ltd.	Rebaudioside A purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni	No questions	467
PureCircle, Ltd.	Purified steviol glycosides with rebaudioside X as the principal component	No questions	473
GLG Life Tech Corporation	High purity steviol glycosides (minimum purity 95%)	No questions	493
GLG Life Tech Corporation	High purity Rebaudioside M	No questions	512
Almenda (Thailand) Limited	Steviol glycosides with rebaudioside A and stevioside as the principal components	No questions	516
GLG Life Tech Corporation	High purity rebaudioside C	No questions	536
GLG Life Tech Corporation	High purity rebaudioside D	No questions	548

Table 6.2-1 Summary of GRAS Notices for Steviol Glycosides

Company	Substance	FDA Response	GRAS Notice No.
Procuctora Alysa SpA	High purity steviol glycosides (minimum purity 95%) consisting primarily of rebaudioside A.	No questions	555
PureCircle, Ltd.	Glucosylated steviol glycosides (minimum purity 80%)	No questions	607
PureCircle, Ltd.	Purified steviol glycosides	No questions	619
Cargill, Inc.	Steviol glycosides produced in *Saccharomyces cerevisiae*	No questions	626
DSM Nutritional Products, LLC	Rebaudioside A from *Yarrowia lipolytica*	No questions	632
Hunan Huacheng Biotech Inc.	High purity steviol glycosides (minimum purity 97%) consisting primarily of rebaudioside A	No questions	638
GLG Life Tech Corporation	Enzyme-modified steviol glycosides	No questions	656
PureCircle USA	Glucosylated steviol glycosides (minimum purity 95%)	No questions	662
Blue California	Rebaudioside M	No questions	667
Xinghua GL Stevia Co., Ltd.	Purified steviol glycosides	No questions	702
Blue California	Rebaudioside D	No questions	715
Shangdong Shengxiangyuan Biotechnology	Purified steviol glycosides	No questions	733
PureCircle Limited	Steviol glycosides consisting primarily of rebaudioside M	No questions	744
PureCircle Limited	Steviol glycosides consisting primarily of rebaudioside M	No questions	745
DSM Food Specialties/DSM Nutritional Products North America	Steviol glycosides consisting primarily of rebaudioside M produced in *Yarrowia lipolytica*	No questions	759
Sichuan Ingia Biosynthetic Co., Ltd.	Rebaudioside D	No questions	764
Tate and Lyle	Rebaudioside M	No questions	780
GLG Life Tech Corporation	Steviol glycosides (minimum purity 95%)	No questions	790
Sichuan Ingia Biosynthetic Co., Ltd.	Rebaudioside M	No questions	799
Steviana Bioscience (Suzhou) Inc.	Purified steviol glycosides	No questions	795
Amyris, Inc.	Rebaudioside M	No questions	812
Haigen-BGG Natural Ingredients Limited	Glucosylated steviol glycosides	No questions	821
Blue California	Rebaudioside E	No questions	823
Jiang Su Svetia Biotechnology Co., Ltd.	Purified steviol glycosides	No questions	838
Sinochem Health Company Ltd.	Purified steviol glycosides	No questions	839
GLG Life Tech Corporation	Rebaudioside M	No questions	846
Qufu Shengren Pharmaceutical Co., Ltd	Glucosylated steviol glycosides	No questions	858
Cargill, Inc.	Rebaudioside M	FDA ceased to evaluate at the notifier's request	867
Daepyung Co., Ltd.	Glucosylated steviol glycosides	No questions	878
Cargill, Inc.	Rebaudioside M	No questions	882
Blue California	Rebaudioside I	No questions	911

Table 6.2-1 Summary of GRAS Notices for Steviol Glycosides

Company	Substance	FDA Response	GRAS Notice No.
Blue California	Rebaudioside B	No questions	968
Shandong Shengxiangyuan Biotechnology Co., Ltd	Enzyme-modified steviol glycosides	No questions	970
Zhucheng Haotian Pharm Co., Ltd	Purified steviol glycosides from the leaves of *Stevia rebaudiana* (Bertoni)	No questions	983
Zhucheng Haotian Pharm Co., Ltd	Enzyme-modified steviol glycosides	No questions	999
Manus Bio, Inc.	Rebaudioside M obtained by enzymatic treatment of steviol glycosides purified from the leaves of *Stevia rebaudiana* (Bertoni)	No questions	1010

FDA = Food and Drug Administration; GRAS = Generally Recognized as Safe.

6.3 Metabolic Fate of Steviol Glycosides

The metabolic fate of steviol glycosides has been well established and recognized by scientific and regulatory bodies, including the FDA. The existing information describes the metabolic fate (absorption, distribution, metabolism, and elimination) of steviol glycosides, notably that these compounds have a similar metabolic fate due to the shared steviol backbone, as outlined in GRN 780. The available data and information on the metabolic fate of individual steviol glycosides as discussed in detail in GRN 780 is incorporated by reference in this dossier and is briefly described as follows. Steviol glycosides are not hydrolyzed in the upper gastrointestinal tract due to the presence of β-glycosidic bonds. The unchanged steviol glycosides degrade by the gut microflora in the colon to release the aglycone, steviol (Wingard *et al*., 1980; Hutapea *et al*., 1997; Gardana *et al*., 2003; Koyama *et al*., 2003a,b; Geuns *et al*., 2003, 2007; Renwick and Tarka, 2008; Nikiforov *et al.*, 2013; Purkayastha *et al.,* 2016). Steviol glycosides are hydrolyzed sequentially. The degradation rate is dependent on the structural complexity of each steviol glycoside (Wingard *et al*., 1980; Koyama *et al*., 2003b). Despite the differences in chemical structure, the rates of hydrolysis of different steviol glycosides to steviol are relatively similar, especially during the first 24 hours of incubation in *in vitro* metabolic studies with human fecal homogenates (Purkayastha *et al.,* 2014, 2015, 2016). Following microbial degradation, the steviol metabolite is absorbed systemically into the portal vein and distributed to the liver, spleen, adrenal glands, fat, and blood (Nakayama *et al*., 1986; Koyama *et al*., 2003b; Wang *et al*., 2004; Roberts and Renwick, 2008). Steviol is conjugated to glucuronic acid to form steviol glucuronide in the liver. The steviol glucuronide metabolite and any unconjugated steviol or unhydrolyzed fraction of the administered glycosides are excreted primarily in the urine, and, to a lesser extent, feces in humans (Wingard *et al*., 1980; Nakayama *et al*., 1986; Kraemer and Maurer, 1994; Simonetti *et al*., 2004; Geuns *et al*., 2006, 2007; Roberts and Renwick, 2008; Wheeler *et al*., 2008).

One new study was identified in the updated search of the scientific literature pertaining to the toxicokinetics of steviol glycosides (Purkayastha and Kwok, 2020). In this study, *in vitro* colonic microbiota samples collected from human adults and children were examined to investigate the metabolic fates of 5 steviol glycoside samples. The steviol glycoside samples were composed of:

- Stevia leaf extract containing at least 20 different individual steviol glycosides;
- A rebaudioside M and rebaudioside D mixture generated by enzymatic treatment of rebaudioside A;
- A steviol glycoside mixture derived from enzymatic treatment of stevioside;
- A steviol glycoside mixture prepared from enzymatic glycosylation of rebaudioside A; and
- A purified rebaudioside A standard derived from *S. rebaudiana* Bertoni.

Healthy adult subjects (6 males and 6 females; 22 to 66 years old) produced stool samples that were pooled (3 male and 3 female) to generate fecal homogenates. The homogenates were used to evaluate the metabolic fates of the steviol glycoside samples detailed above. The metabolism of samples 1 and 5 were also tested in pediatric fecal homogenates (male and female; 2 to 3 years old). Pooled fecal homogenate samples were incubated with steviol glycoside samples under anaerobic conditions, at 37°C for 0, 4, 8, 12, 16, 24, 48, and 72 hours. Steviol glycoside samples met similar metabolic fates regardless of fecal homogenate source. The authors concluded, "*Given a common metabolite structure and a shared metabolic fate in all ages, safety data for individual steviol glycosides can be used to support safety of all steviol glycosides produced by extraction and enzymatic conversion of stevia leaf extract*."

In summary, due to the common molecular structure for steviol glycosides, consisting of a steviol backbone conjugated to different numbers and types of sugar moieties, all individual steviol glycosides that are naturally present in the *S. rebaudiana* Bertoni leaf share a common metabolic fate, as described above. Therefore, the safety database that has been established for individual steviol glycosides (*e.g.,* stevioside, rebaudioside A, rebaudioside D) can be extrapolated to support the safe use of purified steviol glycosides in general, regardless of the steviol glycoside distribution of the preparation, including Tate & Lyle's enzymatically produced steviol glycosides.

6.4 Summary of Steviol Glycoside Safety Opinions by Scientific and Regulatory Authorities

Several scientific bodies and regulatory agencies, including the FDA, the SCF, EFSA, JECFA, FSANZ, and Health Canada, have reviewed the safety of steviol glycosides, which has led to the authorization of steviol glycosides for use in food in numerous countries. A brief summary of the existing authorizations for steviol glycosides as food additives across various jurisdictions and the conclusions of the risk assessments conducted by relevant authoritative bodies are presented below.

In the European Union (EU), commercially available steviol glycoside products must comply with the specifications for steviol glycosides (International Numbering System for Food Additives [INS] No. 960) adopted by the European Commission in 2012 and updated in 2021 and 2022 to include rebaudioside M, Rebaudioside D, and Rebaudioside AM produced through enzymatic conversion.[3], and glucosylated steviol glycosides. As such, steviol glycoside products are approved for use in the EU and must contain no less than 95% total steviol glycosides from 11 total named steviol glycosides (dulcoside, rebaudiosides A, B, C, D, E, F, and M, rubusoside, steviolbioside, and stevioside). Within their safety assessment of 2010 (EFSA, 2010), the EFSA Panel corroborated the JECFA conclusion arising from their 69th meeting and an ADI of 0 to 4 mg/kg body weight, as steviol equivalents, was established for steviol glycosides. In 2020, EFSA evaluated the safety of a proposed amendment to the steviol glycoside specification to expand the list of permissible steviol glycosides to include all of those that are present in the leaves of the *S. rebaudiana* Bertoni plant (EFSA, 2020) and thus align the EU specification with that of the current JECFA specification.. The EFSA Panel on Food Additives and Flavourings (FAF Panel) noted that all steviol glycosides have been observed to share the same metabolic fate, and ultimately concluded that the 60 steviol glycosides identified within the proposed amendment could be established as safe due to the vast toxicological database that has previously been evaluated for these compounds, as a read-across approach could be undertaken. The existing ADI of 4 mg/kg body weight (as steviol equivalents) would be applicable to all 60 of the identified

[3] Commission Regulation (EU) 2021/1156 of 13 July 2021 amending the Annex to Regulation (EU) No 231/2012 laying down specifications for food additives listed in Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council as regards specifications for steviol glycosides (E 960) and rebaudioside M. C/2021/5062. Off J Eur Union 64(L249):87-98. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32021R1156&from=EN.

steviol glycosides. Likewise, in the EFSA FAF panel evaluations of the safety of rebaudioside M, D and AM (EFSA 2019, 2021, 2022) the panel agreed that the ADI of 0 – 4mg/kg bw/day applies to steviol glycoside preparations obtained by enzymatic bioconversion. In the case of the individual applications made in 2019 and 2021, the respective preparations of rebaudioside M, D and AM EFSA issued Scientific Opinions that the preparations obtained did not pose a safety concern. However, in their report on the safety of rebaudioside D produced by enzymatic bioconversion of purified stevia leaf extract using enzymes derived from GM *Komagataella phaffii* (EFSA 2022) EFSA noted that, although there are no toxicological concerns for the additive, the possibility of the presence of residual DNA coding for the kanamycin resistance gene could not be excluded based on the available data. The EFSA FAF Panel therefore concluded that the safety of rebaudioside D produced *via* this specific method was not sufficiently demonstrated since the absence of recombinant DNA was not shown (EFSA, 2022).

The safety of steviol glycosides have been assessed by FSANZ taking into consideration the data that had been previously reviewed by JECFA (FSANZ, 2008). In their review in 2008, FSANZ concluded that an ADI of 0 to 4 mg/kg body weight, measured as steviol equivalents, was suitable. The definition of steviol glycosides in the *Australia New Zealand Food Standards Code* has since been amended twice to expand the list of permissible steviol glycosides that are encapsulated by the term "steviol glycosides," in 2015 and then in 2017, and the term is now defined as including all steviol glycosides present in the leaves of the *S. rebaudiana* plant (FSANZ, 2015, 2017). As part of the 2017 amendment, FSANZ acknowledged that the definition of "*all steviol glycosides in stevia leaf*" includes at least 40 different steviol glycosides (FSANZ, 2017). Specifications for steviol glycoside products, as defined by FSANZ, indicate that *S. rebaudiana* Bertoni extracts must contain no less than 95% steviol glycosides on a dry-weight basis. Recently in 2020, FSANZ further expanded this specification to allow production of steviol glycoside preparations from fermentation utilizing *Saccharomyces cerevisiae* production strains, in addition to the enzymatic conversion of stevia leaf extract to produce high quantities of specific minor steviol glycosides (*i.e.*, rebaudiosides D, M, and A) using enzymes produced by *Pichia pastoris* or *E. coli* (FSANZ, 2020).

In Canada, Health Canada reviewed the safety of steviol glycosides (defined as stevioside, rebaudiosides A, B, C, D, F, M, dulcoside A, rubusoside, and steviolbioside) in 2012 and established an ADI of 4 mg/kg body weight, measured as steviol equivalents (Health Canada, 2012a,b). In 2016, Health Canada expanded the steviol glycosides purity definition to include rebaudioside M as an additional permissible steviol glycoside (Health Canada, 2016). Following a safety assessment in 2017, Health Canada expanded the list of permissible steviol glycosides to include all steviol glycosides in the *S. rebaudiana* Bertoni plant (Health Canada, 2017). In Canada, the specifications set out for steviol glycosides in the Food Chemicals Codex or by JECFA, which indicate that steviol glycoside preparations must contain no less than 95% steviol glycosides on a dry-weight basis, must be met. Steviol glycosides produced from *S. rebaudiana* Bertoni, *S. cerevisiae* CD15380, *S. cerevisiae* CD15407, *S. cerevisiae* Y63348, and *Yarrowia lipolytica* VRM are all permitted for use in the same food products and at the same use levels in Canada. As of October 2022, steviol glycosides from these sources are all permitted for use at the same maximum use levels up to a maximum level of 0.35% in finished products as per the *List of Permitted Sweeteners* (Health Canada, 2022).

The safety of steviol glycosides has been reviewed by JECFA on several occasions: in 1998, 2004, 2007, 2008, and 2016, at their 51st, 63rd, 68th, 69th, and 82nd meetings, respectively (JECFA, 1999, 2006b, 2007, 2009, 2017). The Committee had initially established an ADI of 0 to 2 mg/kg body weight (expressed as steviol equivalents), however, following review of additional data in 2008, an ADI for steviol glycosides of 0 to 4 mg/kg body weight was established, expressed as steviol equivalents. This ADI was maintained at the 82nd JECFA meeting in 2016. In 2019, a framework to develop specifications for steviol glycosides based on 4 unique production methodologies was established and adopted at the 87th meeting of JECFA (JECFA, 2019). The framework categorized steviol glycoside preparations into the following 4 groups based on their

method of manufacture: extraction; fermentation; enzymatic modification; and enzymatic glucosylation (JECFA, 2021). The latest *Compendium of Food Additive Specifications* now contains this framework for steviol glycosides and lists the specifications for steviol glycosides individually for each production method (JECFA, 2021). Separate specifications are listed for each of the following methods of production: (i) Steviol Glycosides from *Stevia rebaudiana* Bertoni; (ii) Steviol Glycosides from Fermentation; (iii) Enzyme Modified Steviol Glycosides; and (iv) Enzyme Modified Glucosylated Steviol Glycosides. The JECFA framework for steviol glycosides has been ratified by Codex into the General Standard for Food Additives (GSFA) (Codex, 2021).

Enzyme Modified Steviol Glycosides have the same identity and purity specification parameters as Steviol Glycosides from *S. rebaudiana* Bertoni and therefore must also contain no less than 95% total steviol glycosides. In accordance with the JECFA specifications for Enzyme Modified Steviol Glycosides laid out in this framework, Tate & Lyle's enzymatically produced steviol glycosides produced through enzymatic conversion of a stevia leaf extract using enzymes obtained from a GM strain of *E. coli* comply with this standard for purity and meet all the JECFA specification parameters.

6.5 New Data Related to the Safety of Steviol Glycosides

The safety of steviol glycosides has been extensively reviewed in a number of GRAS notifications submitted to the U.S. FDA, as outlined in Section 6.2. The safety of steviol glycosides was most recently evaluated by the U.S. FDA in their evaluation of GRN 1010 for rebaudioside M obtained by enzymatic treatment of steviol glycosides purified from the leaves of *Stevia rebaudiana* (Bertoni), which included a comprehensive search of the scientific literature to capture publications relevant to the safety of steviol glycosides up to November 2020 (U.S. FDA, 2022). In order to identify new data related to the safety of steviol glycosides following the FDA review of GRN 1010, a comprehensive search of the scientific literature was conducted from November 2020 to December 2022. The search was limited to articles with full texts within peer-reviewed scientific journals. The following databases were searched: Adis Clinical Trials Insight, AGRICOLA, AGRIS, Allied & Complementary Medicine™, BIOSIS® Toxicology, BIOSIS Previews®, CAB ABSTRACTS, Embase®, Foodline®: SCIENCE, FSTA®, MEDLINE®, NTIS: National Technical Information Service, Toxicology Abstracts, and ToxFile®. The studies identified included genotoxicity studies and several studies in animals evaluating the safety and antidiabetic effects of steviol glycosides. In general, the results of these recent studies provide further support for the safety of steviol glycosides as they do not contradict the safety conclusion on steviol glycosides as established by a number of authoritative scientific bodies (*e.g.,* JECFA, FSANZ, the U.S. FDA, EFSA, and Health Canada). The newly identified studies are summarized below.

6.5.1 Subchronic Toxicity

Two new studies were identified in the updated search of the scientific literature pertaining to the subchronic toxicity of steviol glycosides. It is noted that these studies were not conducted in accordance with OECD Test Guidelines or OECD GLP, and the purity of the steviol glycoside test article was not reported, thus limiting their utility in the risk assessment of Tate & Lyle's enzymatically produced steviol glycosides. However, considering that they evaluate some toxicologically relevant test parameter (e.g., liver damage biomarker or other hematological or clinical chemistry parameter), the results of these studies are included for completeness. Overall, the results of these studies do not contradict the current safety profile of steviol glycosides.

The effects of non-nutritive sweeteners on diabetes-related parameters in non-diabetic rats was assessed by Mbambo *et al.* (2020). Sprague-Dawley rats were divided into groups (sex and group size not reported) and administered a control (normal water), sucrose, aspartame, sucralose, cyclamate, saccharin, or stevia-

based sweeteners (purity of test substances not reported) dissolved in drinking water at sweetness dilutions equivalent to 10% sucrose for 5 weeks. Food and fluid consumption were monitored daily. Body weight changes and 3-hour "tail-tip" fasting blood glucose were measured weekly. Oral glucose tolerance tests (OGTTs) were performed in the final week to measure blood glucose and following the sacrifice of the animals at the end of Week 5, blood was collected to perform serum biochemical analyses. For the purposes of this dossier, only results concerning the steviol glycoside group compared to the control are reported, unless otherwise stated. The body weight of animals in the stevia group was significantly reduced (p<0.05). No significant changes in non-fasting blood glucose were observed following the administration of the non-nutritive sweeteners, including stevia. The results of the OGTT revealed significantly increased serum insulin levels (p<0.05) in the stevia group. All non-nutritive sweeteners, except aspartame, significantly decreased serum triglycerides (p<0.05) when compared to control group. No change in serum total cholesterol was seen in the stevia group, whereas serum high-density lipoprotein cholesterol (HDL-C) significantly increased in the stevia group (p<0.05). The administration of the non-nutritive sweeteners, including stevia, did not significantly affect the remaining blood chemical parameters (*i.e*., serum aspartate transaminase, alanine aminotransferase [ALT], alkaline phosphatase [ALP], urea, uric acid, creatinine, lactate dehydrogenase, and albumin). The study did not find any adverse effects that could be attributed to the test material and concluded some beneficial effects to the diabetes related parameters.

Kurek *et al*. (2021) investigated the effect of steviol glycoside (purity not reported) supplementation in diabetic rats. Male Wistar rats (8 to 10/group) were fed a high-fat diet for 8 weeks followed by intraperitoneal administration of streptozotocin to induce diabetes, while a control group (n=10) was fed a standard diet for the duration of the whole study and given citrate buffer injections. Next, the experimental rats were provided a high-fat diet supplemented with pure stevioside or rebaudioside A at 500 or 2,500 mg/kg body weight/day for 5 weeks. Blood and organ samples were collected at the end of the study period for hematological, biochemical, and histopathological examinations. The authors reported that dietary supplementation with steviol glycosides did not affect blood glucose, insulin, insulin resistance indices, or antioxidant biomarkers in diabetic rats.

As toxicologically relevant test parameters were not significantly affected by the administration of stevia in either of these studies, they can be considered to add to the existing body of literature corroborating the safety of steviol glycosides.

6.5.2 Genotoxicity

Two new studies were identified in the updated search of the scientific literature pertaining to the genotoxicity of steviol glycosides. It is noted that these studies were not conducted in accordance with OECD Test Guidelines or OECD GLP, and the purity of the steviol glycoside test article was not reported, thus limiting their utility in the risk assessment of Tate & Lyle's enzymatically produced steviol glycosides. In addition, given that the purity of the test articles is not reported, it is difficult to ascertain the relevance of the test concentration/dose to human relevance. Nevertheless, these studies are included for completeness on the discussion of steviol glycosides. The results of these 2 new studies do not contradict the current lack of mutagenicity and genotoxicity of steviol glycosides that have been established by multiple scientific and authoritative bodies (see Section 6.4 for further details).

Venous blood-derived lymphocyte cultures were obtained from a healthy donor for use in a comet assay and chromosomal aberration test (Pasqualli *et al.,* 2020). Cells were treated with steviol (purity not reported), which is the backbone of steviol glycosides and the resulting metabolite from gut microbial digestion, at concentrations up to and including 1 mg/mL as part of a dose-range finding study to determine the median lethal concentration (LC_{50}) of 178.7 µg/mL. With the LC_{50} determined, lymphocytes were treated

with 1, 10, and 50 µg steviol/mL in an alkaline comet assay, a chromosomal aberration test, and mitotic index for 24 or 48 hours. In addition, the major lymphocyte subpopulations were identified as $CD3^+$, $CD4^+$, and $CD8^+$. Cell viability was maintained at doses of 50 µg/mL; however, cell proliferation was reduced. The $CD4^+$ population was statistically smaller than control when lymphocytes were treated with 10 and 50 µg/mL steviol, and a statistically significant decrease of the double lymphocyte population (young, immature cells that have not yet finished their cell maturation process) following exposure to all steviol concentrations was observed as compared to control. The $CD3^+$ population was unchanged when lymphocytes were treated with all concentrations of steviol. The alkaline comet observations revealed a significant increase (62%) in the DNA damage index in the 10 µg and 50 µg/mL treatment groups as compared to control (0%), with no dose-dependent increases between the 10 and 50 µg/mL treatment groups. In the chromosomal aberration test, 300 metaphase cells were identified, and aberrations were most abundant in the 10 and 50 µg/mL treatment groups. While steviol treated cells' mitotic index values remained unchanged, treatment conditions used in this study were estimated to be 129 times greater than normal steviol exposure levels in the human diet. The study was not conducted according to OECD TG 489 for *in vivo* mammalian alkaline comet assays. Considering the study is "non-standard" and the observed effects were not dose-dependent, the results hold limited validity and relevance for human consumption.

The impact of steviol glycosides on oxidative and genotoxic measures in BALB/c mice was investigated in a study by Yılmaz *et al.* (2022). Steviol glycosides (rebaudioside A, 98.65% purity) were administered to mice (n=4/sex/group) over 28 days at 0, 470, 620, 940, or 1,880 mg/kg body weight/day in distilled water *via* gavage; equivalent to 0, 155, 205, 310, or 620 mg steviol/kg body weight/day, respectively. Animals were monitored daily for clinical observations, while food consumption and body weights were measured weekly. Blood and bone marrow samples were obtained at study conclusion for hematological biochemistry and mitotic index with chromosome aberration analyses, respectively. Colchicine (5 mg/kg body weight) was administered intraperitoneally 2 hours prior to animal sacrifice to arrest mitosis. All but the lowest dose group, 470 mg/kg, exhibited a statistically significant (p<0.05) increase in chromosomal aberrations, most commonly sister union and polyploidy. The authors tabulated results indicating an increase in mitotic index in all treatment groups, despite description of insignificant differences in mitotic index between control and treatment groups in the text of the article, rendering the authors' overall interpretation of the data unclear. The increases in chromosomal aberrations were not dose dependent. Both high- and low-density cholesterol were unchanged in all treatment groups as compared to control. Observations of tabulated data were used to determine no change in antioxidant status, oxidant status, or oxidative stress index in all study groups; 1 statistically significant decrease was reported in the 620 mg/kg group for paraoxonase-1 enzyme (p<0.01). The relevance of these data is limited since no official test guideline was followed and the significant results reported were not dose dependent.

6.5.3 Reproductive and Developmental Toxicity

Two new studies were identified in the updated search of the scientific literature pertaining to the reproductive and developmental toxicity of steviol glycosides. It is noted that these studies were not conducted in accordance with OECD Test Guidelines or OECD GLP, and the purity of the steviol glycoside test article was not reported, thus limiting their utility in the risk assessment of Tate & Lyle's enzymatically produced steviol glycosides. In addition, the study by Gholizadeh *et al.* (2019) was conducted in diabetes induced male Wistar rats and no relevant healthy control group was included, therefore rendering it difficult to interpret the results and whether the observed findings were due to the test article administration or the disease state of the animal. Nevertheless, these studies are included for completeness on the discussion of steviol glycosides. The results of these 2 new studies do not contradict the current lack reproductive and

developmental toxicity of steviol glycosides that have been established by multiple scientific and authoritative bodies (see Section 6.4 for further details).

A study using a diabetic rat model, induced by single intraperitoneal injections of streptozotocin (60 mg/kg) and nicotinamide (120 mg/kg), was conducted to evaluate the serum hormone levels, key steroidogenesis enzymes, and testicular damage in male Wistar rats following consumption of aqueous stevia extract (purity not reported) (Gholizadeh *et al*., 2019). Animals (n=12) were treated with 1 mL water (diabetic control), 400 mg/kg body weight/day aqueous stevia extract, or 500 mg/kg body weight/day metformin treatment, administered orally for 2 weeks; non-diabetic control animals (n=12) that received 1 mL water in lieu of stevia were also included. Upon study termination, body weights were measured, and testicles were collected along with blood samples, which were then analyzed for a number of hematological and histochemical metrics. A significant decrease in fasting glucose (p<0.05) levels of stevia-treated animals compared to diabetic controls was observed. Serum luteinizing hormone and testosterone were significantly decreased in the diabetic rats as compared to diabetic control (p=0.026 and p<0.001, respectively). Treatment with stevia returned serum luteinizing hormone levels to that of non-diabetic controls, but also significantly decreased serum testosterone (p=0.004). Testis weight and volume were decreased in diabetic rats as compared to non-diabetic control (p=0.016 and p=0.014, respectively); attenuation in both groups was achieved by stevia administration. Seminiferous tubules and germinal epithelium volume, in addition to the number of spermatogonia, spermatocytes, round spermatids, long spermatids, Sertoli cells, and Leydig cells, were statistically decreased in diabetic rats (p≤0.016 in all cases); these were attenuated by administration of stevia. Round spermatids and Sertoli cells were significantly decreased compared to the non-diabetic control (p=0.012 and p=0.001, respectively); results were exacerbated in diabetic animals. Similarly, stevia treatment ameliorated the increase in non-progressive sperms (p<0.05) in the diabetic compared to the non-diabetic control, whereas the increase in immotile sperms (p<0.05) and decrease in rapid progressive sperms (p<0.05) in the diabetic controls were only partially rescued by stevia treatment at study levels (p>0.05). A significant reduction in sperm count and significant increases in sperms with abnormal morphology and percentage of non-viable sperms were observed in diabetic animals (p<0.05) as compared to control. Thus, the authors concluded that oral stevia administration in a diabetic rat model had "*positive effects on testicular steroidogenesis, spermatogenesis, and function*." The authors did not provide any conclusions related to toxicological effects of stevia extract in the animals.

The effects of non-nutritive sweeteners on taste receptor type 1 subunit (T1R3) and taste receptor type 1 subunit 2 (T1R2) expression in uterine and ovarian tissues of guinea pigs was investigated by Li *et al.* (2020); 30 female, Harley-white guinea pigs (n=6/group; 5 groups) were administered water (control), 1.5 mM (low-dose) or 7.5 mM (high-dose) sodium saccharin solution, or 0.5 mM (low-dose; approximately 40 mg steviol/kg body weight/day) or 2.5 mM (high-dose; approximately 174 mg steviol/kg body weight/day) rebaudioside A solution *ad libitum* for 28 days. Daily food consumption measurements and weekly body weight measurements were taken throughout the study; puberty onset was recorded as the day of vaginal opening, and daily vaginal smears were used to track the estrous cycle. The following description of post-mortem analyses of treated animals refers to the rebaudioside A-treated animals as compared to control unless otherwise stated. Food consumption was significantly elevated in Week 1 of the study (p<0.05) but returned to control levels by Week 2. A significant decrease in water intake was observed in the high-dose rebaudioside A group from Weeks 2 to 4 (p<0.05). At Week 2, the average body weight of both rebaudioside A groups was significantly increased (p<0.05) but was no different from control at any other time point. Water intake was decreased in high-dose rebaudioside A animals throughout Weeks 1 and 2, accompanied by rebaudioside A-related weight gain, as compared to control during Week 2 through Week 4 (p<0.05). Observed ovary weight, estradiol levels, and day of puberty onset were not significantly affected by rebaudioside A administration throughout this study. Low-dose rebaudioside A animals

exhibited increased serum progesterone and uterine T1R2 expression, as compared to control (p<0.05); however, no significant corresponding changes were observed in the expression of T1R3 in the ovary and uterus. Ovary follicle distribution in rebaudioside A-treated animals was regular and atretic follicles were qualitatively increased; however, the number of antral follicles was not statistically increased as compared to control. The number of corpus luteum in the ovaries of animals receiving high-dose rebaudioside A were significantly increased (p<0.05). No histological or morphological changes in uterine tissue were observed. Staining of T1R2 and T1R3 in ovarian follicles revealed no significant changes, although corpus luteum T1R3 staining was increased in the lutein cells in animals treated with all doses of rebaudioside A. Uterine expression of T1R2 in high-dose animals was significantly increased, particularly in the epithelial and stromal cells. The authors reported increases in the uterine expression of T1R2 and an increased number of corpus luteum in the ovaries of animals treated with the high-dose rebaudioside A (approximately 174 mg steviol/kg body weight/day). This study was not conducted according to test guidelines established for assessing reproductive and/or developmental toxicity (*e.g.*, OECD TG 421). The increases in body weight in the rebaudioside A groups during week 2 were not dose-dependent or associated with any histopathological changes. Based on these factors, the increase in body weights cannot reliably be attributed to the consumption of rebaudioside A from drinking water.

6.5.4 Immunotoxicity

Sánchez-Delgado *et al.* (2021) conducted a clinical study evaluating the effects of non-calorie sweeteners, including steviol glycosides, on nutrient and calorie intake, adipose mass, triglycerides, and serum proinflammatory cytokines as an immunotoxicity endpoint. The study was conducted over a 7-week period separated into 2 phases involving healthy individuals. In Phase I, a food frequency questionnaire was completed, and anthropometric and body composition measurements (weight, BMI, total fat percentage, muscle mass, and waist circumference) were made at study initiation. A 1-week washout period was implemented to restrict food and drinks with added sugar and non-caloric sweeteners prior to administration initiation. In Phase II, blood samples were drawn from fasted participants to measure biochemical and immunological parameters (blood glucose, triglycerides, cholesterol, interleukin [IL]-1β, IL-6, IL-10, tumor necrosis factor [TNF]-α, and interferon [IFN]-γ] before and after the 6-week administration period. Subjects were randomly assigned 1 of 3 administration groups: Group 1 (n=12, eight 5-g packs of sucrose/day); Group 2 (n=13, four 1-g packs of sucralose/day, each pack containing 0.012 g of sucralose); and Group 3 (n=13, four 1-g packs of steviol glycoside/day, each packet containing 0.025 g of steviol glycosides). The composition of steviol glycosides was not specified. The assigned sweetener was added to drinks or food every day, and subjects were asked to restrict the use of added sugar or sweeteners in the rest of their diet during the administration phase. Intakes were monitored using 24-hour diet recalls and anthropometric and body composition parameters were measured weekly. Mean energy intake in the steviol glycoside group was reduced compared to baseline. Nutrient distribution showed a significant decrease in carbohydrate intake (p=0.002) and an increase in protein intake (p=0.0001) in the steviol glycoside group. No changes were observed in lipid intake, body weight, BMI, or muscle mass in the steviol glycoside group; however, body fat was significantly decreased (p=0.0287). Immunological parameters in the steviol glycoside group from baseline to Week 7 of the study showed a significant decrease in TNF-α concentrations (p= 0.0029) and no significant change in IL-6 concentrations. Concentrations of IFN-γ and IL-10 were below the limit of detection. The authors concluded that, "*The data reported in the present study corroborates previously reported anti- inflammatory effects of steviol glycosides and support the notion that these compounds may have beneficial effects for human health* […]". The consumption of steviol glycosides did not lead to adverse effects or adversely affect the outcomes of immunotoxicity parameters.

6.6 Conclusions

Tate & Lyle intends to market enzymatically produced steviol glycosides as general purpose sweeteners in the U.S. The enzymatically produced steviol glycosides are manufactured through a process consistent with the manufacturing steps described by JECFA for enzyme modified steviol glycosides. Tate & Lyle's enzymatically produced steviol glycosides are high purity products that contain, at a minimum, at least 95% total steviol glycosides. The specifications that have been established for these products meet or exceed the purity and specification requirements for enzyme modified steviol glycosides as described by JECFA (2021). Tate & Lyle's enzymatically produced steviol glycosides have a sweetness profile that is similar to high purity steviol glycosides in general, and is intended for use as a substitutional source of these compounds on the U.S. marketplace. Therefore, the introduction of Tate & Lyle's steviol glycosides will not increase current dietary exposure to steviol glycosides.

Tate & Lyle has concluded that the company's enzymatically produced steviol glycosides are GRAS for use as general purpose sweeteners, as described in Section 1.3, on the basis of scientific procedures. This GRAS conclusion is based on data generally available in the public domain pertaining to the safety of enzymatically produced steviol glycosides and high purity steviol glycosides in general as discussed herein, and on consensus among a panel of experts (the GRAS Panel) who are qualified by scientific training and experience to evaluate the safety of food ingredients. The GRAS Panel consisted of the following qualified

scientific experts: Ashley Roberts (AR Toxicology, Inc.), Professor Emeritus I. Glenn Sipes (University of Arizona), and Professor Emeritus Michael W. Pariza (University of Wisconsin-Madison).

The GRAS Panel independently and critically evaluated all data and information as presented herein, and also concluded that the enzymatically produced steviol glycosides are GRAS for use as general purpose sweeteners as described in Section 1.3, based on scientific procedures. The GRAS Panel's evaluation considered all available scientific data and information, both favorable and unfavorable, relevant to the safety of Tate & Lyle's enzymatically produced steviol glycosides.

The enzymatically produced steviol glycosides therefore may be marketed and sold for its intended purpose in the U.S. without the promulgation of a food additive regulation under Title 21, Section 170.3 of the *Code of Federal Regulations*.

Part 7. §170.255 List of Supporting Data and Information

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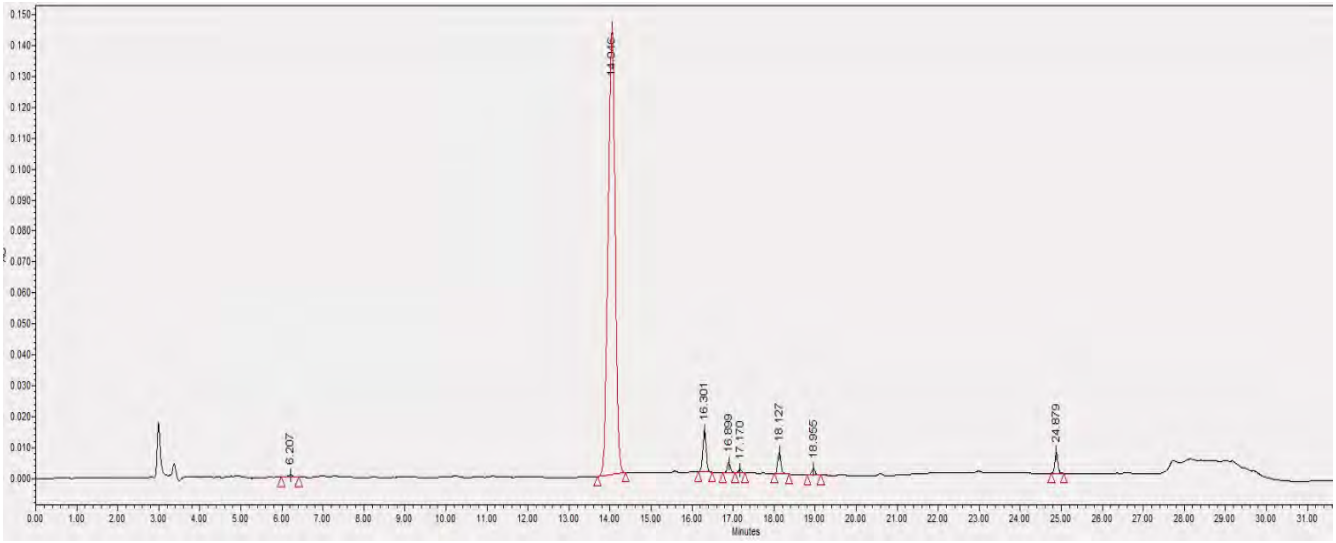
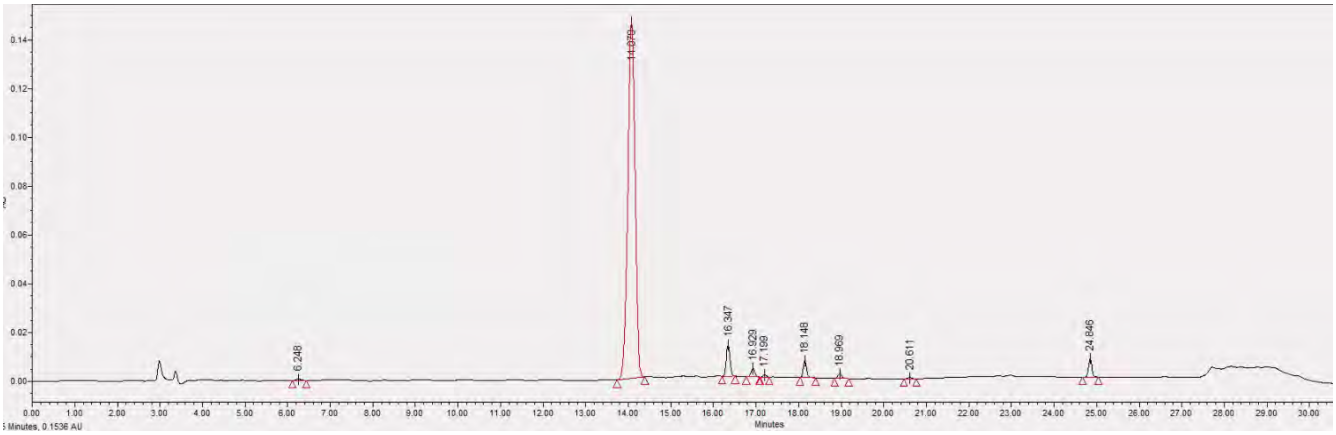
Figure A-1 Chromatogram for Enzymatically Produced Steviol Glycosides (Batch No. A)



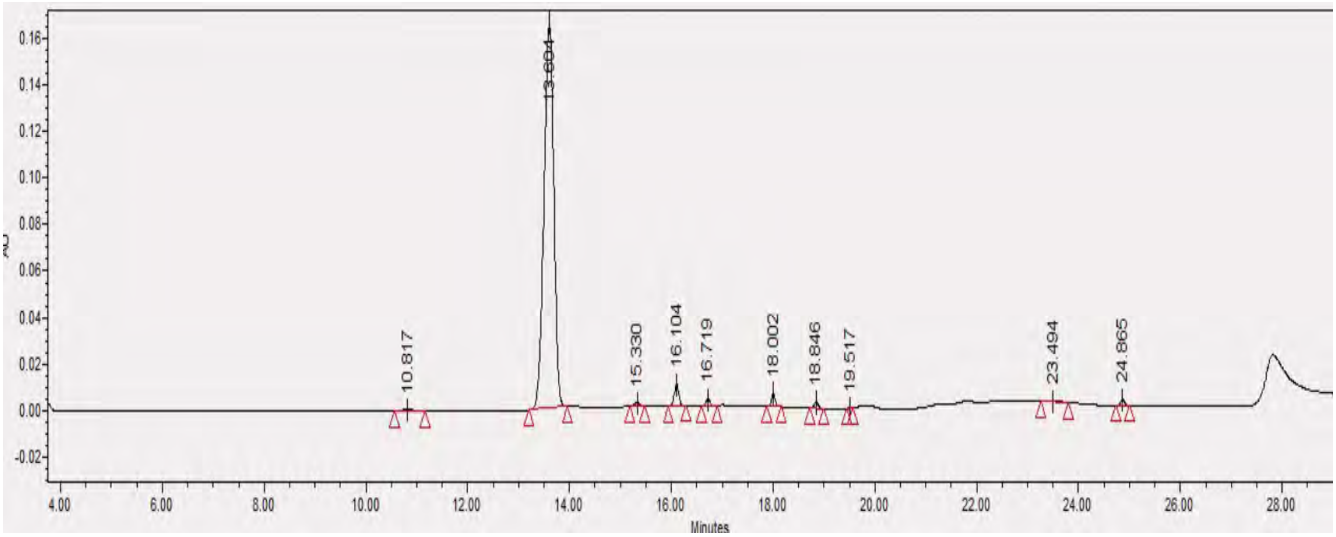
Chromatogram of Enzymatically Produced Steviol Glycosides (Batch No. A), obtained with Agilent poroshell 120 SB-C18, 4.6 mm x 150 mm high-performance liquid chromatography (HPLC) column. Order of retention times from left to right: rebaudioside M (14.05), minor steviol glycosides (16.30 to 18.13), rebaudioside I (18.96), and rebaudioside B (24.88).

Figure A-2 Chromatogram for Enzymatically Produced Steviol Glycosides (Batch No. B)



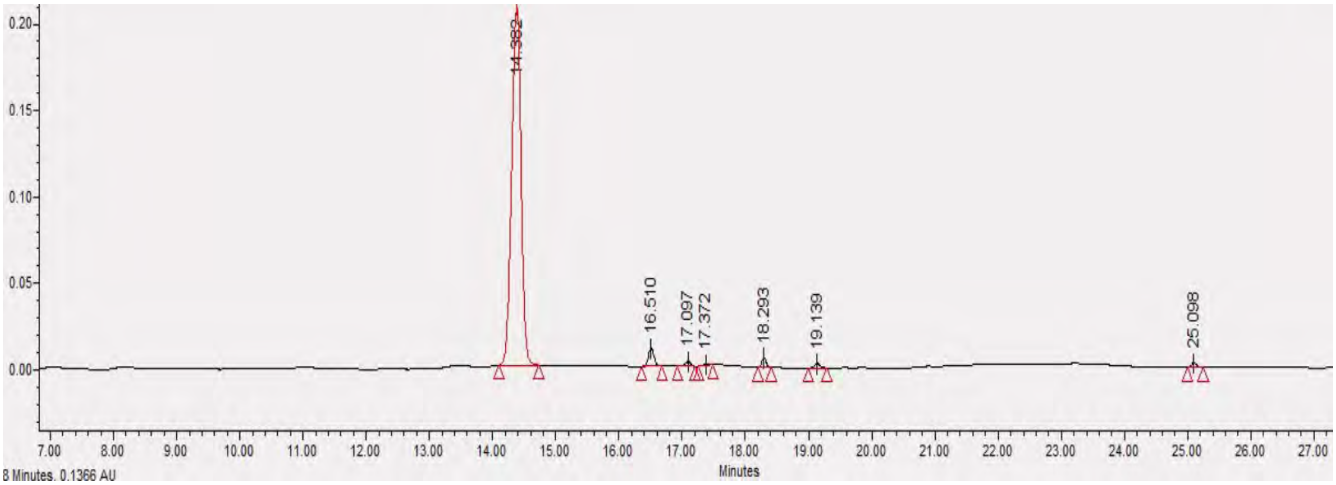
Chromatogram of Enzymatically Produced Steviol Glycosides (Batch No. B), obtained with Agilent poroshell 120 SB-C18, 4.6 mm x 150 mm high-performance liquid chromatography (HPLC) column. Order of retention times from left to right: rebaudioside M (14.08), minor steviol glycosides (16.35 to 18.15), rebaudioside I (18.97), and rebaudioside B (24.85).

Figure A-3 Chromatogram for Enzymatically Produced Steviol Glycosides (Batch No. C)



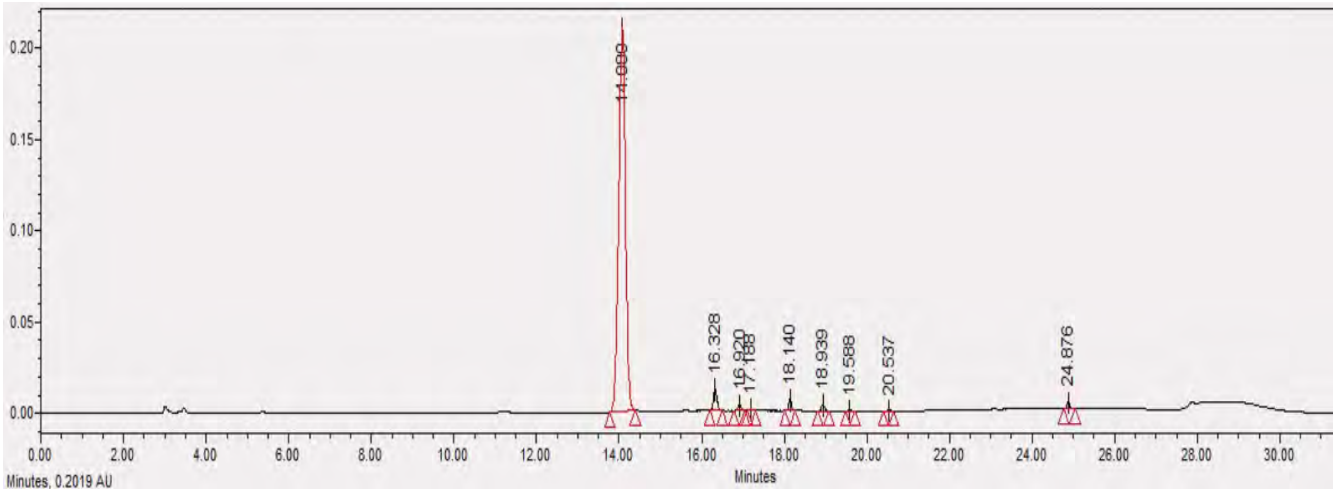
Chromatogram of Enzymatically Produced Steviol Glycosides (Batch No. C), obtained with Agilent poroshell 120 SB-C18, 4.6 mm x 150 mm high-performance liquid chromatography (HPLC) column. Order of retention times from left to right: rebaudioside D (10.82), rebaudioside M (13.60), minor steviol glycosides (15.33 to 18.00), rebaudioside I (18.85), rebaudioside A (19.52) and rebaudioside B (24.87).

Figure A-4 Chromatogram for Enzymatically Produced Steviol Glycosides (Batch No. D)



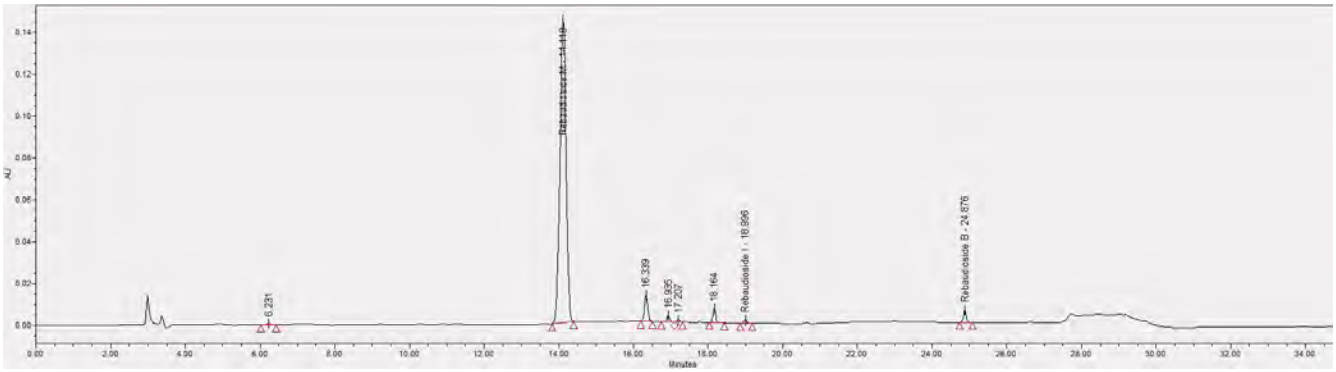
Chromatogram of Enzymatically Produced Steviol Glycosides (Batch No. D), obtained with Agilent poroshell 120 SB-C18, 4.6 mm x 150 mm high-performance liquid chromatography (HPLC) column. Order of retention times from left to right: rebaudioside M (14.38), minor steviol glycosides (16.51 to 18.29), rebaudioside I (19.14) and rebaudioside B (25.10).

Figure A-5 Chromatogram for Enzymatically Produced Steviol Glycosides (Batch No. E)



Chromatogram of Enzymatically Produced Steviol Glycosides (Batch No. E), obtained with Agilent poroshell 120 SB-C18, 4.6 mm x 150 mm high-performance liquid chromatography (HPLC) column. Order of retention times from left to right: rebaudioside M (14.08), minor steviol glycosides (16.33 to 18.14), rebaudioside I (18.94), rebaudioside A (19.59), minor steviol glycosides (20.54) and rebaudioside B (24.88).

Figure A-6 Chromatogram for Enzymatically Produced Steviol Glycosides (Batch No. F)



Chromatogram of Enzymatically Produced Steviol Glycosides (Batch No. F), obtained with Agilent poroshell 120 SB-C18, 4.6 mm x 150 mm high-performance liquid chromatography (HPLC) column. Order of retention times from left to right: rebaudioside M (14.12), minor steviol glycosides (16.34 to 18.16), rebaudioside I (19.00) and rebaudioside B (24.88).

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Analytical Report

Tate & Lyle
Attn: Chetna Saini
5450 Prairie Stone Pkwy
60192 Hoffman Estates
United States

Reportnr.	: **1722192 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:07	Sampling Date *	: 06-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,244
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Sample information *

Seller Unloader	: Tate & Lyle	Product specification	: Stevia
Shipping Date	: 23-Jan-2023	Reference	: Quotation 8586
		Origin	: United States
		AWB / BarCode	: 771108252969

*** Information supplied by customer (TLR takes no responsibility for this information).**

Contaminations

Pesticides

Parameter	Result (as received)			
Pesticides GC-MS-MS	Performed according annex, nothing detected		Q	R
Pesticides LC-MS-MS	Performed according annex, residues detected as per below		Q	R
Benoxacor	< 0,01	mg/kg		O

Pesticides (Glyphosate)

Parameter	Result (as received)			
Glyphosate	< 0,010	mg/kg	Q	R

Pesticides LCMSMS (pos. ionisation)

Parameter	Result (as received)		
Azoxystrobin.	0,012	mg/kg	
Acetamiprid	0,017	mg/kg	Q
Propamocarb.	0,020	mg/kg	

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

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Analytical Report

Reportnr.	: **1722192 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:07	Sampling Date	*: 06-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,244
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Analysed Contamination / Pesticides below detection limits

Pesticides GCMSMS

Biphenyl	< 0,010 mg/kg	Q	Tecnazene	< 0,010 mg/kg	Q	Tefluthrin	< 0,010 mg/kg	Q	Terbufos	< 0,010 mg/kg	Q
Tetradifon	< 0,010 mg/kg	Q	Tetramethrin	< 0,010 mg/kg	Q	Thiometon	< 0,010 mg/kg	Q	Tolclofos-methyl	< 0,010 mg/kg	Q
Toxaphen (sum)	< 0,010 mg/kg		Toxaphen P26.	< 0,010 mg/kg		Toxaphen P50.	< 0,010 mg/kg		Bitertanol.	< 0,010 mg/kg	
Toxaphen P62.	< 0,010 mg/kg		Triallate	< 0,010 mg/kg	Q	Trifluralin	< 0,010 mg/kg	Q	Vinchlozolin	< 0,010 mg/kg	Q
Bromophos-ethyl	< 0,010 mg/kg	Q	Bromophos-methyl	< 0,010 mg/kg	Q	Brompropylate	< 0,010 mg/kg		Buprofezin	< 0,010 mg/kg	Q
Captafol..	< 0,010 mg/kg		Captan (sum)	< 0,010 mg/kg		Carbophenothion.	< 0,010 mg/kg		Chlorbufam	< 0,010 mg/kg	Q
4-chloro-3-methylphenol	< 0,010 mg/kg	Q	Chlordane-cis	< 0,010 mg/kg	Q	Chlordane-trans	< 0,010 mg/kg	Q	Chlorfenvinphos	< 0,010 mg/kg	Q
Chlormephos	< 0,010 mg/kg	Q	Chlorobenzilate	< 0,010 mg/kg	Q	Chloroneb	< 0,010 mg/kg	Q	Chlorothalonil.	< 0,010 mg/kg	
Chlorpropham	< 0,010 mg/kg	Q	Chlorpyrifos.	< 0,010 mg/kg		Chlorpyrifos-methyl.	< 0,010 mg/kg		Acrinathrin	< 0,010 mg/kg	Q
Chlorthiophos.	< 0,010 mg/kg		Cyfluthrin I	< 0,010 mg/kg	Q	Cyfluthrin II	< 0,010 mg/kg	Q	Cyfluthrin III	< 0,010 mg/kg	Q
Cyhalothrin (Lambda)	< 0,010 mg/kg	Q	Cypermethrin (sum)	< 0,010 mg/kg	Q	Deltamethrin	< 0,010 mg/kg	Q	Diallate	< 0,010 mg/kg	Q
Diazinon.	< 0,010 mg/kg		Dichlobenil	< 0,010 mg/kg	Q	Aldrin and Dieldrin (sum)	< 0,010 mg/kg		Dichlormid	< 0,010 mg/kg	Q
Dichlorvos.	< 0,010 mg/kg		Dicofol.	< 0,010 mg/kg		Dieldrin	< 0,010 mg/kg	Q	Diphenylamine	< 0,010 mg/kg	Q
Disulfoton.	< 0,010 mg/kg		Endosulfan-a.	< 0,010 mg/kg		Endosulfan-ß	< 0,010 mg/kg	Q	Endosulfansulphate	< 0,010 mg/kg	Q
Endrin	< 0,010 mg/kg	Q	Anthraquinone	< 0,010 mg/kg	Q	EPN	< 0,010 mg/kg	Q	Esfenvalerate	< 0,010 mg/kg	Q
Ethion	< 0,010 mg/kg	Q	Etrimfos	< 0,010 mg/kg	Q	Famoxadone.	< 0,010 mg/kg		Fenitrothion.	< 0,010 mg/kg	
Fenpropathrin.	< 0,010 mg/kg		Flucythrinate.	< 0,010 mg/kg		Flumioxazin	< 0,010 mg/kg	Q	Fluvalinate.	< 0,010 mg/kg	
Atrazine	< 0,010 mg/kg	Q	Folpet	< 0,010 mg/kg	Q	Fonofos.	< 0,010 mg/kg		HCH-a	< 0,010 mg/kg	Q
HCH-d	< 0,010 mg/kg	Q	HCH-ß	< 0,010 mg/kg	Q	HCH-y (lindane)	< 0,010 mg/kg	Q	Heptachlor	< 0,010 mg/kg	Q
Heptachloroepoxide-cis	< 0,010 mg/kg	Q	Heptachloroepoxide-trans	< 0,010 mg/kg	Q	Hexachlorobenzene (HCB)	< 0,010 mg/kg	Q	Azinphos-ethyl	< 0,010 mg/kg	Q
Iprodione.	< 0,010 mg/kg		Isodrin	< 0,010 mg/kg	Q	Methoxychlor.	< 0,010 mg/kg		Naled	< 0,010 mg/kg	Q
Nitrofen.	< 0,010 mg/kg		Nonachlor (cis + trans).	< 0,010 mg/kg		o,p-DDD	< 0,010 mg/kg	Q	o,p-DDE	< 0,010 mg/kg	Q
o,p-DDT	< 0,010 mg/kg	Q	p,p-DDD	< 0,010 mg/kg	Q	Bifenox	< 0,010 mg/kg	Q	p,p-DDE	< 0,010 mg/kg	Q
p,p-DDT.	< 0,010 mg/kg		Parathion-ethyl	< 0,010 mg/kg	Q	Parathion-methyl.	< 0,010 mg/kg		Pentachloorbenzene	< 0,010 mg/kg	Q
Permethrin I	< 0,010 mg/kg	Q	Permethrin II	< 0,010 mg/kg	Q	Phenothrin	< 0,010 mg/kg	Q	Phenthoate	< 0,010 mg/kg	Q
Phenylphenol,2-	< 0,010 mg/kg	Q	Bifenthrin	< 0,010 mg/kg	Q	Phorate	< 0,010 mg/kg	Q	Piperonylbutoxide.	< 0,010 mg/kg	
Pirimiphos-ethyl	< 0,010 mg/kg	Q	Pirimiphos-methyl	< 0,010 mg/kg	Q	Procymidone	< 0,010 mg/kg	Q	Profenophos	< 0,010 mg/kg	Q
Propham	< 0,010 mg/kg	Q	Propyzamide	< 0,010 mg/kg	Q	Quintozene (sum)	< 0,010 mg/kg	Q	Sulfotep	< 0,010 mg/kg	Q

Pesticides LCMSMS

Amitraz incl. metabolites	< 0,010 mg/kg		Fluxapyroxad	< 0,010 mg/kg	Q	Phosmet.	< 0,010 mg/kg				

Pesticides LCMSMS (neg. ionisation)

2,4-D.	< 0,010 mg/kg		Chlorfluazuron	< 0,010 mg/kg	Q	Chloroxuron.	< 0,010 mg/kg		Clethodim.	< 0,010 mg/kg	
Cyclanilide.	< 0,010 mg/kg		Cythioate.	< 0,010 mg/kg		Dicamba	< 0,050 mg/kg		Diflubenzuron.	< 0,010 mg/kg	
Dinoseb.	< 0,010 mg/kg		Dinoterb.	< 0,010 mg/kg		DMSA (N,N-dimethyl-N'-fenyls	< 0,010 mg/kg		DNOC	< 0,010 mg/kg	Q
Fenpiclonil.	< 0,010 mg/kg		Fipronil	< 0,005 mg/kg	Q	Fipronil (sum)	< 0,005 mg/kg	Q	Fipronil sulfon	< 0,005 mg/kg	Q
Fluazinam.	< 0,010 mg/kg		Flubendiamide	< 0,010 mg/kg	Q	Flucycloxuron (E+Z).	< 0,010 mg/kg		Fludioxonil.	< 0,010 mg/kg	
Flufenoxuron	< 0,010 mg/kg	Q	Fluometuron.	< 0,005 mg/kg		Fluroxypyr.	< 0,010 mg/kg		Flutolanil.	< 0,010 mg/kg	
Halofenozide.	< 0,010 mg/kg		Hexaconazole.	< 0,010 mg/kg		Hexaflumuron.	< 0,010 mg/kg		Imazamethabenz-methyl.	< 0,010 mg/kg	
Imazethapyr	< 0,010 mg/kg	Q	Isocarbophos.	< 0,010 mg/kg		Isoxaflutole.	< 0,010 mg/kg		Lufenuron.	< 0,010 mg/kg	
MCPA.	< 0,010 mg/kg		MCPB	< 0,010 mg/kg	Q	Mecoprop	< 0,010 mg/kg	Q	Mepronil.	< 0,010 mg/kg	
Methoprene.	< 0,010 mg/kg		Monuron.	< 0,010 mg/kg		Neburon.	< 0,010 mg/kg		Norflurazon.	< 0,010 mg/kg	
Noviflumuron.	< 0,010 mg/kg		Picolinafen.	< 0,010 mg/kg		Propanil.	< 0,010 mg/kg		Prothioconazole.	< 0,010 mg/kg	
Silthiofam.	< 0,010 mg/kg		Sulfosulfuron	< 0,010 mg/kg	Q	Teflubenzuron.	< 0,010 mg/kg		Terbacil.	< 0,010 mg/kg	

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Analytical Report

Reportnr.	: **1722192 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:07	Sampling Date	*: 06-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,244
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Triasulfuron.	< 0,010 mg/kg	Triflumuron.	< 0,010 mg/kg	Triflusulfuron-methyl.	< 0,010 mg/kg

Pesticides LCMSMS (pos. ionisation)

Acephate	< 0,010 mg/kg Q	Acibenzolar-S-methyl.	< 0,010 mg/kg	Alachlor	< 0,010 mg/kg Q	Aldicarb	< 0,010 mg/kg Q
Aldicarb sulphone	< 0,010 mg/kg Q	Aldicarb-sulfoxide	< 0,010 mg/kg Q	Ametoctradin	< 0,010 mg/kg Q	Ametryn	< 0,010 mg/kg Q
Aminocarb.	< 0,010 mg/kg	Azaconazole.	< 0,010 mg/kg	Azamethiphos.	< 0,010 mg/kg	Azinphos-methyl	< 0,010 mg/kg Q
Aziprotryne	< 0,010 mg/kg Q	Benalaxyl.	< 0,010 mg/kg	Bendiocarb.	< 0,010 mg/kg	Benodanil.	< 0,010 mg/kg
Benthiavalicarb-isopropyl	< 0,010 mg/kg Q	Benzoyl-prop-ethyl.	< 0,010 mg/kg	Bifenazate	< 0,010 mg/kg Q	Bixafen	< 0,010 mg/kg Q
Boscalid	< 0,010 mg/kg Q	Bromacil	< 0,010 mg/kg Q	Bupirimate	< 0,010 mg/kg Q	Butocarboxim sulfoxide	< 0,010 mg/kg Q
Butoxycarboxim.	< 0,010 mg/kg	Butralin	< 0,010 mg/kg Q	Buturon.	< 0,010 mg/kg	Cadusafos.	< 0,010 mg/kg
Carbaryl	< 0,010 mg/kg Q	Carbendazim.	< 0,010 mg/kg	Carbofuran	< 0,002 mg/kg Q	Carboxin	< 0,010 mg/kg Q
Carfentrazone-ethyl	< 0,010 mg/kg Q	Chloridazon.	< 0,010 mg/kg	Chlorotoluron	< 0,010 mg/kg Q	Clothianidin	< 0,010 mg/kg Q
Coumaphos	< 0,010 mg/kg Q	Cyanazine	< 0,010 mg/kg Q	Cyanofenphos	< 0,010 mg/kg Q	Cyprodinil	< 0,010 mg/kg Q
Daminozide	< 0,010 mg/kg Q	Demeton O & S.	< 0,010 mg/kg	Demeton-s/Demeton-o	< 0,010 mg/kg Q	Demeton-S-methyl-sulfon	< 0,010 mg/kg Q
Dichlofluanid	< 0,010 mg/kg Q	Dicrotophos	< 0,010 mg/kg Q	Difenoconazole	< 0,010 mg/kg Q	Difenoxuron	< 0,010 mg/kg Q
Dimefuron	< 0,010 mg/kg Q	Dimethachlor	< 0,010 mg/kg Q	Dimethenamid-P	< 0,010 mg/kg Q	Dimethirimol	< 0,010 mg/kg Q
Dimethoate	< 0,010 mg/kg Q	Dimethomorph.	< 0,010 mg/kg	Diniconazole	< 0,010 mg/kg Q	Diphenamid	< 0,010 mg/kg Q
Dipropetryn	< 0,010 mg/kg Q	Disulfoton-sulfone	< 0,010 mg/kg Q	DMST (Dimethylsulftoluidide).	< 0,010 mg/kg	Dodine.	< 0,010 mg/kg
Epoxiconazole	< 0,010 mg/kg Q	Etaconazole	< 0,010 mg/kg Q	Ethiofencarb	< 0,010 mg/kg Q	Ethiofencarb sulfone	< 0,010 mg/kg Q
Ethiprole	< 0,010 mg/kg Q	Ethirimol	< 0,010 mg/kg Q	Ethoprofos	< 0,010 mg/kg Q	Ethoprop	< 0,010 mg/kg Q
Ethoxyquin.	< 0,010 mg/kg	Fenamidone.	< 0,010 mg/kg	Fenamiphos sulphone.	< 0,010 mg/kg	Fenamiphos sulphoxide	< 0,010 mg/kg Q
Fenamiphos.	< 0,010 mg/kg	Fenarimol	< 0,010 mg/kg Q	Fenazaquin	< 0,010 mg/kg Q	Fenbuconazole.	< 0,010 mg/kg
Fenfuram.	< 0,010 mg/kg	Fenhexamid.	< 0,010 mg/kg	Fenobucarb.	< 0,010 mg/kg	Fenoxycarb.	< 0,010 mg/kg
Fenpropimorph.	< 0,010 mg/kg	Fenpyroximat	< 0,010 mg/kg Q	Fensulfothion (sum).	< 0,010 mg/kg	Fenthion	< 0,010 mg/kg Q
Fenthion-sulfoxide.	< 0,010 mg/kg	Fenuron	< 0,010 mg/kg Q	Flamprop-methyl.	< 0,010 mg/kg	Flonicamid (sum incl. metaboli	< 0,010 mg/kg Q
Florasulam.	< 0,010 mg/kg	Fluazifop-P (sum).	< 0,010 mg/kg	Flufenacet.	< 0,010 mg/kg	Fluoxastrobin	< 0,010 mg/kg Q
Flupyradifurone	< 0,010 mg/kg Q	Fluquinconazole.	< 0,010 mg/kg	Flusilazole	< 0,010 mg/kg Q	Flusilazole.	< 0,010 mg/kg
Flutriafol.	< 0,010 mg/kg	Foramsulfuron.	< 0,010 mg/kg	Fosthiazate.	< 0,010 mg/kg	Fuberidazole.	< 0,010 mg/kg
Furalaxyl.	< 0,010 mg/kg	Haloxyfop	< 0,010 mg/kg Q	Heptenophos	< 0,010 mg/kg Q	Hexazinone	< 0,010 mg/kg Q
Hexythiazox	< 0,010 mg/kg Q	Hymexazole.	< 0,010 mg/kg	Imazalil.	< 0,010 mg/kg	Imazapic	< 0,01 mg/kg Q
Imidacloprid.	< 0,010 mg/kg	Indoxacarb	< 0,010 mg/kg Q	Iodosulfuron methyl	< 0,010 mg/kg Q	Iprobenphos.	< 0,010 mg/kg
Iprovalicarb.	< 0,010 mg/kg	Isazofos.	< 0,010 mg/kg	Isofenphos-methyl.	< 0,010 mg/kg	Isoprocarb.	< 0,010 mg/kg
Isoproturon.	< 0,010 mg/kg	Isouron.	< 0,010 mg/kg	Kresoxym-methyl.	< 0,010 mg/kg	Lenacil.	< 0,010 mg/kg
Linuron.	< 0,010 mg/kg	Malaoxon.	< 0,010 mg/kg	Malathion.	< 0,010 mg/kg	Mecarbam	< 0,010 mg/kg Q
Mefenacet.	< 0,010 mg/kg	Mephosfolan.	< 0,010 mg/kg	Mesosulfuron-methyl	< 0,010 mg/kg Q	Metalaxyl.	< 0,010 mg/kg
Metamitron.	< 0,010 mg/kg	Metasystox I	< 0,010 mg/kg	Metazachloor	< 0,010 mg/kg Q	Metconazole.	< 0,010 mg/kg
Methabenzthiazuron.	< 0,010 mg/kg	Methamidophos.	< 0,010 mg/kg	Methidathion.	< 0,010 mg/kg	Methiocarb	< 0,010 mg/kg Q
Methomyl.	< 0,010 mg/kg	Methoprotryne.	< 0,010 mg/kg	Methoxyfenozide.	< 0,010 mg/kg	Metobromuron.	< 0,010 mg/kg
Metolachlor	< 0,010 mg/kg Q	Metolachlor..	< 0,010 mg/kg	Metoxuron	< 0,010 mg/kg Q	Metrafenone	< 0,010 mg/kg Q
Metsulfuron methyl	< 0,010 mg/kg Q	Mevinphos	< 0,010 mg/kg Q	Monalide	< 0,010 mg/kg Q	Monocrotophos.	< 0,010 mg/kg
Monolinuron	< 0,010 mg/kg Q	Myclobutanil.	< 0,010 mg/kg	Napropamide (sum of isomer	< 0,010 mg/kg	Nitenpyram.	< 0,010 mg/kg
Nuarimol	< 0,010 mg/kg Q	Ofurace.	< 0,010 mg/kg	Omethoate.	< 0,010 mg/kg	Orbencarb.	< 0,010 mg/kg
Oxadixyl.	< 0,010 mg/kg	Oxamyl	< 0,010 mg/kg Q	Oxydemeton-methyl.	< 0,010 mg/kg	Paclobutrazol.	< 0,010 mg/kg
Paraoxon-Ethyl.	< 0,010 mg/kg	Paraoxon-methyl.	< 0,010 mg/kg	Penconazole	< 0,010 mg/kg Q	Pencycuron	< 0,010 mg/kg Q
Pendimethalin	< 0,010 mg/kg Q	Phorate sulfone.	< 0,010 mg/kg	Phorate sulfoxide.	< 0,010 mg/kg	Phosalone	< 0,010 mg/kg Q
Phosphamidon	< 0,010 mg/kg Q	Phoxim	< 0,010 mg/kg Q	Picoxystrobin	< 0,010 mg/kg Q	Pirimicarb.	< 0,010 mg/kg
Prochloraz.	< 0,010 mg/kg	Promecarb.	< 0,010 mg/kg	Prometryn	< 0,010 mg/kg Q	Propachlor.	< 0,010 mg/kg
Propargite	< 0,010 mg/kg Q	Propazine	< 0,010 mg/kg Q	Propiconazole	< 0,010 mg/kg Q	Propoxur.	< 0,010 mg/kg
Propoxycarbazone sodium.	< 0,010 mg/kg	Prosulfocarb.	< 0,010 mg/kg	Prosulfuron	< 0,010 mg/kg Q	Pymetrozine	< 0,010 mg/kg Q

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Analytical Report

Reportnr.	: **1722192 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:07	Sampling Date	*: 06-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,244
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Pyracarbolid.	< 0,010 mg/kg		Pyraclostrobin	< 0,010 mg/kg	Q	Pyridaben	< 0,010 mg/kg	Q	Pyridaphenthion.	< 0,010 mg/kg	
Pyridate	< 0,010 mg/kg	Q	Pyrifenox	< 0,010 mg/kg	Q	Pyrimethanil	< 0,010 mg/kg	Q	Pyriproxyfen	< 0,010 mg/kg	Q
Quinalphos	< 0,010 mg/kg	Q	Quinclorac	< 0,010 mg/kg	Q	Quinoxyfen	< 0,010 mg/kg	Q	Simazine.	< 0,010 mg/kg	
Spinetoram (sum)	< 0,010 mg/kg	Q	Spinosad (sum)	< 0,010 mg/kg		Spirotetramat (MRL sum)	< 0,010 mg/kg		Spiroxamine.	< 0,010 mg/kg	
Sulcotrione.	< 0,010 mg/kg		Tebuconazol	< 0,010 mg/kg	Q	Tebufenozide.	< 0,010 mg/kg		Tebuthiuron.	< 0,010 mg/kg	
Terbumeton.	< 0,010 mg/kg		Terbutryn	< 0,010 mg/kg	Q	Tetraconazole.	< 0,010 mg/kg		Thiabendazole	< 0,010 mg/kg	Q
Thiacloprid.	< 0,010 mg/kg		Thiamethoxam	< 0,010 mg/kg	Q	Thifensulfuron methyl	< 0,010 mg/kg	Q	Thiobencarb.	< 0,010 mg/kg	
Thiofanox	< 0,010 mg/kg	Q	Thiofanox-sulfone.	< 0,010 mg/kg		Thiofanox-sulfoxide.	< 0,010 mg/kg		Thiophanate-methyl.	< 0,010 mg/kg	
Tolyfluanid	< 0,010 mg/kg	Q	Triadimefon.	< 0,010 mg/kg		Triadimenol.	< 0,010 mg/kg		Triapenthenol.	< 0,010 mg/kg	
Triazophos	< 0,010 mg/kg	Q	Trichlorfon.	< 0,010 mg/kg		Tricyclazole.	< 0,010 mg/kg		Trietazine.	< 0,010 mg/kg	
Trifloxystrobin	< 0,010 mg/kg	Q	Triflumizole	< 0,010 mg/kg	Q	Triforine	< 0,010 mg/kg	Q	Trinexapac	< 0,010 mg/kg	Q
Triticonazole.	< 0,010 mg/kg		Vamidothion.	< 0,010 mg/kg		XMC (3,5-Xylyl MethylCarbam	< 0,010 mg/kg		Zoxamide.	< 0,010 mg/kg	

Q - Analyses ISO 17025 accredited by RvA (ILAC)
R - Carried out by TLR International Laboratories, location Ridderkerk
O - Outsourced

Samplingd

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

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Analytical Report

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Sample Arrival Date	: 26-Jan-2023 11:07	Sampling Date	*: 06-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,244
Packing	: Plastic, ambient	Seal / Seal Code	: No /

ANNEX

Method Descriptions

Contaminations

Pesticides

Method Description	**Method Code**
Flexscope:Determination of the pesticide content ; GC-MS-MS method	Own method
Flexscope:Determination of the pesticide content; LC-MS-MS method	Own method

Pesticides (Glyphosate)

Method Description	**Method Code**
Determination of Glyphosate in plant material with LCMSMS (FMOC-method)	Own method

Pesticides LCMSMS (neg. ionisation)

Method Description	**Method Code**
Determination of Phenoxy alkane carboxylic acids components are performed with the optimized multimethod	.

Abbreviations:

acc: in accordance with
eq: Equivalent to

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

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Analytical Report

Tate & Lyle
Attn: Chetna Saini
5450 Prairie Stone Pkwy
60192 Hoffman Estates
United States

Reportnr.	: **1722193 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:10	Sampling Date	*: 19-May-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,244
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Sample information *

Seller Unloader	: Tate & Lyle	Product specification	: Stevia
Shipping Date	: 23-Jan-2023	Reference	: Quotation 8586
		Origin	: United States
		AWB / BarCode	: 771108252969

*** Information supplied by customer (TLR takes no responsibility for this information).**

Contai

Pesticides

Parameter	Result (as received)			
Pesticides GC-MS-MS	Performed according annex, residues detected as per below		Q	R
Pesticides LC-MS-MS	Performed according annex, residues detected as per below		Q	R
Benoxacor	< 0,01	mg/kg		O

Pesticides (Glyphosate)

Parameter	Result (as received)			
Glyphosate	< 0,010	mg/kg	Q	R

Pesticides GCMSMS

Parameter	Result (as received)		
Anthraquinone	0,020	mg/kg	Q

Pesticides LCMSMS (pos. ionisation)

Parameter	Result (as received)		
Azoxystrobin.	0,013	mg/kg	
Acetamiprid	0,025	mg/kg	Q
Difenoconazole	0,028	mg/kg	Q
Dimethomorph.	0,034	mg/kg	
Tebufenozide.	0,013	mg/kg	

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

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Analytical Report

Tate & Lyle
Attn: Chetna Saini
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60192 Hoffman Estates
United States

Reportnr.	: **1722195 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:08	Sampling Date *	: 21-May-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,24
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Sample information *

Seller Unloader	: Tate & Lyle	Product specification	: Stevia
Shipping Date	: 23-Jan-2023	Reference	: Quotation 8586
		Origin	: United States
		AWB / BarCode	: 771108252969

*** Information supplied by customer (TLR takes no responsibility for this information).**

Contaminations

Pesticides

Parameter	Result (as received)			
Pesticides GC-MS-MS	Performed according annex, nothing detected		Q	R
Pesticides LC-MS-MS	Performed according annex, nothing detected		Q	R
Benoxacor	< 0,01	mg/kg		O

Pesticides (Glyphosate)

Parameter	Result (as received)			
Glyphosate	< 0,010	mg/kg	Q	R

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

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Analytical Report

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Sample Arrival Date	: 26-Jan-2023 11:08	Sampling Date	*: 21-May-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,24
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Analysed Contamination / Pesticides below detection limits

Pesticides GCMSMS

Biphenyl	< 0,010 mg/kg	Q	Tecnazene	< 0,010 mg/kg	Q	Tefluthrin	< 0,010 mg/kg	Q	Terbufos	< 0,010 mg/kg	Q
Tetradifon	< 0,010 mg/kg	Q	Tetramethrin	< 0,010 mg/kg	Q	Thiometon	< 0,010 mg/kg	Q	Tolclofos-methyl	< 0,010 mg/kg	Q
Toxaphen (sum)	< 0,010 mg/kg		Toxaphen P26.	< 0,010 mg/kg		Toxaphen P50.	< 0,010 mg/kg		Bitertanol.	< 0,010 mg/kg	
Toxaphen P62.	< 0,010 mg/kg		Triallate	< 0,010 mg/kg	Q	Trifluralin	< 0,010 mg/kg	Q	Vinchlozolin	< 0,010 mg/kg	Q
Bromophos-ethyl	< 0,010 mg/kg	Q	Bromophos-methyl	< 0,010 mg/kg	Q	Brompropylate	< 0,010 mg/kg		Buprofezin	< 0,010 mg/kg	Q
Captafol..	< 0,010 mg/kg		Captan (sum)	< 0,010 mg/kg		Carbophenothion.	< 0,010 mg/kg		Chlorbufam	< 0,010 mg/kg	Q
4-chloro-3-methylphenol	< 0,010 mg/kg	Q	Chlordane-cis	< 0,010 mg/kg	Q	Chlordane-trans	< 0,010 mg/kg	Q	Chlorfenvinphos	< 0,010 mg/kg	Q
Chlormephos	< 0,010 mg/kg	Q	Chlorobenzilate	< 0,010 mg/kg	Q	Chloroneb	< 0,010 mg/kg	Q	Chlorothalonil.	< 0,010 mg/kg	
Chlorpropham	< 0,010 mg/kg	Q	Chlorpyrifos.	< 0,010 mg/kg		Chlorpyrifos-methyl.	< 0,010 mg/kg		Acrinathrin	< 0,010 mg/kg	Q
Chlorthiophos.	< 0,010 mg/kg		Cyfluthrin I	< 0,010 mg/kg	Q	Cyfluthrin II	< 0,010 mg/kg	Q	Cyfluthrin III	< 0,010 mg/kg	Q
Cyhalothrin (Lambda)	< 0,010 mg/kg	Q	Cypermethrin (sum)	< 0,010 mg/kg	Q	Deltamethrin	< 0,010 mg/kg	Q	Diallate	< 0,010 mg/kg	Q
Diazinon.	< 0,010 mg/kg		Dichlobenil	< 0,010 mg/kg	Q	Aldrin and Dieldrin (sum)	< 0,010 mg/kg		Dichlormid	< 0,010 mg/kg	Q
Dichlorvos.	< 0,010 mg/kg		Dicofol.	< 0,010 mg/kg		Dieldrin	< 0,010 mg/kg	Q	Diphenylamine	< 0,010 mg/kg	Q
Disulfoton.	< 0,010 mg/kg		Endosulfan-a.	< 0,010 mg/kg		Endosulfan-ß	< 0,010 mg/kg	Q	Endosulfansulphate	< 0,010 mg/kg	Q
Endrin	< 0,010 mg/kg	Q	Anthraquinone	< 0,010 mg/kg	Q	EPN	< 0,010 mg/kg	Q	Esfenvalerate	< 0,010 mg/kg	Q
Ethion	< 0,010 mg/kg	Q	Etrimfos	< 0,010 mg/kg	Q	Famoxadone.	< 0,010 mg/kg		Fenitrothion.	< 0,010 mg/kg	
Fenpropathrin.	< 0,010 mg/kg		Flucythrinate.	< 0,010 mg/kg		Flumioxazin	< 0,010 mg/kg	Q	Fluvalinate.	< 0,010 mg/kg	
Atrazine	< 0,010 mg/kg	Q	Folpet	< 0,010 mg/kg	Q	Fonofos.	< 0,010 mg/kg		HCH-a	< 0,010 mg/kg	Q
HCH-d	< 0,010 mg/kg	Q	HCH-ß	< 0,010 mg/kg	Q	HCH-y (lindane)	< 0,010 mg/kg	Q	Heptachlor	< 0,010 mg/kg	Q
Heptachloroepoxide-cis	< 0,010 mg/kg	Q	Heptachloroepoxide-trans	< 0,010 mg/kg	Q	Hexachlorobenzene (HCB)	< 0,010 mg/kg	Q	Azinphos-ethyl	< 0,010 mg/kg	Q
Iprodione.	< 0,010 mg/kg		Isodrin	< 0,010 mg/kg	Q	Methoxychlor.	< 0,010 mg/kg		Naled	< 0,010 mg/kg	Q
Nitrofen.	< 0,010 mg/kg		Nonachlor (cis + trans).	< 0,010 mg/kg		o,p-DDD	< 0,010 mg/kg	Q	o,p-DDE	< 0,010 mg/kg	Q
o,p-DDT	< 0,010 mg/kg	Q	p,p-DDD	< 0,010 mg/kg	Q	Bifenox	< 0,010 mg/kg	Q	p,p-DDE	< 0,010 mg/kg	Q
p,p-DDT.	< 0,010 mg/kg		Parathion-ethyl	< 0,010 mg/kg	Q	Parathion-methyl.	< 0,010 mg/kg		Pentachloorbenzene	< 0,010 mg/kg	Q
Permethrin I	< 0,010 mg/kg	Q	Permethrin II	< 0,010 mg/kg	Q	Phenothrin	< 0,010 mg/kg	Q	Phenthoate	< 0,010 mg/kg	Q
Phenylphenol,2-	< 0,010 mg/kg	Q	Bifenthrin	< 0,010 mg/kg	Q	Phorate	< 0,010 mg/kg	Q	Piperonylbutoxide.	< 0,010 mg/kg	
Pirimiphos-ethyl	< 0,010 mg/kg	Q	Pirimiphos-methyl	< 0,010 mg/kg	Q	Procymidone	< 0,010 mg/kg	Q	Profenophos	< 0,010 mg/kg	Q
Propham	< 0,010 mg/kg	Q	Propyzamide	< 0,010 mg/kg	Q	Quintozene (sum)	< 0,010 mg/kg	Q	Sulfotep	< 0,010 mg/kg	Q

Pesticides LCMSMS

Amitraz incl. metabolites	< 0,010 mg/kg		Fluxapyroxad	< 0,010 mg/kg	Q	Phosmet.	< 0,010 mg/kg				

Pesticides LCMSMS (neg. ionisation)

2,4-D.	< 0,010 mg/kg		Chlorfluazuron	< 0,010 mg/kg	Q	Chloroxuron.	< 0,010 mg/kg		Clethodim.	< 0,010 mg/kg	
Cyclanilide.	< 0,010 mg/kg		Cythioate.	< 0,010 mg/kg		Dicamba	< 0,050 mg/kg		Diflubenzuron.	< 0,010 mg/kg	
Dinoseb.	< 0,010 mg/kg		Dinoterb.	< 0,010 mg/kg		DMSA (N,N-dimethyl-N'-fenyls	< 0,010 mg/kg		DNOC	< 0,010 mg/kg	Q
Fenpiclonil.	< 0,010 mg/kg		Fipronil	< 0,005 mg/kg	Q	Fipronil (sum)	< 0,005 mg/kg	Q	Fipronil sulfon	< 0,005 mg/kg	Q
Fluazinam.	< 0,010 mg/kg		Flubendiamide	< 0,010 mg/kg	Q	Flucycloxuron (E+Z).	< 0,010 mg/kg		Fludioxonil.	< 0,010 mg/kg	
Flufenoxuron	< 0,010 mg/kg	Q	Fluometuron.	< 0,005 mg/kg		Fluroxypyr.	< 0,010 mg/kg		Flutolanil.	< 0,010 mg/kg	
Halofenozide.	< 0,010 mg/kg		Hexaconazole.	< 0,010 mg/kg		Hexaflumuron.	< 0,010 mg/kg		Imazamethabenz-methyl.	< 0,010 mg/kg	
Imazethapyr	< 0,010 mg/kg	Q	Isocarbophos.	< 0,010 mg/kg		Isoxaflutole.	< 0,010 mg/kg		Lufenuron.	< 0,010 mg/kg	
MCPA.	< 0,010 mg/kg		MCPB	< 0,010 mg/kg	Q	Mecoprop	< 0,010 mg/kg	Q	Mepronil.	< 0,010 mg/kg	
Methoprene.	< 0,010 mg/kg		Monuron.	< 0,010 mg/kg		Neburon.	< 0,010 mg/kg		Norflurazon.	< 0,010 mg/kg	
Noviflumuron.	< 0,010 mg/kg		Picolinafen.	< 0,010 mg/kg		Propanil.	< 0,010 mg/kg		Prothioconazole.	< 0,010 mg/kg	
Silthiofam.	< 0,010 mg/kg		Sulfosulfuron	< 0,010 mg/kg	Q	Teflubenzuron.	< 0,010 mg/kg		Terbacil.	< 0,010 mg/kg	

INTERNATIONAL LABORATORIES

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• ROTTERDAM • LIMA •

Analytical Report

Reportnr.	: **1722195 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:08	Sampling Date	*: 21-May-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,24
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Triasulfuron.	< 0,010 mg/kg	Triflumuron.	< 0,010 mg/kg	Triflusulfuron-methyl.	< 0,010 mg/kg

Pesticides LCMSMS (pos. ionisation)

Acephate	< 0,010 mg/kg Q	Acetamiprid	< 0,010 mg/kg Q	Acibenzolar-S-methyl.	< 0,010 mg/kg	Alachlor	< 0,010 mg/kg Q
Aldicarb	< 0,010 mg/kg Q	Aldicarb sulphone	< 0,010 mg/kg Q	Aldicarb-sulfoxide	< 0,010 mg/kg Q	Ametoctradin	< 0,010 mg/kg Q
Ametryn	< 0,010 mg/kg Q	Aminocarb.	< 0,010 mg/kg	Azaconazole.	< 0,010 mg/kg	Azamethiphos.	< 0,010 mg/kg
Azinphos-methyl	< 0,010 mg/kg Q	Aziprotryne	< 0,010 mg/kg Q	Azoxystrobin.	< 0,010 mg/kg	Benalaxyl.	< 0,010 mg/kg
Bendiocarb.	< 0,010 mg/kg	Benodanil.	< 0,010 mg/kg	Benthiavalicarb-isopropyl	< 0,010 mg/kg Q	Benzoyl-prop-ethyl.	< 0,010 mg/kg
Bifenazate	< 0,010 mg/kg Q	Bixafen	< 0,010 mg/kg Q	Boscalid	< 0,010 mg/kg Q	Bromacil	< 0,010 mg/kg Q
Bupirimate	< 0,010 mg/kg Q	Butocarboxim sulfoxide	< 0,010 mg/kg Q	Butoxycarboxim.	< 0,010 mg/kg	Butralin	< 0,010 mg/kg Q
Buturon.	< 0,010 mg/kg	Cadusafos.	< 0,010 mg/kg	Carbaryl	< 0,010 mg/kg Q	Carbendazim.	< 0,010 mg/kg
Carbofuran	< 0,002 mg/kg Q	Carboxin	< 0,010 mg/kg Q	Carfentrazone-ethyl	< 0,010 mg/kg Q	Chloridazon.	< 0,010 mg/kg
Chlorotoluron	< 0,010 mg/kg Q	Clothianidin	< 0,010 mg/kg Q	Coumaphos	< 0,010 mg/kg Q	Cyanazine	< 0,010 mg/kg Q
Cyanofenphos	< 0,010 mg/kg Q	Cyprodinil	< 0,010 mg/kg Q	Daminozide	< 0,010 mg/kg Q	Demeton O & S.	< 0,010 mg/kg
Demeton-s/Demeton-o	< 0,010 mg/kg Q	Demeton-S-methyl-sulfon	< 0,010 mg/kg Q	Dichlofluanid	< 0,010 mg/kg Q	Dicrotophos	< 0,010 mg/kg Q
Difenoconazole	< 0,010 mg/kg Q	Difenoxuron	< 0,010 mg/kg Q	Dimefuron	< 0,010 mg/kg Q	Dimethachlor	< 0,010 mg/kg Q
Dimethenamid-P	< 0,010 mg/kg Q	Dimethirimol	< 0,010 mg/kg Q	Dimethoate	< 0,010 mg/kg Q	Dimethomorph.	< 0,010 mg/kg
Diniconazole	< 0,010 mg/kg Q	Diphenamid	< 0,010 mg/kg Q	Dipropetryn	< 0,010 mg/kg Q	Disulfoton-sulfone	< 0,010 mg/kg Q
DMST (Dimethylsulftoluidide).	< 0,010 mg/kg	Dodine.	< 0,010 mg/kg	Epoxiconazole	< 0,010 mg/kg Q	Etaconazole	< 0,010 mg/kg Q
Ethiofencarb	< 0,010 mg/kg Q	Ethiofencarb sulfone	< 0,010 mg/kg Q	Ethiprole	< 0,010 mg/kg Q	Ethirimol	< 0,010 mg/kg Q
Ethoprofos	< 0,010 mg/kg Q	Ethoprop	< 0,010 mg/kg Q	Ethoxyquin.	< 0,010 mg/kg	Fenamidone.	< 0,010 mg/kg
Fenamiphos sulphone.	< 0,010 mg/kg	Fenamiphos sulphoxide	< 0,010 mg/kg Q	Fenamiphos.	< 0,010 mg/kg	Fenarimol	< 0,010 mg/kg Q
Fenazaquin	< 0,010 mg/kg Q	Fenbuconazole.	< 0,010 mg/kg	Fenfuram.	< 0,010 mg/kg	Fenhexamid.	< 0,010 mg/kg
Fenobucarb.	< 0,010 mg/kg	Fenoxycarb.	< 0,010 mg/kg	Fenpropimorph.	< 0,010 mg/kg	Fenpyroximat	< 0,010 mg/kg Q
Fensulfothion (sum).	< 0,010 mg/kg	Fenthion	< 0,010 mg/kg Q	Fenthion-sulfoxide.	< 0,010 mg/kg	Fenuron	< 0,010 mg/kg Q
Flamprop-methyl.	< 0,010 mg/kg	Flonicamid (sum incl. metaboli	< 0,010 mg/kg Q	Florasulam.	< 0,010 mg/kg	Fluazifop-P (sum).	< 0,010 mg/kg
Flufenacet.	< 0,010 mg/kg	Fluoxastrobin	< 0,010 mg/kg Q	Flupyradifurone	< 0,010 mg/kg Q	Fluquinconazole.	< 0,010 mg/kg
Flusilazole	< 0,010 mg/kg Q	Flusilazole.	< 0,010 mg/kg	Flutriafol.	< 0,010 mg/kg	Foramsulfuron.	< 0,010 mg/kg
Fosthiazate.	< 0,010 mg/kg	Fuberidazole.	< 0,010 mg/kg	Furalaxyl.	< 0,010 mg/kg	Haloxyfop	< 0,010 mg/kg Q
Heptenophos	< 0,010 mg/kg Q	Hexazinone	< 0,010 mg/kg Q	Hexythiazox	< 0,010 mg/kg Q	Hymexazole.	< 0,010 mg/kg
Imazalil.	< 0,010 mg/kg	Imazapic	< 0,01 mg/kg Q	Imidacloprid.	< 0,010 mg/kg	Indoxacarb	< 0,010 mg/kg Q
Iodosulfuron methyl	< 0,010 mg/kg Q	Iprobenphos.	< 0,010 mg/kg	Iprovalicarb.	< 0,010 mg/kg	Isazofos.	< 0,010 mg/kg
Isofenphos-methyl.	< 0,010 mg/kg	Isoprocarb.	< 0,010 mg/kg	Isoproturon.	< 0,010 mg/kg	Isouron.	< 0,010 mg/kg
Kresoxym-methyl.	< 0,010 mg/kg	Lenacil.	< 0,010 mg/kg	Linuron.	< 0,010 mg/kg	Malaoxon.	< 0,010 mg/kg
Malathion.	< 0,010 mg/kg	Mecarbam	< 0,010 mg/kg Q	Mefenacet.	< 0,010 mg/kg	Mephosfolan.	< 0,010 mg/kg
Mesosulfuron-methyl	< 0,010 mg/kg Q	Metalaxyl.	< 0,010 mg/kg	Metamitron.	< 0,010 mg/kg	Metasystox I	< 0,010 mg/kg
Metazachloor	< 0,010 mg/kg Q	Metconazole.	< 0,010 mg/kg	Methabenzthiazuron.	< 0,010 mg/kg	Methamidophos.	< 0,010 mg/kg
Methidathion.	< 0,010 mg/kg	Methiocarb	< 0,010 mg/kg Q	Methomyl.	< 0,010 mg/kg	Methoprotryne.	< 0,010 mg/kg
Methoxyfenozide.	< 0,010 mg/kg	Metobromuron.	< 0,010 mg/kg	Metolachlor	< 0,010 mg/kg Q	Metolachlor..	< 0,010 mg/kg
Metoxuron	< 0,010 mg/kg Q	Metrafenone	< 0,010 mg/kg Q	Metsulfuron methyl	< 0,010 mg/kg Q	Mevinphos	< 0,010 mg/kg Q
Monalide	< 0,010 mg/kg Q	Monocrotophos.	< 0,010 mg/kg	Monolinuron	< 0,010 mg/kg Q	Myclobutanil.	< 0,010 mg/kg
Napropamide (sum of isomer	< 0,010 mg/kg	Nitenpyram.	< 0,010 mg/kg	Nuarimol	< 0,010 mg/kg Q	Ofurace.	< 0,010 mg/kg
Omethoate.	< 0,010 mg/kg	Orbencarb.	< 0,010 mg/kg	Oxadixyl.	< 0,010 mg/kg	Oxamyl	< 0,010 mg/kg Q
Oxydemeton-methyl.	< 0,010 mg/kg	Paclobutrazol.	< 0,010 mg/kg	Paraoxon-Ethyl.	< 0,010 mg/kg	Paraoxon-methyl.	< 0,010 mg/kg
Penconazole	< 0,010 mg/kg Q	Pencycuron	< 0,010 mg/kg Q	Pendimethalin	< 0,010 mg/kg Q	Phorate sulfone.	< 0,010 mg/kg
Phorate sulfoxide.	< 0,010 mg/kg	Phosalone	< 0,010 mg/kg Q	Phosphamidon	< 0,010 mg/kg Q	Phoxim	< 0,010 mg/kg Q
Picoxystrobin	< 0,010 mg/kg Q	Pirimicarb.	< 0,010 mg/kg	Prochloraz.	< 0,010 mg/kg	Promecarb.	< 0,010 mg/kg
Prometryn	< 0,010 mg/kg Q	Propachlor.	< 0,010 mg/kg	Propamocarb.	< 0,010 mg/kg	Propargite	< 0,010 mg/kg Q
Propazine	< 0,010 mg/kg Q	Propiconazole	< 0,010 mg/kg Q	Propoxur.	< 0,010 mg/kg	Propoxycarbazone sodium.	< 0,010 mg/kg

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

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Analytical Report

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ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,24
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Prosulfocarb.	< 0,010 mg/kg		Prosulfuron	< 0,010 mg/kg	Q	Pymetrozine	< 0,010 mg/kg	Q	Pyracarbolid.	< 0,010 mg/kg	
Pyraclostrobin	< 0,010 mg/kg	Q	Pyridaben	< 0,010 mg/kg	Q	Pyridaphenthion.	< 0,010 mg/kg		Pyridate	< 0,010 mg/kg	Q
Pyrifenox	< 0,010 mg/kg	Q	Pyrimethanil	< 0,010 mg/kg	Q	Pyriproxyfen	< 0,010 mg/kg	Q	Quinalphos	< 0,010 mg/kg	Q
Quinclorac	< 0,010 mg/kg	Q	Quinoxyfen	< 0,010 mg/kg	Q	Simazine.	< 0,010 mg/kg		Spinetoram (sum)	< 0,010 mg/kg	Q
Spinosad (sum)	< 0,010 mg/kg		Spirotetramat (MRL sum)	< 0,010 mg/kg		Spiroxamine.	< 0,010 mg/kg		Sulcotrione.	< 0,010 mg/kg	
Tebuconazol	< 0,010 mg/kg	Q	Tebufenozide.	< 0,010 mg/kg		Tebuthiuron.	< 0,010 mg/kg		Terbumeton.	< 0,010 mg/kg	
Terbutryn	< 0,010 mg/kg	Q	Tetraconazole.	< 0,010 mg/kg		Thiabendazole	< 0,010 mg/kg	Q	Thiacloprid.	< 0,010 mg/kg	
Thiamethoxam	< 0,010 mg/kg	Q	Thifensulfuron methyl	< 0,010 mg/kg	Q	Thiobencarb.	< 0,010 mg/kg		Thiofanox	< 0,010 mg/kg	Q
Thiofanox-sulfone.	< 0,010 mg/kg		Thiofanox-sulfoxide.	< 0,010 mg/kg		Thiophanate-methyl.	< 0,010 mg/kg		Tolyfluanid	< 0,010 mg/kg	Q
Triadimefon.	< 0,010 mg/kg		Triadimenol.	< 0,010 mg/kg		Triapenthenol.	< 0,010 mg/kg		Triazophos	< 0,010 mg/kg	Q
Trichlorfon.	< 0,010 mg/kg		Tricyclazole.	< 0,010 mg/kg		Trietazine.	< 0,010 mg/kg		Trifloxystrobin	< 0,010 mg/kg	Q
Triflumizole	< 0,010 mg/kg	Q	Triforine	< 0,010 mg/kg	Q	Trinexapac	< 0,010 mg/kg	Q	Triticonazole.	< 0,010 mg/kg	
Vamidothion.	< 0,010 mg/kg		XMC (3,5-Xylyl MethylCarbam	< 0,010 mg/kg		Zoxamide.	< 0,010 mg/kg				

Q - Analyses ISO 17025 accredited by RvA (ILAC)
R - Carried out by TLR International Laboratories, location Ridderkerk
O - Outsourced

Samplingdate unknown / time difference between sampling- and arrival-date might be too long. Time lapsed before testing may affect results.

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

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Packing	: Plastic, ambient	Seal / Seal Code	: No /

ANNEX

Method Descriptions

Contaminations

Pesticides

Method Description	**Method Code**
Flexscope:Determination of the pesticide content ; GC-MS-MS method	Own method
Flexscope:Determination of the pesticide content; LC-MS-MS method	Own method

Pesticides (Glyphosate)

Method Description	**Method Code**
Determination of Glyphosate in plant material with LCMSMS (FMOC-method)	Own method

Pesticides LCMSMS (neg. ionisation)

Method Description	**Method Code**
Del opt	

Abbre

acc:

eq: Equivalent to

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e-mail: info@tlr.nl

Analytical Report

Tate & Lyle
Attn: Chetna Saini
5450 Prairie Stone Pkwy
60192 Hoffman Estates
United States

Reportnr.	: **1722196 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:00	Sampling Date *	: 07-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,243
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Sample information *

Seller Unloader	: Tate & Lyle	Product specification	: Stevia
Shipping Date	: 23-Jan-2023	Reference	: Quotation 8586
		Origin	: United States

*** Information supplied by customer (TLR takes no responsibility for this information).**

Contaminations

Pesticides

Parameter	Result (as received)		
Pesticides GC-MS-MS	Performed according annex, nothing detected	Q	R
Pesticides LC-MS-MS	Performed according annex, nothing detected	Q	R
Benoxacor	< 0,01 mg/kg		O

Pesticides (Glyphosate)

Parameter	Result (as received)		
Glyphosate	< 0,010 mg/kg	Q	R

Requested 26-Jan-2023 by Tate & Lyle
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Drs. ing. H. Janssens Director TLR International Laboratories

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ROTTERDAM

Analytical Report

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ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,243
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Analysed Contamination / Pesticides below detection limits

Pesticides GCMSMS

Biphenyl	< 0,010 mg/kg Q	Tecnazene	< 0,010 mg/kg Q	Tefluthrin	< 0,010 mg/kg Q	Terbufos	< 0,010 mg/kg Q
Tetradifon	< 0,010 mg/kg Q	Tetramethrin	< 0,010 mg/kg Q	Thiometon	< 0,010 mg/kg Q	Tolclofos-methyl	< 0,010 mg/kg Q
Toxaphen (sum)	< 0,010 mg/kg	Toxaphen P26.	< 0,010 mg/kg	Toxaphen P50.	< 0,010 mg/kg	Bitertanol.	< 0,010 mg/kg
Toxaphen P62.	< 0,010 mg/kg	Triallate	< 0,010 mg/kg Q	Trifluralin	< 0,010 mg/kg Q	Vinchlozolin	< 0,010 mg/kg Q
Bromophos-ethyl	< 0,010 mg/kg Q	Bromophos-methyl	< 0,010 mg/kg Q	Brompropylate	< 0,010 mg/kg	Buprofezin	< 0,010 mg/kg Q
Captafol,.	< 0,010 mg/kg	Captan (sum)	< 0,010 mg/kg	Carbophenothion.	< 0,010 mg/kg	Chlorbufam	< 0,010 mg/kg Q
4-chloro-3-methylphenol	< 0,010 mg/kg Q	Chlordane-cis	< 0,010 mg/kg Q	Chlordane-trans	< 0,010 mg/kg Q	Chlorfenvinphos	< 0,010 mg/kg Q
Chlormephos	< 0,010 mg/kg Q	Chlorobenzilate	< 0,010 mg/kg Q	Chloroneb	< 0,010 mg/kg Q	Chlorothalonil.	< 0,010 mg/kg
Chlorpropham	< 0,010 mg/kg Q	Chlorpyrifos.	< 0,010 mg/kg	Chlorpyrifos-methyl.	< 0,010 mg/kg	Acrinathrin	< 0,010 mg/kg Q
Chlorthiophos.	< 0,010 mg/kg	Cyfluthrin I	< 0,010 mg/kg Q	Cyfluthrin II	< 0,010 mg/kg Q	Cyfluthrin III	< 0,010 mg/kg Q
Cyhalothrin (Lambda)	< 0,010 mg/kg Q	Cypermethrin (sum)	< 0,010 mg/kg Q	Deltamethrin	< 0,010 mg/kg Q	Diallate	< 0,010 mg/kg Q
Diazinon.	< 0,010 mg/kg	Dichlobenil	< 0,010 mg/kg Q	Aldrin and Dieldrin (sum)	< 0,010 mg/kg	Dichlormid	< 0,010 mg/kg Q
Dichlorvos.	< 0,010 mg/kg	Dicofol.	< 0,010 mg/kg	Dieldrin	< 0,010 mg/kg Q	Diphenylamine	< 0,010 mg/kg Q
Disulfoton.	< 0,010 mg/kg	Endosulfan-a.	< 0,010 mg/kg	Endosulfan-ß	< 0,010 mg/kg Q	Endosulfansulphate	< 0,010 mg/kg Q
Endrin	< 0,010 mg/kg Q	Anthraquinone	< 0,010 mg/kg Q	EPN	< 0,010 mg/kg Q	Esfenvalerate	< 0,010 mg/kg Q
Ethion	< 0,010 mg/kg Q	Etrimfos	< 0,010 mg/kg Q	Famoxadone.	< 0,010 mg/kg	Fenitrothion.	< 0,010 mg/kg
Fenpropathrin.	< 0,010 mg/kg	Flucythrinate.	< 0,010 mg/kg	Flumioxazin	< 0,010 mg/kg Q	Fluvalinate.	< 0,010 mg/kg
Atrazine	< 0,010 mg/kg Q	Folpet	< 0,010 mg/kg Q	Fonofos.	< 0,010 mg/kg	HCH-a	< 0,010 mg/kg Q
HCH-d	< 0,010 mg/kg Q	HCH-ß	< 0,010 mg/kg Q	HCH-y (lindane)	< 0,010 mg/kg Q	Heptachlor	< 0,010 mg/kg Q
Heptachloroepoxide-cis	< 0,010 mg/kg Q	Heptachloroepoxide-trans	< 0,010 mg/kg Q	Hexachlorobenzene (HCB)	< 0,010 mg/kg Q	Azinphos-ethyl	< 0,010 mg/kg Q
Iprodione.	< 0,010 mg/kg	Isodrin	< 0,010 mg/kg Q	Methoxychlor.	< 0,010 mg/kg	Naled	< 0,010 mg/kg Q
Nitrofen.	< 0,010 mg/kg	Nonachlor (cis + trans).	< 0,010 mg/kg	o,p-DDD	< 0,010 mg/kg Q	o,p-DDE	< 0,010 mg/kg Q
o,p-DDT	< 0,010 mg/kg Q	p,p-DDD	< 0,010 mg/kg Q	Bifenox	< 0,010 mg/kg Q	p,p-DDE	< 0,010 mg/kg Q
p,p-DDT.	< 0,010 mg/kg	Parathion-ethyl	< 0,010 mg/kg Q	Parathion-methyl.	< 0,010 mg/kg	Pentachloorbenzene	< 0,010 mg/kg Q
Permethrin I	< 0,010 mg/kg Q	Permethrin II	< 0,010 mg/kg Q	Phenothrin	< 0,010 mg/kg Q	Phenthoate	< 0,010 mg/kg Q
Phenylphenol,2-	< 0,010 mg/kg Q	Bifenthrin	< 0,010 mg/kg Q	Phorate	< 0,010 mg/kg Q	Piperonylbutoxide.	< 0,010 mg/kg
Pirimiphos-ethyl	< 0,010 mg/kg Q	Pirimiphos-methyl	< 0,010 mg/kg Q	Procymidone	< 0,010 mg/kg Q	Profenophos	< 0,010 mg/kg Q
Propham	< 0,010 mg/kg Q	Propyzamide	< 0,010 mg/kg Q	Quintozene (sum)	< 0,010 mg/kg Q	Sulfotep	< 0,010 mg/kg Q

Pesticides LCMSMS

Amitraz incl. metabolites	< 0,010 mg/kg	Fluxapyroxad	< 0,010 mg/kg Q	Phosmet.	< 0,010 mg/kg		

Pesticides LCMSMS (neg. ionisation)

2,4-D.	< 0,010 mg/kg	Chlorfluazuron	< 0,010 mg/kg Q	Chloroxuron.	< 0,010 mg/kg	Clethodim.	< 0,010 mg/kg
Cyclanilide.	< 0,010 mg/kg	Cythioate.	< 0,010 mg/kg	Dicamba	< 0,050 mg/kg	Diflubenzuron.	< 0,010 mg/kg
Dinoseb.	< 0,010 mg/kg	Dinoterb.	< 0,010 mg/kg	DMSA (N,N-dimethyl-N'-fenyls	< 0,010 mg/kg	DNOC	< 0,010 mg/kg Q
Fenpiclonil.	< 0,010 mg/kg	Fipronil	< 0,005 mg/kg Q	Fipronil (sum)	< 0,005 mg/kg Q	Fipronil sulfon	< 0,005 mg/kg Q
Fluazinam.	< 0,010 mg/kg	Flubendiamide	< 0,010 mg/kg Q	Flucycloxuron (E+Z).	< 0,010 mg/kg	Fludioxonil.	< 0,010 mg/kg
Flufenoxuron	< 0,010 mg/kg Q	Fluometuron.	< 0,005 mg/kg	Fluroxypyr.	< 0,010 mg/kg	Flutolanil.	< 0,010 mg/kg
Halofenozide.	< 0,010 mg/kg	Hexaconazole.	< 0,010 mg/kg	Hexaflumuron.	< 0,010 mg/kg	Imazamethabenz-methyl.	< 0,010 mg/kg
Imazethapyr	< 0,010 mg/kg Q	Isocarbophos.	< 0,010 mg/kg	Isoxaflutole.	< 0,010 mg/kg	Lufenuron.	< 0,010 mg/kg
MCPA.	< 0,010 mg/kg	MCPB	< 0,010 mg/kg Q	Mecoprop	< 0,010 mg/kg Q	Mepronil.	< 0,010 mg/kg
Methoprene.	< 0,010 mg/kg	Monuron.	< 0,010 mg/kg	Neburon.	< 0,010 mg/kg	Norflurazon.	< 0,010 mg/kg
Noviflumuron.	< 0,010 mg/kg	Picolinafen.	< 0,010 mg/kg	Propanil.	< 0,010 mg/kg	Prothioconazole.	< 0,010 mg/kg
Silthiofam.	< 0,010 mg/kg	Sulfosulfuron	< 0,010 mg/kg Q	Teflubenzuron.	< 0,010 mg/kg	Terbacil.	< 0,010 mg/kg

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ROTTERDAM

Analytical Report

Reportnr.	: **1722196 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:00	Sampling Date	*: 07-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,243
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Triasulfuron.	< 0,010 mg/kg	Triflumuron.	< 0,010 mg/kg	Triflusulfuron-methyl.	< 0,010 mg/kg

Pesticides LCMSMS (pos. ionisation)

Acephate	< 0,010 mg/kg	Q	Acetamiprid	< 0,010 mg/kg	Q	Acibenzolar-S-methyl.	< 0,010 mg/kg	Q	Alachlor	< 0,010 mg/kg	Q
Aldicarb	< 0,010 mg/kg	Q	Aldicarb sulphone	< 0,010 mg/kg	Q	Aldicarb-sulfoxide	< 0,010 mg/kg	Q	Ametoctradin	< 0,010 mg/kg	Q
Ametryn	< 0,010 mg/kg	Q	Aminocarb.	< 0,010 mg/kg		Azaconazole.	< 0,010 mg/kg		Azamethiphos.	< 0,010 mg/kg	
Azinphos-methyl	< 0,010 mg/kg	Q	Aziprotryne	< 0,010 mg/kg	Q	Azoxystrobin.	< 0,010 mg/kg		Benalaxyl.	< 0,010 mg/kg	
Bendiocarb.	< 0,010 mg/kg		Benodanil.	< 0,010 mg/kg		Benthiavalicarb-isopropyl	< 0,010 mg/kg	Q	Benzoyl-prop-ethyl.	< 0,010 mg/kg	
Bifenazate	< 0,010 mg/kg	Q	Bixafen	< 0,010 mg/kg	Q	Boscalid	< 0,010 mg/kg	Q	Bromacil	< 0,010 mg/kg	Q
Bupirimate	< 0,010 mg/kg	Q	Butocarboxim sulfoxide	< 0,010 mg/kg	Q	Butoxycarboxim.	< 0,010 mg/kg		Butralin	< 0,010 mg/kg	Q
Buturon.	< 0,010 mg/kg		Cadusafos.	< 0,010 mg/kg		Carbaryl	< 0,010 mg/kg	Q	Carbendazim.	< 0,010 mg/kg	
Carbofuran	< 0,002 mg/kg	Q	Carboxin	< 0,010 mg/kg	Q	Carfentrazone-ethyl	< 0,010 mg/kg	Q	Chloridazon.	< 0,010 mg/kg	
Chlorotoluron	< 0,010 mg/kg	Q	Clothianidin	< 0,010 mg/kg	Q	Coumaphos	< 0,010 mg/kg	Q	Cyanazine	< 0,010 mg/kg	Q
Cyanofenphos	< 0,010 mg/kg	Q	Cyprodinil	< 0,010 mg/kg	Q	Daminozide	< 0,010 mg/kg	Q	Demeton O & S.	< 0,010 mg/kg	
Demeton-s/Demeton-o	< 0,010 mg/kg	Q	Demeton-S-methyl-sulfon	< 0,010 mg/kg	Q	Dichlofluanid	< 0,010 mg/kg	Q	Dicrotophos	< 0,010 mg/kg	Q
Difenoconazole	< 0,010 mg/kg	Q	Difenoxuron	< 0,010 mg/kg	Q	Dimefuron	< 0,010 mg/kg	Q	Dimethachlor	< 0,010 mg/kg	Q
Dimethenamid-P	< 0,010 mg/kg	Q	Dimethirimol	< 0,010 mg/kg	Q	Dimethoate	< 0,010 mg/kg	Q	Dimethomorph.	< 0,010 mg/kg	
Diniconazole	< 0,010 mg/kg	Q	Diphenamid	< 0,010 mg/kg	Q	Dipropetryn	< 0,010 mg/kg	Q	Disulfoton-sulfone	< 0,010 mg/kg	Q
DMST (Dimethylsulftoluidide).	< 0,010 mg/kg		Dodine.	< 0,010 mg/kg		Epoxiconazole	< 0,010 mg/kg	Q	Etaconazole	< 0,010 mg/kg	Q
Ethiofencarb	< 0,010 mg/kg	Q	Ethiofencarb sulfone	< 0,010 mg/kg	Q	Ethiprole	< 0,010 mg/kg	Q	Ethirimol	< 0,010 mg/kg	Q
Ethoprofos	< 0,010 mg/kg	Q	Ethoprop	< 0,010 mg/kg	Q	Ethoxyquin.	< 0,010 mg/kg		Fenamidone.	< 0,010 mg/kg	
Fenamiphos sulphone.	< 0,010 mg/kg		Fenamiphos sulphoxide	< 0,010 mg/kg	Q	Fenamiphos.	< 0,010 mg/kg		Fenarimol	< 0,010 mg/kg	Q
Fenazaquin	< 0,010 mg/kg	Q	Fenbuconazole.	< 0,010 mg/kg		Fenfuram.	< 0,010 mg/kg		Fenhexamid.	< 0,010 mg/kg	
Fenobucarb.	< 0,010 mg/kg		Fenoxycarb.	< 0,010 mg/kg		Fenpropimorph.	< 0,010 mg/kg		Fenpyroximat	< 0,010 mg/kg	Q
Fensulfothion (sum).	< 0,010 mg/kg		Fenthion	< 0,010 mg/kg	Q	Fenthion-sulfoxide.	< 0,010 mg/kg		Fenuron	< 0,010 mg/kg	Q
Flamprop-methyl.	< 0,010 mg/kg		Flonicamid (sum incl. metaboli	< 0,010 mg/kg	Q	Florasulam.	< 0,010 mg/kg		Fluazifop-P (sum).	< 0,010 mg/kg	
Flufenacet.	< 0,010 mg/kg		Fluoxastrobin	< 0,010 mg/kg	Q	Flupyradifurone	< 0,010 mg/kg	Q	Fluquinconazole.	< 0,010 mg/kg	
Flusilazole	< 0,010 mg/kg	Q	Flusilazole.	< 0,010 mg/kg		Flutriafol.	< 0,010 mg/kg		Foramsulfuron.	< 0,010 mg/kg	
Fosthiazate.	< 0,010 mg/kg		Fuberidazole.	< 0,010 mg/kg		Furalaxyl.	< 0,010 mg/kg		Haloxyfop	< 0,010 mg/kg	Q
Heptenophos	< 0,010 mg/kg	Q	Hexazinone	< 0,010 mg/kg	Q	Hexythiazox	< 0,010 mg/kg	Q	Hymexazole.	< 0,010 mg/kg	
Imazalil.	< 0,010 mg/kg		Imazapic	< 0,01 mg/kg	Q	Imidacloprid.	< 0,010 mg/kg		Indoxacarb	< 0,010 mg/kg	Q
Iodosulfuron methyl	< 0,010 mg/kg	Q	Iprobenphos.	< 0,010 mg/kg		Iprovalicarb.	< 0,010 mg/kg		Isazofos.	< 0,010 mg/kg	
Isofenphos-methyl.	< 0,010 mg/kg		Isoprocarb.	< 0,010 mg/kg		Isoproturon.	< 0,010 mg/kg		Isouron.	< 0,010 mg/kg	
Kresoxym-methyl.	< 0,010 mg/kg		Lenacil.	< 0,010 mg/kg		Linuron.	< 0,010 mg/kg		Malaoxon.	< 0,010 mg/kg	
Malathion.	< 0,010 mg/kg		Mecarbam	< 0,010 mg/kg	Q	Mefenacet.	< 0,010 mg/kg		Mephosfolan.	< 0,010 mg/kg	
Mesosulfuron-methyl	< 0,010 mg/kg	Q	Metalaxyl.	< 0,010 mg/kg		Metamitron.	< 0,010 mg/kg		Metasystox I	< 0,010 mg/kg	
Metazachloor	< 0,010 mg/kg	Q	Metconazole.	< 0,010 mg/kg		Methabenzthiazuron.	< 0,010 mg/kg		Methamidophos.	< 0,010 mg/kg	
Methidathion.	< 0,010 mg/kg		Methiocarb	< 0,010 mg/kg	Q	Methomyl.	< 0,010 mg/kg		Methoprotryne.	< 0,010 mg/kg	
Methoxyfenozide.	< 0,010 mg/kg		Metobromuron.	< 0,010 mg/kg		Metolachlor	< 0,010 mg/kg	Q	Metolachlor..	< 0,010 mg/kg	
Metoxuron	< 0,010 mg/kg	Q	Metrafenone	< 0,010 mg/kg	Q	Metsulfuron methyl	< 0,010 mg/kg	Q	Mevinphos	< 0,010 mg/kg	Q
Monalide	< 0,010 mg/kg	Q	Monocrotophos.	< 0,010 mg/kg		Monolinuron	< 0,010 mg/kg	Q	Myclobutanil.	< 0,010 mg/kg	
Napropamide (sum of isomer	< 0,010 mg/kg		Nitenpyram.	< 0,010 mg/kg		Nuarimol	< 0,010 mg/kg	Q	Ofurace.	< 0,010 mg/kg	
Omethoate.	< 0,010 mg/kg		Orbencarb.	< 0,010 mg/kg		Oxadixyl.	< 0,010 mg/kg		Oxamyl	< 0,010 mg/kg	Q
Oxydemeton-methyl.	< 0,010 mg/kg		Paclobutrazol	< 0,010 mg/kg		Paraoxon-Ethyl.	< 0,010 mg/kg		Paraoxon-methyl.	< 0,010 mg/kg	
Penconazole	< 0,010 mg/kg	Q	Pencycuron	< 0,010 mg/kg	Q	Pendimethalin	< 0,010 mg/kg	Q	Phorate sulfone.	< 0,010 mg/kg	
Phorate sulfoxide.	< 0,010 mg/kg		Phosalone	< 0,010 mg/kg	Q	Phosphamidon	< 0,010 mg/kg	Q	Phoxim	< 0,010 mg/kg	Q
Picoxystrobin	< 0,010 mg/kg	Q	Pirimicarb.	< 0,010 mg/kg		Prochloraz.	< 0,010 mg/kg		Promecarb.	< 0,010 mg/kg	
Prometryn	< 0,010 mg/kg	Q	Propachlor.	< 0,010 mg/kg		Propamocarb.	< 0,010 mg/kg		Propargite	< 0,010 mg/kg	Q
Propazine	< 0,010 mg/kg	Q	Propiconazole	< 0,010 mg/kg	Q	Propoxur.	< 0,010 mg/kg		Propoxycarbazone sodium.	< 0,010 mg/kg	

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Analytical Report

Reportnr.	: **1722196 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:00	Sampling Date	*: 07-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,243
Packing	: Plastic, ambient	Seal / Seal Code	: No /

Prosulfocarb.	< 0,010 mg/kg		Prosulfuron	< 0,010 mg/kg	Q	Pymetrozine	< 0,010 mg/kg	Q	Pyracarbolid.	< 0,010 mg/kg	
Pyraclostrobin	< 0,010 mg/kg	Q	Pyridaben	< 0,010 mg/kg	Q	Pyridaphenthion.	< 0,010 mg/kg		Pyridate	< 0,010 mg/kg	Q
Pyrifenox	< 0,010 mg/kg	Q	Pyrimethanil	< 0,010 mg/kg	Q	Pyriproxyfen	< 0,010 mg/kg	Q	Quinalphos	< 0,010 mg/kg	Q
Quinclorac	< 0,010 mg/kg	Q	Quinoxyfen	< 0,010 mg/kg	Q	Simazine.	< 0,010 mg/kg		Spinetoram (sum)	< 0,010 mg/kg	Q
Spinosad (sum)	< 0,010 mg/kg		Spirotetramat (MRL sum)	< 0,010 mg/kg		Spiroxamine.	< 0,010 mg/kg		Sulcotrione.	< 0,010 mg/kg	
Tebuconazol	< 0,010 mg/kg	Q	Tebufenozide.	< 0,010 mg/kg		Tebuthiuron.	< 0,010 mg/kg		Terbumeton.	< 0,010 mg/kg	
Terbutryn	< 0,010 mg/kg	Q	Tetraconazole.	< 0,010 mg/kg		Thiabendazole	< 0,010 mg/kg	Q	Thiacloprid.	< 0,010 mg/kg	
Thiamethoxam	< 0,010 mg/kg	Q	Thifensulfuron methyl	< 0,010 mg/kg	Q	Thiobencarb.	< 0,010 mg/kg		Thiofanox	< 0,010 mg/kg	Q
Thiofanox-sulfone.	< 0,010 mg/kg		Thiofanox-sulfoxide.	< 0,010 mg/kg		Thiophanate-methyl.	< 0,010 mg/kg		Tolyfluanid	< 0,010 mg/kg	Q
Triadimefon.	< 0,010 mg/kg		Triadimenol.	< 0,010 mg/kg		Triapenthenol.	< 0,010 mg/kg		Triazophos	< 0,010 mg/kg	Q
Trichlorfon.	< 0,010 mg/kg		Tricyclazole.	< 0,010 mg/kg		Trietazine.	< 0,010 mg/kg		Trifloxystrobin	< 0,010 mg/kg	Q
Triflumizole	< 0,010 mg/kg	Q	Triforine	< 0,010 mg/kg	Q	Trinexapac	< 0,010 mg/kg	Q	Triticonazole.	< 0,010 mg/kg	
Vamidothion.	< 0,010 mg/kg		XMC (3,5-Xylyl MethylCarbam	< 0,010 mg/kg		Zoxamide.	< 0,010 mg/kg				

Q-Analyses ISO 17025 accredited by RvA (ILAC)
R-Carriec out by TLR International Laboratories, location Ridderkerk
O-Outsourced

Samplingdate unknown / time difference between sampling-and arrival-date might be too long. Time lapsed before testing may affect results.

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Analytical Report

Reportnr.	: **1722196 version 1**		
Sample Arrival Date	: 26-Jan-2023 11:00	Sampling Date	*: 07-Jul-2022
ReportDate Version	: **27-Mar-2023 16:56**	Samplesize (kg)	: 0,243
Packing	: Plastic, ambient	Seal / Seal Code	: No /

ANNEX

Method Descriptions

Contaminations

Pesticides

Method Description	**Method Code**
Flexscope:Determination of the pesticide content ; GC-MS-MS method	Own method
Flexscope:Determination of the pesticide content; LC-MS-MS method	Own method

Pesticides (Glyphosate)

Method Description	**Method Code**
Determination of Glyphosate in plant material with LCMSMS (FMOC-method)	Own method

Pesticides LCMSMS (neg. ionisation)

Method Description	**Method Code**
Determination of Phenoxy alkane carboxylic acids components are performed with the optimized multimethod	.

Abbreviations:

acc: in accordance with
eq: Equivalent to

Requested 26-Jan-2023 by Tate & Lyle
Analyses according to annex
Drs. ing. H. Janssens Director TLR International Laboratories

From: Santa Maria, Juan Cristian <JuanCristian.SantaMaria@tateandlyle.com>
Sent: Monday, September 25, 2023 3:38 PM
To: Zhang, Janet <Janet.Zhang@fda.hhs.gov>
Subject: [EXTERNAL] RE: GRN 1140

Dear Mrs. Zhang,

Thanks once again for your note.

In response to your question, of the 9 batches that were analyzed to produce the data reported in section 2.3.2 Batch Analysis of GRN 1140, no alcohol was used for several of the production batches, and only ethanol was used for several others. Nevertheless, depending on the nature of the starting material and processing conditions (within the ranges described in our submission), and in order to meet specific finished product target physical attributes, our production process may alternatively use methanol or SDA 3-A ethanol (that contains 5% methanol) in the desorption and/or optional crystallization and wash steps. The alcohols employed are effectively removed during the drying steps, such that under all these scenarios, the finished product is analyzed to confirm that it meets the ≤200 ppm residual methanol and ≤5,000 ppm residual ethanol limits established in the specification (section 2.3.1) before being released for commercialization.

It may be worth noting that the use of ethanol and/or methanol is well established in the manufacture of steviol glycosides, where it may be used in the desorption, wash and crystallization steps of the manufacturing process. Such use has been evaluated and deemed safe by different regulatory bodies including the Joint FAO/WHO Expert Committed on Food Additives, and the European Food Safety Authority, and the specification limits established for ethanol and methanol in GRN 1140 are identical to those established for steviol glycosides manufactured by extraction, enzyme modification, fermentation and enzymatic glucosylation in JECFA Monograph 26 (FAO and WHO, 2021). Likewise, the FCC monograph for steviol glycosides has identical limits for ethanol and methanol, as does Commission Regulation (EU) No 231/2012 for stevia extracts and numerous GRAS Notices for steviol glycosides that received “no questions” from the FDA (as highlighted in Table 6.2-1 of GRN 1140).

I hope the above information answers your question, but please do not hesitate to contact me should you need any additional information.

Kind regards,

Juan Cristián Santa María
Senior Director, Global Regulatory & Scientific Affairs
Innovation and Commercial Development
Tate & Lyle

Mob. +1 (470) 373-7122

External use permitted

From: Santa Maria, Juan Cristian <JuanCristian.SantaMaria@tateandlyle.com>
Sent: Wednesday, September 20, 2023 7:09 PM
To: Zhang, Janet <Janet.Zhang@fda.hhs.gov>
Subject: RE: GRN 1140

Dear Mrs. Zhang,

I hope this message finds you well.

I hereby confirm receipt of your email below. We will be responding to your question in the next few days.

Kind regards,

Juan Cristián Santa María
Senior Director, Global Regulatory & Scientific Affairs
Tate & Lyle
Mob. +1 (470) 373-7122

From: Zhang, Janet <Janet.Zhang@fda.hhs.gov>
Sent: Wednesday, September 20, 2023 5:03 PM
To: Santa Maria, Juan Cristian <JuanCristian.SantaMaria@tateandlyle.com>
Subject: [EXTERNAL] GRN 1140

Dear Mr. Santa María,

We have a question regarding GRN 1140 you submitted on behalf of Tate & Lyle, please provide your response within 10 business days.

- The manufacturing process described on p. 9 and depicted in Figure 2.2-1 (p. 11) of the notice includes the use of alcohol in the desorption and optional crystallization and wash steps. Please confirm the identity of the alcohol used (e.g., ethanol or methanol).

Thanks,

Jianrong (Janet) Zhang, Ph.D.
FDA/OFVM/CFSAN/OFAS/DST
College Park, MD 20740
Phone: 240-402-1327
janet.zhang@fda.hhs.gov