

Center for Regulatory Services, Inc.

5200 Wolf Run Shoals Road Woodbridge, VA 22192-5755 703 590 7337 (Fax 703 580 8637) smedley@cfr-services.com

September 10, 2021

Dr. Susan Carlson
Director, Division of Biotechnology and GRAS Notice Review (HFS-255)
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

Dear Dr. Carlson:

SUBJECT: Transmittal of the FINK TEC GmbH -

GRAS Notice for Applied Phage Meat S2

Antimicrobial to control Salmonella enterica spp. in

Meat and poultry

Enclosed you will find the GRAS notice for Applied Phage Meat S2 that contains cocktail contains six out of a set of eleven well characterized bacteriophages, namely: vB_SalM_ELB17, vB_SalM_MP82, vB_SalM_KAZ99a, vB_SalM_RMP11k, vB_SalM_RMS3b, vB_SalM_TAT2F, vB_SalM_DIN2, vB_SalM_MP75, vB_SalS_FV7M4, vB_SalS_RMP9 and vB_SalS_OBO18 for use as antimicrobial to control Salmonella enterica spp. in ground and whole red meat and poultry, including whole carcasses, primals, subprimals, trimmings, and organs, submitted by FINK TEC GmbH.

I have provided a DVD of the GRAS notice and all the cited references.

Should you have any questions on this filing, please contact me, at your convenience.

Sincerely,

Kristi

Smedley

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a mail to assembly the reviews area only in
Date 2024 56:16 124853, Graph

Kristi O. Smedley, Ph.D.

Consultant to FINK TEC GmbH

Attachments

FDA Form 3667 (Hard Copy and DVD-Copy)
Applied Phage Meat S2GRN NARRATIVE of Notice (Hard Copy and DVD-Copy)
Appendices (as appended to Narrative) (DVD-copy)
Full Complement of References (DVD-copy)

FINK TEC GmbH GRAS Notification "Applied Phage Meat S2"

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FINK TEC GmbH: "Applied Phage Meat S2"

Attachment list:

Attachment I: Host spectra

Attachment II: Bioinformatic analyses of phage genomes – confidential

Attachment III: Phage genome sequences – confidential

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Attachment V: Genome safety table

Attachment VI: Allergen search

Attachment VII: Efficacy study on pork

Attachment VIII: Efficacy study on beef

Attachment IX: Efficacy study on chicken

I. GRAS Exemption Claim

I.1 Claim of Exemption From the Premarket Approval Requirements Pursuant to 21CFR 170 Subpart E

This Notice is submitted in compliance with Subpart E of FDA's GRAS Notification process regulations 21 CFR Subpart E 170.225-170.255.

The bacteriophages vB SalM ELB17 (DSM 26158), vB SalM MP82 (DSM 26173), vB SalM KAZ99a (DSM 33039), vB SalM RMP11k (DSM 33040), vB SalM RMS3b 33043), vB SalM TAT2F (DSM (DSM 33044). vB SalM MP75 vB SalM DIN2 (DSM 33045), (DSM 104023), (DSM 26125), vB SalS RMP9 (DSM 26157) and vB SalS FV7M4 vB SalS OBO18 (DSM33041), formulated under the product name of, "Applied Phage Meat S2", have been determined by the scientists of the FINK TEC GmbH to be generally recognized as safe, through scientific procedures, and are exempt from the premarket approval requirements under the intended use conditions described within this notification. The accompanying sections provide the basis for this finding. On behalf of FINK TEC GmbH (notifier), I certify that to the best of my knowledge, this GRAS Notice is complete, representative, and balanced with respect to the information provided, favorable or unfavorable, known to me and pertinent to the evaluation of the safety and GRAS status of our bacteriophage-based antimicrobial product.

Signed,		

Date: 2.09.2021

Michael Fink Chief Executive Officer FINK TEC GmbH Oberster Kamp 23 D-59069 Hamm Germany

I.2 Name and Address of Notifier

FINK TEC GmbH

Dr. Michael Fink

Chief Executive Officer

Oberster Kamp 23

D-59069 Hamm

Germany

Ph: +49 (0)2385 73 300 Fax: +49 (0)2385 73 389 Michael.Fink@finktec.com

Notifier's US Representative

Kristi O. Smedley, Ph.D.

Center for Regulatory Services, Inc.

5200 Wolf Run Shoals Rd.

Woodbridge, VA 22192

Office: 703-590-7337 Fax: 703-580-8637

smedley@cfr-services.com

I.3 Common or Usual Name of the Notified Substance

The FINK TEC GmbH produces a bacteriophage cocktail with potent lytic activity against *Salmonella enterica* spp. under the trade name "*Applied Phage Meat S2*". The cocktail contains six out of a set of eleven well characterized bacteriophages, namely: vB_SalM_ELB17, vB_SalM_MP82, vB_SalM_KAZ99a, vB_SalM_RMP11k, vB_SalM_RMS3b, vB_SalM_TAT2F, vB_SalM_DIN2, vB_SalM_MP75, vB_SalS_FV7M4, vB_SalS_RMP9 and vB_SalS_OBO18.

I.4 Conditions of Use

The bacteriophage cocktail, formulated as "Applied Phage Meat S2", is intended for use as antimicrobial to control Salmonella enterica spp. in ground and whole red meat and poultry, including whole carcasses, primals, subprimals, trimmings, and organs, wherever and whenever a risk of Salmonella contamination occurs.

I.5 Basis for the GRAS Determination

In accordance with 21 CFR § 170.30(b), the intended use of bacteriophages vB_SalM_ELB17, vB_SalM_MP82, vB_SalM_KAZ99a, vB_SalM_RMP11k, vB_SalM_RMS3b, vB_SalM_TAT2F, vB_SalM_DIN2, vB_SalM_MP75, vB_SalS_FV7M4, vB_SalS_RMP9 and vB_SalS_OBO18 has been determined to be generally recognized as safe (GRAS), based on scientific procedures and a comprehensive search of the scientific literature.

I.6 Availability of Information

The data and information that serve as the basis for this GRAS notification are available for review and copying at the offices of FINK TEC GmbH. Copies are available upon request to:

FINK TEC GmbH
Dr. Michael Fink
Chief Executive Officer
Oberster Kamp 23
D-59069 Hamm
Germany

Ph: +49 (0)2385 73 300 Fax: +49 (0)2385 73 389 Michael.Fink@finktec.com

I.7 Public Disclosure

FOIA (Freedom of Information Act): Parts 2 through 8 of this notification as well as the data provided in the Attachments I and IV-IX to this notification do not contain data or information that is exempt from disclosure under the FOIA (Freedom of Information Act, 5 U.S.C. 552).

The data provided in the Attachments II and III to this notification are considered confidential business information and should be exempt from disclosure under the FOIA (Freedom of Information Act, 5 U.S.C. 552).

I.8 Sharing Trade Secret Information to USDA/Food Safety and Inspection Services

FINK TEC GmbH authorizes FDA to share any trade secret information to the US Department of Agriculture, Food Safety and Inspection Service, as needed.

II. Identity of Substance

II.1 Identity

Common and Usual Name of the Food Grade Substance: *Salmonella*-specific phage preparation

Quantitative Composition: The *Salmonella*-specific phage preparation is comprised of eleven (11) bacteriophages (phages) to be used six (6) at a time in the final commercial product "*Applied Phage Meat S2*". All phages used in the phage preparation are strictly lytic as determined by an analysis of phage genomes.

An application of the food ingredient will use a mixture of equal proportions of six (6) phages selected from the designated eleven (11) phage preparation components, with specificity against the target bacterium *Salmonella enterica* spp. The applied preparation will contain a total phage concentration ranging between 5×10^9 and 1×10^{10} active "Plaque Forming Units per milliliter of solution" (PFU/mL).

The ability to utilize a blend of selected phages in a particular processing plant is necessary to guarantee the broad scope of lytic activity of the blend against the target *Salmonella* strains. In addition, a rotation in the composition of the cocktail, using a subset of the eleven (11) phages that are the subject of this notice, reduces the risk that the targeted bacterial pathogen might develop resistance against the applied preparation product. The possibility to create diversity within the preparation composition will also provide the meat producer with the means to rapidly react to outbreaks of novel *Salmonella* strains.

The final phage preparation is a colorless and odorless liquid suspension of phages that is produced as a concentrate to be diluted with water at the site of application to generate a working solution ranging in concentration from 1×10^5 to 1×10^7 PFU/mL, depending on the actual application.

Phages that comprise the preparation are deposited with the Leibniz Institute DSMZ – German Collection of Microorganisms and Cultures as designated below (https://www.dsmz.de/home.html):

Order: Caudovirales Family: Myoviridae

Species: DSM 26158 (ELB17)

DSM 26173 (MP82)
DSM 33039 (KAZ99a)
DSM 33040 (RMP11k)
DSM 33043 (RMS3b)
DSM 33044 (TAT2F)
DSM 33045 (DIN2)

DSM 104023 (MP75)

Host bacteria: Salmonella enterica spp.

Order: Caudovirales Family: Siphoviridae

Species: DSM 26125 (FV7M4)

DSM 26157 (RMP9) DSM33041 (OBO18)

Host bacteria: Salmonella enterica spp.

Eight (8) of the preparation phages belong to the structural family of Myoviridae, three (3) preparation phages to the family of Siphoviridae. All bacteriophages are strictly lytic as determined by the analysis of their genomes as described below.

Host range: FINK TEC GmbH conducted host range studies on phage preparation component phages. The results of these studies are shown in Attachment 1. Since the individual host ranges varied and none of the phages were lytic against all *Salmonella* strains tested, the different phages complement each other, increasing the total coverage, which is important for the composition of an efficient targeted anti-microbial phage product.

Phage Type: All phage preparation phage components are exclusively lytic. The biology of phages has been exhaustively studied in the 100 years since their discovery. Two major phage classes have been described, lytic and temperate. Temperate phages do not necessarily kill their host bacterium. They have the ability to passively invade a host and thereby are transferring their own genes from one host bacterium to the next, in a process called lysogenic conversion (Brüssow et al. 2004)(Fortier and Sekulovic 2013). As some temperate phages may carry toxin genes (Davis et al. 2000; Smith et al. 2012),

they are not suited to be components of a phage cocktail produced and applied on an industrial scale.

Lytic phages, on the other hand, lack the genes responsible for lysogenic conversion and an infection by a lytic phage always leads to the death of the bacterial host. Thus, lytic phages are safe for use in food, as they do not disseminate toxin or other genes that pose risks for humans.

II.2 Method of Manufacture

II.2.1 Maintenance of host bacteria and bacteriophage stocks to insure purity

Frozen aliquots of the non-pathogenic *E. coli* host strain MG1655 (ATCC 47076) (Guyer et al. 1981) or the non-human pathogenic *Salmonella* host strains *Salmonella bongori* (ATCC 43975) (Reeves et al. 1989) and *Salmonella paratyphi* B var. Java (ATCC BAA-1584) (Boyd et al. 1993) are stored at -80°C as glycerol stocks. For each production cycle the respective strain is streaked out on an agar plate and a single colony is used to start a pre-culture to be used in the fermentation process.

Stocks of bacteriophage lysates are sterilized by $0.22~\mu m$ filtration and stored at 4°C. Immediately before use in the fermentation process, the bacteriophage stocks are sterilized anew by $0.22~\mu m$ filtration to minimize the risk of contamination.

II.2.2 Description of the manufacturing process

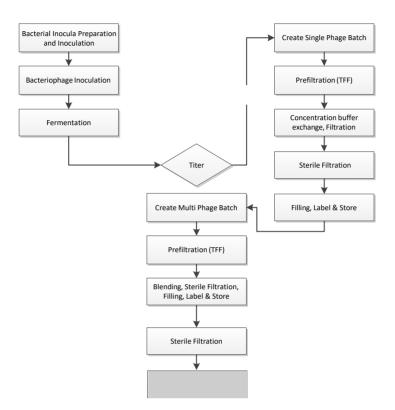
The individual bacteriophages are produced in an aerobic fermentation process in an animal-product free growth medium. For each bacteriophage a specific host strain, either E. coli or Salmonella, is grown to a target optical density at 600 nanometers and infected with the bacteriophage at a previously determined multiplicity of infection (MOI, the ratio of phage to bacteria) and the combination is incubated with aeration and mixing. The bacteriophages will infect their host bacteria, multiply within them and eventually lyse the host bacteria, generating a bacteriophage lysate. After the fermentation process is complete, the bacteriophage lysates are titered, to determine the concentration of the progeny bacteriophages. Thereafter the bacteriophage lysates are clarified by an initial continuous centrifugation process followed by a filtration process using a Tangential Flow Filtration (TFF) system to remove unbroken host cells and host cell debris. In a second filtration step the bacterial growth medium is exchanged to phosphate buffered saline, a common storage buffer that does not contain any unapproved food additives. In a third filtration step the individual bacteriophage solutions are sterilized through a 0.22 µm filter (Lehnherr and Bartsch 2012). All processing aids used in the manufacturing are of food grade quality or of a quality specified in the 5th Edition of the Food Chemical Codex.

Each individual bacteriophage stock has to meet the specified release parameters before it can be used as one of six components to mix the "Applied Phage Meat S2" bacteriophage cocktail.

Table 1: Product specification for each batch of an individual bacteriophage.

Parameter	Specification
Bacteriophage titer	>5 x 10 ⁹ PFU/mL
Microbial sterility	no growth
PCR identity	identical to PCR reference profile

II.2.3 Process flow diagram



Bacterial Inocula Preparation and Inoculation Bacteriophage Inoculation Fermentation Titer Concentration buffer exchange, Filtration Sterile Filtration CCP 1 Prefiltration (TFF) Blending, Sterile Filtration, Filling, Label & Store Sterile Filtration CCP 2

II.2.4 Critical Control Points

II.2.5 HACCP plan summary

Subject	ISSUE DATE	PRODUCT
CCP HACCP Plan Summary	2.03.2016	Applied Phage Meat S2
FinkTec GmbH		Page 1 of 1
Oberster Kamp 23		
59069 Hamm		
Germany		

Critical			Monitoring						
Control									
Points		Critical					Corrective		
ССР	Hazard(s)	Limit	what	how	Frequency	who	Action(s)	CCP Verification	Records
			Total						
			aerobic						
	bacterial		germ				Redo sterile		
CCP 1	contamination	>10 cfu/g	count	ISO 4833	each batch	QC	filtration	positive control	
			Yeast and				Redo sterile		
		>10 cfu/g	moulds	NMKL 98	each batch	QC	filtration	positive control	
			Total						
			aerobic						
	bacterial		germ				Redo sterile		
CCP 2	contamination	>10 cfu/g	count	ISO 4833	each batch	QC	filtration	positive control	
			Yeast and				Redo sterile		
		>10 cfu/g	moulds	NMKL 98	each batch	QC	filtration	positive control	
			Enteroba						
			cteriacea				Redo sterile		
		>10 cfu/g	е	ISO 6888-1	each batch	QC	filtration	positive control	

II.2.6 Raw Materials

The fermentation medium is an animal-product free growth medium. Its components are described here and have an existing regulatory status as regulated GRAS ingredients or additives:

Soy Peptone: Peptones are GRAS affirmed at 21 CFR § 184.1553 for use as processing aids, among other uses, at levels not to exceed good manufacturing practice. Peptones are protein hydrolysates consisting of free amino acids and short peptides in an aqueous salt solution.

Yeast Extract: Yeast extract is a commonly used food ingredient. For example, baker's yeast extract is GRAS affirmed as a flavoring agent or adjuvant at up to 5% in foods generally 21 CFR § 184.1983.

Sodium Chloride: Sodium chloride "salt" is the prototype in 21 CFR § 182.1 (a) of an ingredient that is so obviously GRAS that FDA has not listed it as GRAS.

Magnesium chloride: Magnesium chloride salt is GRAS affirmed at 21 CFR § 184.1426 for use as a processing aid, among other uses, at levels not to exceed good manufacturing practice. Magnesium chloride is a component of the buffer used for the finalized bacteriophage product.

Monopotassium phosphate: Monopotassium phosphate is a GRAS substance (21 CFR § 582.4521) and an indirect additive (21 CFR 175.105) and it is identified as a currently used fermentation aid (FDA Substances added to Food list). Among other uses, monopotassium phosphate is used as a processing aid at levels not to exceed good manufacturing practice. Monopotassium phosphate is a component of the buffer used for the finalized bacteriophage product.

Disodium phosphate: Disodium phosphate is a GRAS substance (21 CFR § 182.6290) used as a processing aid, among other uses, at levels not to exceed good manufacturing practice. Disodium phosphate is a component of the buffer used for the finalized bacteriophage product.

II.3 Specification of "Applied Phage Meat S2"

The final product specifications are given in Table 2 below:

Table 1: Product specifications of "Applied Phage Meat S2"

Description	dized bacteriophage cocktail					
_	based on naturally occurring					
	ba	bacteriophages, stabilized				
Concentration	Approx. >	1 x 10 ⁹ bacteriophages/mL ¹				
Packaging	Stainless s	teel KEG barrels, flat fitting				
Storage		lry (recommended 4-8°C), do				
	not store in	n direct sun light				
Shelf life	6 months,	process immediately after				
	opening					
Appearance		to light yellowish liquid				
Texture	Liquid					
рН	7.0-7.4					
odor / taste	characteris	etic				
Microbiological Parameters						
Total plate count	ISO	< 50 CFU/g				
	48833 ²					
Yeast and Mould	NMKL	< 100 CFU/g				
	983					
Staphylococcus	ISO	< 10 CFU/g				
	6888 ²					
Salmonella	NMKL	not detectable in 25 g				
	713	100 GTV				
Enterobacteriacea	ISO	< 100 CFU/g				
	21528 ²	1000 GTVV				
Sulfite-reducing Clostridia	ISO	< 1000 CFU/g				
DODAY IS I	152132					
PCR Verification ⁴	Complies	Yes/no (for single phage				
		solutions)				

¹Clokie and Kropinski 2009

²http://www.iso.org/iso/catalogue_detail.htm?csnumber=23036

³http://www.nmkl.org/index.php/en/

⁴Mullis et al. 1986

II.4 Bacteriophage names and classification

Order: Caudovirales Family: Myoviridae

Species: vB SalM MP82

vB_SalM_KAZ99a vB_SalM_RMP11k vB_SalM_RMS3b vB_SalM_TAT2F vB_SalM_DIN2 vB_SalM_MP75

Host bacteria: Salmonella enterica spp.

Order: Caudovirales Family: Siphoviridae

Species: vB_SalS_FV7M4

vB_SalS_RMP9

 vB_SalS_OBO18

Host bacteria: Salmonella enterica spp.

II.5 Original sources of bacteriophages in the preparation

All bacteriophages were isolated from wastewater. They are used in their natural form, neither modified nor genetically engineered.

II.6 Bacteriophage properties

II.6.1 Salmonella host range

The bacteriophages are specific for a wide range of *Salmonella enterica* spp. serovars as shown in Table 3. The data was generated in a titration experiment as shown in Attachment I.

Table 2: Salmonella host strains covered by "Applied Phage Meat S2":

S. agona	S. anatum	S. brandenburg	S. choleraesius
S. decatur	S. derby	S. dublin	S. duisburg
S. emek	S. enterica	S. enteritidis	S. gallinarum
S. haifa	S. heidelberg	S. indiana	S. infantis
S. java	S. kiambu	S. livingstone	S. London
S. miami	S. minnesota	S. montevideo	S. muenchen
S. newport	S. panama	S. parathyphi A	S. paratyphi B
S. paratyphi C	S. pullorum	S. rubislaw	S. saintpaul
S. sendai	S. senftenberg	S. stanley	S. stanleyville
S. thompson	S. typhimurium	S. tyhpisuis	S. virchow
S. wien			

II.6.2 Type

Eight of the bacteriophages belong to the structural family of Myoviridae, three bacteriophages to the structural family of Siphoviridae. All bacteriophages are strictly lytic as determined by the analysis of their genomes (see Attachment II).

II.6.3 Complete gene sequences of all the bacteriophage genes

The genomes of all bacteriophages were determined using Next-Generation-Sequencing (Illumina technology). They were analyzed using standard bioinformatical methods. The complete and annotated genomic sequences of all eleven bacteriophages are provided in Attachment III. The analyses of these genomes confirmed not only the lytic nature of all bacteriophages but also demonstrated that no virulence genes (Attachment IV) no toxin toxin genes (Attachment V),

no antibiotic resistance markers, no genes coding for proteins with allergenic properties (Attachment VI) nor any other detrimental genes were present.

II.7 Host

II.7.1 Pathogenicity profile

Six bacteriophages, namely vB_SalM_ELB17, vB_SalM_KAZ99a, vB_SalM_RMS3b, vB_SalS_RMP9, vB_SalM_MP75 and vB_SalS_FV7M4 are grown on the *E. coli* K12 derivative MG1655 (ATCC 47076) (Guyer et al. 1981). Two bacteriophages, namely vB_SalM_MP82, vB_SalM_RMP11k are grown on the non-human pathogenic strain *Salmonella bongori* (ATCC 43975) and three bacteriophages, namely vB_SalM_TAT2F, vB_SalM_DIN2 and vB_SalS_OBO18 are grown on the non-human pathogenic strain *Salmonella paratyphi* B var. Java (ATCC BAA-1584) (Boyd et al. 1993).

E. coli K12 is not considered a human, animal or plant pathogen, nor is it toxicogenic (Environmental Protection Agency (1997a). *E. coli K12* has a history of safe use in the production of specialty chemicals and human drugs and was exempted from EPA review under TSCA § 725.420 (Toxic Substance Control Act) (Environmental Protection Agency (1997b). In addition, *E. coli* K1 derivatives have been used repeatedly in the production of GRAS notified food additives like α-cyclodextrin, GRAS Notice 000155, L-leucin, GRAS Notice 000308 and Lycopene, GRAS Notice 000299.

The two non-human pathogenic *Salmonella enterica* strains are known to produce no enterotoxins that could compromise the final product and have been considered safe for the production of salmonella-specific bacteriophages (GRAS Notice 000435).

II.7.2 Endotoxins (LPS)

Endotoxins are a class of lipopolysaccharides (LPS) that are located in the outer membrane of gram-negative bacteria like *Salmonella* and *E. coli*. Endotoxins can lead to sepsis (toxic shock syndrome) when they reach the human blood stream (*Pathophysiology of Shock, Sepsis, and Organ Failure* 2012). However, LPS is found everywhere in the environment and in large quantities in human food and in even higher concentrations in the human intestine (Im et al. 2012). For example,

milk contains 10^5 to 10^6 EU/mL (Gehring et al. 2008) or beef up to 7.5 x 10^4 EU/g (Jay et al. 1979). Consequently, no regulations for the presence of LPS in the human diet exist. During the destruction of the *Salmonella* or *E. coli* host by the bacteriophages in the fermentation process, up to 10^8 EU/mL LPS is released into the growth medium. However, most of the endotoxin is removed during the purification process described above, to a residual level of approximately 1 x 10^4 EU/mL, in the final "Applied Phage Meat S2" product. As the concentrated product is further diluted with water to reach the application concentration, the use of "Applied Phage Meat S2" will not significantly contribute to the LPS concentration naturally found in food.

II.8 Stability

Based on studies assessing the stability of the bacteriophage concentration and bacterial sterility, the shelf life of "Applied Phage Meat S2" is six months when stored at 2-10 °C (35.6 – 50 °F) in a dark, UV-protected area.

II.9 Intended Use

II.9.1 Description of Use

The bacteriophage cocktail, formulated as "Applied Phage Meat S2", is intended for use as an antimicrobial to control Salmonella enterica spp. that may be present in commercial slaughter operations when processing pork, beef or poultry. The phage preparation is applied at processing plant ambient temperature as a spray, using existing approved spray systems in meat processing facilities. The envisioned use is consistent with Good Manufacturing Practices and the expected efficacious dose lies between 1×10^5 to 1×10^7 phage particles per gram of treated meat, depending on the exact application.

II.9.2 Efficacy of Use

The "Applied Phage Meat S2" preparation has been shown to be effective in reducing the number of Salmonella counts in three meat model system assays for pork, beef and poultry. Briefly, meat cubes of consistent dimensions were first inoculated with 10³ cells of a Salmonella test strain per cm² of meat surface. Following a brief period to allow for adherence of the test bacteria to the substrate, the meat cubes were treated with "Applied Phage Meat S2" to a final concentration of 1 x 10⁷ PFU/cm². After incubation, the surface bacteria were counted. The results of the

studies indicate that the phage preparation can reduce the count of a *Salmonella* test strain by approximately 96% from pork, 91% from beef and 93% from chicken, respectively (Attachments VII, VIII and IX).

II.9.3 Demonstration of Regulation as a Processing Aid

The technical effect on the food of the phage preparation is measured by a reduction in the target *Salmonella* on the food and not by a measure of the absence or inactivation of phage particles on the food. It is not intended for the phage preparation to have an ongoing effect on the treated meat and technical studies using three meat model systems were undertaken to demonstrate that no ongoing effect occurs under conditions of the tests.

The data demonstrate a significant reduction in test *Salmonella* counts within four (4) hours of the phage treatment. Analysis at two (2) days and seven (7) days following phage treatment (samples held at 4°C to simulate plant conditions in cold boxes) found no further reduction in *Salmonella* counts, thus demonstrating that there is no ongoing technical effect on the treated meat (Attachments VII, VIII and IX).

These results are consistent with the known properties of the phages and their hosts, as well as processing parameters in the meat processing plant. Phage/host infection requires a physical contact between the phage and its host. Phages must either come into contact with the host as a direct result of the spray application or move to the host by passive diffusion in a liquid environment. Because phages and *Salmonella* are not mobile on dry surfaces such as fully chilled carcasses, the phage/host interaction will occur only during the time that the carcass is wet.

Once the carcass has dried, the phages and *Salmonella* hosts are essentially immobilized. Only phage/host interactions initiated while the carcass surface was wet will result in host killing, thereby limiting the technical effect to the early phases of the meat production process. The common practice of spray chilling of carcasses will also reduce phage numbers on the surface of carcasses.

In addition, phage infection and killing of the host depends on host metabolic functions. As meat carcasses are chilled to 4°C and all following steps of the process occur at refrigeration temperatures, new phage infections of the host are effectively eliminated.

USDA has determined and codified in FSIS Directive 7120.1 numerous

similar applications of phages to treat meat products, including poultry meat immediately prior to consumer packaging

(<u>https://www.fsis.usda.gov/policy/fsis-directives/7120.1</u> accessed July 29, 2021).

In summary, the phage preparation "Applied Phage Meat S2" will not have an ongoing technical effect on meat carcasses in the envisioned application for the following reasons:

- Phage infection of the *Salmonella* host is limited to the early phases of the meat processing process.
- Phages are removed from the carcasses during processing at various stages, depending on plant protocols.
- Phage / host interactions are inhibited at refrigeration temperatures in the post-chill supply chain.
- USDA has determined that similar phage technologies do not have an ongoing effect and are processing aids on meat and poultry products.

III. Dietary Exposure

The expected dietary exposure to *Salmonella*-specific phages as a result of the application of the phage preparation is insignificant and below the level of toxicological concern. Calculation of incremental exposure to the commercial preparation or incremental Estimated Dietary Intake (EDI) was done according to the following:

Assuming the following:

- •CEDI and EDI are assumed to be equal in this case as the phage preparation described herein is a new product and has no other approved applications.
- •According to the USDA, the average disappearance in 2020 was 281.3 pounds of red meat and poultry per capita per year. (https://www.ers.usda.gov/data-products/livestock-meat-domestic-data/)
- •All meat consumed in the US is treated with the phage preparation (highly conservative; see below)
- •Phage particle weight = 2×10^{-16} grams (Taylor, Epstein, and Lauffer 1955)(Giddings, Yang, and Myers 1977)(Mazzone, Engler, and Bahr 1980).
- •a realistic but high concentration of 1×10^7 PFU per gram of meat would be used.

NB: The calculations are extremely conservative for the following reason:

1. EDI assumes that all phages applied adhere to the meat but the application is by spray on hanging carcasses and runoff of the phage preparation is estimated to exceed 90%.

EDI Calculation

- 1. Weight of the phage in gram X Concentration of the phage applied per gram of treated meat = gram phage per gram of treated meat
- 2. Average meat consumption in US in (g)/person/year
- 3. Weight of phage/gram of treated meat X (Avg. meat consumption in US (g)/person/year / 365 days/year) = Incremental EDI as grams of phage consumed/person/day.

Following the above formula, we obtain:

- 1. Gram phage/ gram of treated meat = 2×10^{-16} g X 1 x 10^7 phage/gram of treated meat = 2×10^{-9} grams or $0.002 \mu g$
- 2. $281.3 \text{ lbs } X 1000 / 2.2 = 1.28 \times 10^5 \text{ g/year}$
- 3. Incremental EDI = $(0.002 \ \mu g/g \ of \ treated \ meat \ X \ 1.28 \ x \ 10^5 \ grams \ of$ Page 23 of 36

meat per year) / 365 days/year =

0.70 μg/person/day

Because the highly conservative, calculated incremental exposure to phages in consumed meat treated with phage preparation is less than 0.5 ppb in the total diet, no toxicological safety studies were done in accordance with FDA guidance in "Guidance for Industry: Summary Table of Recommended Toxicological Testing for Additives Used Food" (https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulator yInformation/default.htm) and "Guidance for Industry: Preparation of Food Contact Notifications for Food Contact Substances: Toxicology Recommendations":

(http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatory Information/ucm081825.htm#iva).

We further note that the incremental EDI above also implicitly assumes that every gram of meat consumed is treated, which is not the case. Specifically, the use as a spray treatment on carcasses means that only the surface of the carcass is exposed to the product. None of the interior muscle meat is intended to come in contact with the phage preparation. Thus, it is quite clear that the presence of the phage preparation is at "de minimus" levels on meat that would be consumed; and it is more likely that consumers will be exposed to phage from the environment rather than as a result of the use of the phage preparation.

Further, all other materials present in the phage preparation are either GRAS ingredients or approved food additives and thus present no risk to consumers of treated meat.

IV. Self-Limiting Levels of Use

None

V. Experience Based on Common Use in Food Before 1958

None and not applicable. Bacteriophages have not been used in foods before 1958. However, it is noted that bacteriophages are ubiquitous and are a normal component of our environment and food supply.

VI. Basis of Determination GRAS: Scientific Procedures

VI.1 Background on Salmonella

Foodborne illnesses caused by pathogenic *Salmonella* are a serious health burden worldwide. In the US alone the center for Disease Control estimates that *Salmonella* causes about 1.2 million illnesses, 23,000 hospitalizations, and 450 deaths every year, and that food is the source for about 1 million of these illnesses (CDC Salmonella). While food producers and food processors implemented strict monitoring programs, they do not always have access to active means to reduce the levels of *Salmonella* in food.

The bacteriophage cocktail, formulated as "Applied Phage Meat S2", offers a means to improve this situation. The application of "Applied Phage Meat S2" will reduce or eliminate contaminating Salmonella enterica spp. from meat. As shown for example in the accompanying studies where the application of "Applied Phage Meat S2" to raw pork, raw beef or raw chicken led to a reduction of the Salmonella count by 96%, 91% and 93% respectively (see Attachments VII, VIII and IX). As a consequence, the treated meat products would be safer and the number of foodborne illnesses could be reduced.

VI.2 Bacteriophages are omnipresent in the environment.

Large numbers of bacteriophages have been found in virtually every aquatic or terrestrial habitat where bacteria exist (Gómez and Buckling 2011)(Marston and Sallee 2003)(Clokie et al. 2011). The gut of mammals and humans is an especially rich source of bacteriophages (Dalmasso, Hill, and Ross 2014), many of which have been consumed via various foods (Kennedy, Oblinger, and Bitton 1984)(Atterbury et al. 2003)(Hsu, Shieh, and Sobsey 2002)(Suárez and Reinheimer 2002)(Kiliç et al. 1996). This abundance of bacteriophages in the environment and the continuous exposure of humans to them could explain the absence of any adverse effects in various safety studies in humans and animals (Carlton et al. 2005)(Chibani-Chennoufi et al. 2004)(Bruttin and Brüssow 2005) as well as in long term applications in human medicine (Weber-Dabrowska, Mulczyk, and Górski 2003)(Górski et al. 2009)(Kutter et al. 2010)(Kutateladze 2015).

VI.3 Lytic bacteriophages are GRAS

The biology of bacteriophages has been exhaustively studied in the 100 years since their discovery. Two major bacteriophage classes have been described, lytic and temperate. Temperate bacteriophages do not necessarily kill their host bacterium. They have the ability to passively invade a host and thereby are transferring their own genes from one host bacterium to the next, in a process called lysogenic conversion (Brüssow et

al. 2004)(Fortier and Sekulovic 2013). As some temperate bacteriophages may carry toxin genes (Davis et al. 2000)(Smith et al. 2012), they are not suited to be components of a bacteriophage cocktail produced and applied on an industrial scale. Lytic bacteriophages, on the other hand, lack the genes responsible for lysogenic conversion and an infection by a lytic bacteriophage always leads to the death of the bacterial host. Thus, lytic bacteriophages are safe for practical applications as they do not disseminate toxin genes. With the aid of comparative genomics, it is nowadays possible to clearly distinguish lytic from temperate bacteriophages and thus select only the former for a phage preparation like "Applied Phage Meat S2". Using in silico analyses the genomic information can also be used to show that lytic phages do not contain genes encoding for antibiotic resistance markers or allergens.

VI.4 Substantial equivalence to previously approved bacteriophage products.

Since the USFDA in 1996 approved a *Listeria*-specific bacteriophage preparation as food additive, several other products based on lytic bacteriophages, targeting various bacterial pathogens, have been designated GRAS and/or have been cleared for food safety usage by a number of regulatory agencies:

- ListexTM is a bacteriophage preparation containing a single *Listeria monocytogenes* lytic bacteriophage, P100, used for biocontrol of *Listeria* in susceptible foodstuffs, that is GRAS (GRAS Notice No. 000218)
- ListexTM is also listed by the USDA FSIS for use as processing aid for use on ready-to-eat meat products (FSIS Directive 8120.1)
- ListexTM is also approved as a processing aid for susceptible foodstuffs in many countries, including Canada, by Health Canada and FSANZ, Australia and New Zealand. The Dutch Ministry of Health has issued a formal statement, confirming that ListexTM can be used as a processing aid. Additionally, ListexTM has been approved for use in Switzerland in cheese-making and also as processing aid in keeping with European legislation on food safety.
- ListexTM is listed by the Organic Materials Review Institute (OMRI). This means that ListexTM may be used in the certified organic production of food, food processing and handling according to the USDA National Organic Program Rule.
- ListShieldTM is a bacteriophage preparation containing six lytic *Listeria monocytogenes*-specific bacteriophages, that is FDA-cleared as a food additive (21 CFRF§172.785)
- ListShieldTM is also listed by the USDA FSIS for use as processing aid with no labeling requirements when applied to various ready-to-eat meats

- and poultry products (FSIS Directive 7120.1).
- ListShieldTM is GRAS for direct application to fish and shellfish (including smoked varieties; e.g. smoked salmon), fresh and processed fruits, fresh and processed vegetables, and dairy products (including cheese) (GRAS notice No. 000528)
- ListShieldTM is also EPA-registered for use on non-food surfaces in food processing plants to prevent or significantly reduce contamination of *Listeria monocytogenes* (EPA registration #74234-1).
- ListShieldTM is Health Canada approved for use on ready-to-eat meat and poultry, smoked salmon, fresh cut apples and long leaf lettuce (iLONO).
- ListShieldTM is National Food Service of Israel approved as a food processing aid for the treatment of ready-to-eat meat and poultry products (Ref: 70275202).
- EcoShieldTM is a bacteriophage preparation containing three lytic bacteriophages specific against *E. coli* O157:H7, that is FDA-cleared through a "Food Contact Notification" for use on red meat parts and trim, intended to be ground (FCN no. 1018).
- EcoShieldTM is also listed by the USDA FSIS as safe and suitable for use in the production of red meat parts and trim prior to grinding as processing aid with no labeling requirements (FSIS Directive 7120.1).
- EcoShieldTM is Health Canada approved for use on red meat parts and trim prior to grinding (iLONO)
- EcoShieldTM is National Food Service of Israel approved as food processing aid for the treatment of meat immediately before grinding (Ref: 70275202).
- AgriPhageTM is a bacteriophage preparation targeting *Xanthomonas campestris* pv. *vesicatoria* and *Pseudomonas syringae* pv. *tomato* that is EPA-registered for use on tomatoes and peppers. AgriPhageTM can be applied directly as foliar spray and can be used as a curative on symptomatic plants or preventively prior to visual signs of damage (EPA Reg. No. 67986-1).
- AgriPhageTM has been amended to now include organic usage on tomato and pepper plants as governed by the USDA National Organic Program (NOP).
- AgriPhage-CMMTM is a bacteriophage preparation targeting *Clavibacter michiganensis* pv. *michiganensis*, that is EPA-registered for use on tomatoes. AgriPhage-CMMTM can be applied directly as a foliar spray and can be used as a curative on symptomatic plants or preventively prior to visual signs of damage (EPA Reg. No. 67986-6).
- The Canadian Pest Management Regulatory Agency (PMRA) has approved bio-pesticide AgriPhage-CMMTM for bacterial stem canker in

- tomato caused by Clavibacter michiganensis pv. michiganensis (30301)
- FinalyseTM is a bacteriophage preparation targeting *E. coli* O157:H7, that received USDA Food Safety and Inspection Services approval for commercialization and application as a spray mist or wash on live animals prior to slaughter to decrease pathogen transfer to meat.
- ArmamentTM is a bacteriophage preparation targeting *Salmonella*, that received USDA Food Safety and Inspection Services approval for the commercialization and application as a spray mist or wash on the feathers of live poultry prior to slaughter to decrease pathogen transfer to meat.
- SalmonelexTM is a bacteriophage preparation containing two specific bacteriophages, S16 and FO1a, for use as antibicrobial to control *Salmonella* serovars in ceartain pork and poultry products at levels up to 10⁸ PFU/g of food, that was designated as GRAS (GRAS Notice No. 000468).
- SalmoFreshTM is a bacteriophage preparation for controlling the foodborne bacterial pathogen *Salmonella enterica*, that is GRAS for direct application onto poultry, fish and shellfish and fresh and processed fruits and vegetables (GRAS Notice No. 000435).
- SalmoFreshTM is also FSIS-listed as safe and suitable as antimicrobial for use in the production of poultry products as a processing aid with no labeling requirements (FSIS Directive 7120.1).
- SalmoFreshTM is Health Canada approved as a processing aid for use on fish, shellfish and fresh and processed fruits and vegetables or on ready-to-eat poultry products prior to slicing and on raw poultry prior to grinding or after grinding (iLONO).
- SalmoFreshTM is National Food Service of Israel approved as a food processing aid for the treatment of fish, shellfish, fresh and processed fruits and vegetables and poultry immediately before or aftergrinding and on ready- to-eat products before slicing (Ref: 70275202).
- Secure Shield E1, a bacteriophage preparation that specifically targets shiga toxin-producing *E. coli* O157:H7 as well as non-O157:H7 shiga toxin producing *E. coli*. that is GRAS for the application on beef carcasses (GRAS Notice No. 000724).
- A preparation containing the bacterial monophages, BP-63 and LVR16-A, specific to *Salmonella* for use as an antimicrobial processing aid (GRAS Notice No. 000752).
- A preparation containing two bacterial phages specific to *E. coli* O157 for use as an antimicrobial on beef carcasses, subprimals, beef cuts and trimmings (GRAS Notice No. 000757).
- A preparation containing three bacterial phages specific to several *E. coli* serotypes for use as an antimicrobial processing aid to control specific *E. coli* serotypes on poultry, red meats, fruits, vegetables, eggs, fish, and

shellfish applied to food surfaces (GRAS Notice No. 000827).

- A preparation containing bacterial phages specific to shiga-toxin producing *E. coli* for use as an antimicrobial to control *E. coli* on food when applied to ground and whole meat and poultry, including whole carcasses, primals and subprimals, trimmings and organs; ready-to-eat meats and poultry; fresh and processed fruits; fresh and processed vegetables; dairy products (including cheese); and fish and other seafood (GRAS Notice No. 000834).
- A preparation containing three bacterial phages specific to *Salmonella* intended for use as an antimicrobial on food to control *Salmonella* (GRAS Notice No. 000888).
- A preparation containing three bacteriophages specific to *Salmonella enterica* serovars for use as antimicrobial on intact poultry, intact red meat, eggs, fruits, vegetables, fish (excluding catfish) and shellfish (GRAS Notice No. 000917).
- A preparation containing three to eight bacteriophages specific to *Campylobacter jejuni*, intended for use as an antimicrobial on raw and ground poultry, and raw red meat products (GRAS Notice No. 000966).

Several regulatory agencies are represented in the preceding list, each of which separately determined that different bacteriophage preparations are safe. The bacteriophage cocktail "Applied Phage Meat S2" is substantially equivalent to the above-mentioned bacteriophage products and should therefore also be considered GRAS.

VI.5 Raw material Safety.

All the raw materials used in the fermentation and manufacture of the GRAS substances are food grade and are permitted in the manufacture of food (see section II.2.6).

VI.6 Summary and basis for GRAS.

"Applied Phage Meat S2" is a bacteriophage cocktail specific against Salmonella enterica spp. To reach such a broad coverage, a panel of elven lytic bacteriophages was compiled and characterized in detail. All the evidence presented above as well as evidence collected from the scientific literature indicates that the individual lytic bacteriophages, their composition in a cocktail and the bacterial fermentation process used to produce them are safe. Humans are exposed to large numbers of bacteriophages on a daily basis and consume them naturally through food and water, without any noticeable effects. The treatment of raw meat

with "Applied Phage Meat S2" would not significantly increase this natural consumption of bacteriophages. However, the desired reduction of pathogenic bacteria present on the meat would make it safer for human consumption. Based on these findings and also the significant equivalence of "Applied Phage Meat S2" to other GRAS- approved products, the scientists of the FINK TEC GmbH came to the conclusion that "Applied Phage Meat S2" should be considered GRAS.

VII. References

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VIII. Links

Leibniz Institute DSMZ – German Collection of Microorganisms and Cultures: (https://www.dsmz.de/home.html)

USDA FSIS Directive 7120.1:

(https://www.fsis.usda.gov/policy/fsis-directives/7120.1)

Environmental Protection Agency (1997a) Final risk assessment of *Escherichia coli K-12* derivatives:

(http://www.epa.gov/sites/production/files/2015-09/documents/fra004.pdf).

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(https://www.gpo.gov/fdsys/pkg/FR-1997-04-11/pdf/97-8669.pdf).

USDA, average disappearance in 2020:

(https://www.ers.usda.gov/data-products/livestock-meat-domestic-data/)

FDA "Guidance for Industry: Summary Table of Recommended Toxicological Testing for Additives Used in Food" June 2006

(https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/default.htm)

FDA "Guidance for Industry: Preparation of Food Contact Notifications for Food Contact Substances: Toxicology Recommendations":

(http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm081825.htm#iva)

Host spectrum analysis of the "Applied Phage Meat S2" component phages based on titration assays on Salmonella enterica spp.

Study Number # R018-007_HS

PTC Phage Technology Center GmbH

Siemensstraße 42

D- 59199 Bönen

Tel.: 49 (0) 2383 919 175

Fax: 49 (0) 2383 919 179

Dr. Michael Fink

FINK TEC GmbH

Oberster Kamp 23

D-59069 Hamm

Tel.: 49 (0) 2385 730

1. STUDY TITLE

Host spectrum analysis of the "Applied Phage Meat S2" component phages based on titration assays on Salmonella enterica spp.

2. STUDY DIRECTOR

Hansjörg Lehnherr, Ph.D.

3. STUDY PERSONNEL

The following personnel contributed to the conduct and reporting of the studies reported herein:

Name: Title: Role:

Hansjörg Lehnherr, Ph.D. Chief scientist Study director

Andrea Kroj, Ph.D. Research scientist Hands-on-research

4. PERFORMING LABORATORY

PTC Phage Technology Center GmbH Siemensstraße 42 D- 59199 Bönen

Tel.: 49 (0) 2383 919 174 Fax: 49 (0) 2383 919 179

5. STUDY OBJECTIVE

To determine the coverage of a collection of *Salmonella enterica* spp. strains by the "Applied Phage Meat S2" component phages. The host range analyses were based titration assays with the overlay agar method.

6. PHAGES

The phage preparations used for the host spectrum analyses are listed below:

Table 1: Phage data

Pha	ige	Date/# ChB.	Titer [PFU/mL]		
DSM #	Internal #	Date/# CnB.			
DSM 26158	ELB17	10.06.2020	8 x 10 ⁸		
DSM 26173	MP82	04.09.2019	4 x 10 ⁹		
DSM 33039	KAZ99a	05.08.2020	2.5 x 10 ⁸		
DSM 33040	RMP11k	22.04.2020	2 x 10 ⁸		
DSM 33043	RMS3b	12.06.2019	2 x 10 ¹⁰		
DSM 33044	TAT2F	01.04.2020	1 x 10 ⁹		
DSM 33045	DIN2	01.04.2020	4 x 10 ⁸		
DSM 26125	MP75	14.08.2020	7 x 10 ¹⁰		
DSM 104021	FV7M4	08.04.2020	6 x 10 ⁹		
DSM 26157	RMP9	04.09.2019	1 x 10 ¹⁰		
DSM33041	OBO18	12.02.2020	3 x 10 ¹⁰		

7. BACTERIAL STRAINS USED FOR HOST RANGE ANALYSES

The following 41 *Salmonella enterica* spp. bacterial serovars were used to determine the host range of the "Applied Phage Meat S2" component phages:

S. agona	S. anatum	S. brandenburg	S. choleraesius			
S. decatur	S. derby	S. dublin	S. duisburg			
S. emek	S. enterica	S. enteritidis	S. gallinarum			
S. haifa	S. heidelberg	S. indiana	S. infantis			
S. java	S. kiambu	S. livingstone	S. London			
S. miami	S. minnesota	S. montevideo	S. muenchen			
S. newport	S. panama	S. parathyphi A	S. paratyphi B			
S. paratyphi C	S. pullorum	S. rubislaw	S. saintpaul			
S. sendai	S. senftenberg	S. stanley	S. stanleyville			
S. thompson	S. typhimurium	S. tyhpisuis	S. virchow			
S. wien						

8. MEDIA AND REAGENTS

All media and reagents were sterilized before usage.

- LB broth Lennox (Roth, Karlsruhe, Germany; catalog # X964.4)
- LB agar Lennox (Roth, Karlsruhe, Germany; catalog # X965.2)
- Agar-Agar, Kobe I (Roth, Karlsruhe, Germany; catalog # 5210.2)
- LB top agar (LB broth with 0.6 % Agar-Agar)

9. GENERAL OUTLINE OF STUDY

- Overnight cultures of the bacterial test strains were grown in LB medium at 37°C. The LB top agar was melted and kept in a water bath at 55°C.
- The phage preparations were serially diluted in LB medium.
- 100 μ L of the overnight bacterial culture were mixed with 100 μ L of a phage dilution and 4 mL melted, warm top agar. The mixture was vortexed and distributed on LB agar plates.
- After solidification of the agar, the LB agar plates were incubated at 37°C for 16 h.
- The ability of a phage to form single plaques in the bacterial lawn was classified as positive phage-host interaction.

10. RESULTS

1. Raw Data

Table 2: Coverage of 41 Salmonella enterica serovars by the "Applied Phage Meat S2" component phages.

Salmonella strains	Phages										
Sumonena strains	FV7M4	MP82	RMP9	OBO18	DIN2	TAT2F	RMS3b	RMP11k	MP75	KAZ99a	ELB17
S. agona	-	-	-	-	+	-	-	-	-	+	-
S. anatum	-	-	+	-	+	+	-	+	-	-	-
S. brandenburg	-	-	-	-	+	-	-	-	+	-	-
S. choleraesuis	+	+	+	-	+	+	+	+	-	+	-
S. decatur	-	-	+	-	-	+	+	+	-	+	-
S. derby	-	+	+	+	+	+	+	+	+	-	-
S. dublin	+	+	-	+	+	+	+	+	+	+	-
S. duisburg	-	-	+	-	-	+	+	+	+	+	-
S. emek	-	-	-	-	-	-	-	-	+	-	+
S. enterica	-	-	-	+	-	+	+	+	+	+	-
S. enteritidis	-	+	-	+	-	+	+	+	+	+	+
S. gallinarum	-	-	-	+	-	+	-	+	+	+	-
S. haifa	-	-	+	-	-	-	-	-	-	-	+
S. heidelberg	-	+	+	+	+	+	+	+	+	+	+
S. indiana	+	-	+	1	-	+	+	+	+	+	-
S. infantis	+	+	+	-	+	+	+	+	-	+	-
S. java	+	-	+	-	+	+	+	+	+	+	-
S. kiambu	-	-	-	-	+	-	-	-	+	-	-
S. livingstone	-	+	+	-	+	-	+	-	-	+	-
S. Iondon	-	+	-	-	+	-	-	-	-	-	+
S. miami	-	+	-	-	+	+	+	+	+	+	-
S. minnesota	-	-	-	-	+	+	+	+	-	+	-
S. montevideo	-	-	-	-	-	+	-	+	-	-	-
S. muenchen	+	+	+	+	+	+	+	+	+	+	+
S. newport	-	+	-	+	+	+	+	+	-	+	-
S. panama	-	-	+	+	-	+	+	+	+	+	-
S. paratyphi A	-	-	+	-	-	+	+	+	-	+	-
S. paratyphi B	+	+	-	-	-	+	+	+	+	+	+
S. paratyphi C	+	+	+	+	+	+	+	+	+	+	-
S. pullorum	-	-	-	+	+	+	+	+	+	+	-
S. rubislaw	-	+	+	-	-	+	+	+	-	+	-
S. saintpaul	+	-	-	-	+	+	+	+	+	+	+
S. sendai	-	-	-	-	-	-	-	+	-	+	+
S. senftenberg	-	+	-	-	-	-	-	-	-	-	+
S. stanley	-	-	-	-	-	+	+	+	+	+	-
S. stanleyville	-	-	+	-	-	+	+	+	+	+	-
S. thompson	-	+	-	-	+	+	+	+	-	+	-
S. typhimurium	-	+	+	+	-	+	+	+	+	+	+
S. typhisuis	-	+	-	-	+	+	+	+	-	+	-
S. virchow	-	+	-	-	-	+	+	+	-	+	-
S. wien	-	+	-	-	-	+	+	+	-	+	-

 Table 2: Ranked coverage

Salmonella	Phages							Pos.				
strains	RMP11k	KAZ99a	TAT2F	RMS3b	MP75	DIN2	MP82	RMP9	OBO18	ELB17	FV7M4	int./strain
S. muenchen	+	+	+	+	+	+	+	+	+	+	+	11
S. heidelberg	+	+	+	+	+	+	+	+	+	+	-	10
S. paratyphi C	+	+	+	+	+	+	+	+	+	-	+	10
S. dublin	+	+	+	+	+	+	+	-	+	-	+	9
S. typhimurium	+	+	+	+	+	-	+	+	+	+	-	9
S. choleraesuis	+	+	+	+	-	+	+	+	-	-	+	8
S. derby	+	-	+	+	+	+	+	+	+	-	-	8
S. enteritidis	+	+	+	+	+	-	+	-	+	+	-	8
S. infantis	+	+	+	+	-	+	+	+	-	-	+	8
S. java	+	+	+	+	+	+	-	+	-	-	+	8
S. paratyphi B	+	+	+	+	+	-	+	-	-	+	+	8
S. saintpaul	+	+	+	+	+	+	-	-	-	+	+	8
S. indiana	+	+	+	+	+	-	-	+	-	-	+	7
S. miami	+	+	+	+	+	+	+	-	-	-	-	7
S. panama	+	+	+	+	+	-	-	+	+	-	-	7
S. newport	+	+	+	+	-	+	+	-	+	-	-	7
S. pullorum	+	+	+	+	+	+	-	-	+	-	-	7
S. duisburg	+	+	+	+	+	-	-	+	-	-	-	6
S. enterica	+	+	+	+	+	-	-	-	+	-	-	6
S. rubislaw	+	+	+	+	-	-	+	+	-	-	-	6
S. stanleyville	+	+	+	+	+	-	-	+	-	-	-	6
S. thompson	+	+	+	+	-	+	+	-	-	-	-	6
S. typhisuis	+	+	+	+	-	+	+	-	-	-	-	6
S. decatur	+	+	+	+	-	-	-	+	-	-	-	5
S. gallinarum	+	+	+	-	+	-	-	-	+	-	-	5
S. livingstone	-	+	-	+	-	+	+	+	-	-	-	5
S. minnesota	+	+	+	+	-	+	-	-	-	-	-	5
S. paratyphi A	+	+	+	+	-	-	-	+	-	-	-	5
S. stanley	+	+	+	+	+	-	-	-	-	-	-	5
S. virchow	+	+	+	+	-	-	+	-	-	-	-	5
S. wien	+	+	+	+	-	-	+	-	-	-	-	5
S. anatum	+	-	+	-	-	+	-	+	-	-	-	4
S. london	-	-	-	-	-	+	+	-	-	+	-	3
S. sendai	+	+	-	-	-	-	-	-	-	+	-	3
S. agona	-	+	-	-	-	+	-	-	-	-	-	2
S. brandenburg	-	-	-	-	+	+	-	-	-	-	-	2
S. emek	-	-	-	-	+	-	-	-	-	+	-	2
S. haifa	-	-	-	-	-	-	-	+	-	+	-	2
S. kiambu	-	-	-	-	+	+	-	-	-	-	-	2
S. montevideo	+	-	+	-	-	-	-	-	-	-	-	2
S. senftenberg	-	-	-	l -	-	l -	+	-	-	+	-	2
Pos. int./phage	33	32	32	30	22	21	20	18	12	11	9	

Abbreviations: Pos. int./phage Positive interactions per phage Pos. int./strain Positive interactions per strain

2. Interpretation of the results

All 41 Salmonella enterica serovars tested were sensitive to at least two genetically independent component phages of the "Applied Phage Meat S2" bacteriophage product. The most sensitive serovar, S. muenchen, in fact was supporting the growth of all eleven component phages. Four component phages, namely RMP11k, KAZ99a, TAT2F and RMS3b showed a very broad host range with over 30/41 positive interactions. Since the individual host ranges varied, the different component phages complement each other, increasing the total coverage, which is important for the composition of an efficient phage product like "Applied Phage Meat S2". This information will be used to choose six out of eleven component phages in order to produce an "Applied Phage Meat S2" product with an optimal range of activity, adjusted to the serovars present in an individual meat production facility.

11. SUMMARY CONCLUSION OF THE STUDY

For the present study a set 41 of Salmonella enterica spp. serovars with relevance in the area of meat production was collected. All these serovars where covered by at least two of the eleven component phages of "Applied Phage Meat S2". By a combination of component phages with complementary host preferences it is possible to generate an "Applied Phage Meat S2" product with a broad range of activity.

12. SIGNATURES	
	10.02.2021
Andrea Kroj, Ph.D.	Date
Research scientist	
	10.02.2021
Hansjörg Lehnherr, Ph.D.	Date
Study director	

Attachment II

Bioninformatic analyses of Salmonella phages.

The genomes of all bacteriophages were determined using Next Generation Sequencing (Illumina technology). They were analyzed using standard bioinformatics methods with the help of a commercially available software package "Geneious" version 4.8 (Biomatters Ltd, New Zealand), as well as the search engines BLASTN, BLASTX and BLASTP provided online by NCBI (Bethesda, USA) together with the "Genbank" database containing all genomic information available up to date.

PHAGE ELB17 HOST Salmonella

GENOME MOLECULE DNA
GENOME SIZE 241840 bp, 267 genes

Seventy-three pages of confidential business information removed.

PHAGE MP82
HOST Salmonella
GENOME MOLECULE DNA

GENOME SIZE 138668 bp, 260 genes

Fifty-one pages of confidential business information removed.

PHAGE KAZ99a
HOST Salmonella
GENOME MOLECULE DNA

GENOME SIZE 82441 bp, 153 genes

Twenty-seven pages of confidential business information removed.

PHAGE RMP11k HOST Salmonella

GENOME MOLECULE DNA

GENOME SIZE 84771 bp, 150 genes

Twenty-eight pages of confidential business information removed.

PHAGE RMS3b
HOST Salmonella
GENOME MOLECULE DNA

GENOME SIZE 82827 bp, 159 genes

Twenty-seven pages of confidential business information removed.

PHAGE TAT2F
HOST Salmonella
GENOME MOLECULE DNA

GENOME SIZE 85108 bp, 154 genes

Twenty-eight pages of confidential business information removed.

PHAGE DIN2
HOST Salmonella
GENOME MOLECULE DNA
GENOME SIZE 53642 bp, 77 genes

Sixteen pages of confidential business information removed.

PHAGE MP75
HOST Salmonella
GENOME MOLECULE DNA

GENOME SIZE 158040 bp, 218 genes

Fifty pages of confidential business information removed.

PHAGE FV7M4
HOST Salmonella
GENOME MOLECULE DNA

GENOME SIZE 46741 bp, 82 genes

Fifteen pages of confidential business information removed.

PHAGE RMP9
HOST Salmo

HOST Salmonella
GENOME MOLECULE DNA

GENOME SIZE 61148 bp, 78 genes

Nineteen pages of confidential business information removed.

PHAGE OBO18
HOST Salmonella

GENOME MOLECULE DNA

GENOME SIZE 41513 bp, 57 genes

Thirteen pages of confidential business information removed.

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Output

VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Virulence genes for Escherichia coli

Query / Template length Contig Position in contig Virulence factor Identity **Protein function** Accession number

No hit found

Shiga-toxin genes

Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: ELB17.txt

CITATIONS

For publication of results, please cite:

 Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli.
 Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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Center for Genomic Epidemiology, DTU, Kemitorvet, Building 204, 2800 Kgs. Lyngby, Denmark
Contact: Vibeke Dybdahl Hammer, Telephone: +45 3588 6420, E-mail: vdha@food.dtu.dk
Funded by: The Danish Council for Strategic Research
Last modified May 22, 2012 11:08:01 GMT

Center for Genomic Epidemiology



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VirulenceFinder-2.0 Server - Results

Identity

Organism(s): Escherichia coli

Virulence genes for Escherichia coli Query / Template length Contig Position in contig Protein function Accession number

Virulence factor No hit found

Shiga-toxin genes

Virulence factor Identity Query / Template length Contig Position in contig Accession number Protein function

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: MP82.txt

CITATIONS

For publication of results, please cite:

 Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli. Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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Center for Genomic Epidemiology, DTU, Kemitorvet, Building 204, 2800 Kgs. Lyngby, Denmark
Contact: Vibeke Dybdahl Hammer, Telephone: +45 3588 6420, E-mail: vdha@food.dtu.dk
Funded by: The Danish Council for Strategic Research
Last modified May 22, 2012 11:08:01 GMT

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Virulence genes for Escherichia coli

Virulence factor Identity Query / Template length Contig Position in contig Protein function Accession number

No hit found

Shiga-toxin genes

Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: KAZ99a.txt

CITATIONS

For publication of results, please cite:

 Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli.
 Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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Center for Genomic Epidemiology, DTU, Kemitorvet, Building 204, 2800 Kgs. Lyngby, Denmark
Contact: Vibeke Dybdahl Hammer, Telephone: +45 3588 6420, E-mail: vdha@food.dtu.dk
Funded by: The Danish Council for Strategic Research
Last modified May 22, 2012 11:08:01 GMT



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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Virulence genes for Escherichia coli

Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number

No hit found

Shiga-toxin genes

Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: RMP11k.txt

CITATIONS

For publication of results, please cite:

· Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli. Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Shiga-toxin genes

Virulence factor Query / Template length Identity Contig Position in contig Protein function Accession number

No hit found

Virulence genes for Escherichia coli

Virulence factor Identity Query / Template length Contig Position in contig Protein function Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: RMS3b.txt

CITATIONS

For publication of results, please cite:

 Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Virulence genes for Escherichia coli

Query / Template length Position in contig Virulence factor Identity Contig Protein function Accession number

No hit found

Shiga-toxin genes

Virulence factor Identity Query / Template length Contig Position in contig Protein function Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: TAT2F.txt

CITATIONS

For publication of results, please cite:

 Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli.
 Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM.
 J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Shiga-toxin genes

Query / Template length Virulence factor Identity Contig Position in contig Protein function Accession number

No hit found

Virulence genes for Escherichia coli

Virulence factor Query / Template length Contig Position in contig Accession number Identity **Protein function**

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: DIN2.txt

CITATIONS

For publication of results, please cite:

· Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli. Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Virulence genes for Escherichia coli

Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number

No hit found

Shiga-toxin genes

Query / Template length Virulence factor Identity Contig Position in contig Protein function Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: MP75.txt

CITATIONS

For publication of results, please cite:

· Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli. Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Virulence genes for Escherichia coli

Virulence factor Identity Query / Template length Contig Position in contig Protein function Accession number

No hit found

Shiga-toxin genes

Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: FV7M4.txt

CITATIONS

For publication of results, please cite:

 Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli.
 Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Shiga-toxin genes

Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number

No hit found

Virulence genes for Escherichia coli

Virulence factor Identity Query / Template length Contig Position in contig Protein function Accession number

No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: RMP9.txt

CITATIONS

For publication of results, please cite:

· Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM. J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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VirulenceFinder-2.0 Server - Results

Organism(s): Escherichia coli

Virulence genes for Escherichia coli Virulence factor Identity Query / Template length Contig Position in contig Protein function Accession number No hit found Shiga-toxin genes Virulence factor Identity Query / Template length Contig Position in contig **Protein function** Accession number No hit found

extended output

Results as text Results tsv Hits in genome seqs Virulence factor seqs

Input Files: OBO18.txt

CITATIONS

For publication of results, please cite:

 Real-time whole-genome sequencing for routine typing, surveillance, and outbreak detection of verotoxigenic Escherichia coli.
 Joensen KG, Scheutz F, Lund O, Hasman H, Kaas RS, Nielsen EM, Aarestrup FM.
 J. Clin. Micobiol. 2014. 52(5): 1501-1510. View the abstract

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Attachment V: Genome safety of the component phages of the "Applied Phage Meat S2" product against Salmonella enterica spp.

		Presence of	L-11 Edition)	Presence of the			
DSM name	Phage internal name	protein synthesis inhibitors	neuro- toxins	Oxygen- liable cytolysins	toxins affecting membrane integrity & functions	general cytotoxins	listed in the VirulenceFinder database
DSM 33041	OBO18	none	none	none	none	none	none
DSM 26125	FV7M4	none	none	none	none	none	none
DSM 26157	RMP9	none	none	none	none	none	none
DSM 26158	ELB17	none	none	none	none	none	none
DSM 33045	DIN2	none	none	none	none	none	none
DSM 26173	MP82	none	none	none	none	none	none
DSM 104023	MP75	none	none	none	none	none	none
DSM 33043	RMS3b	none	none	none	none	none	none
DSM 33039	KAZ99a	none	none	none	none	none	none
DSM 33040	RMP11k	none	none	none	none	none	none
DSM 33044	TAT2F	none	none	none	none	none	none

Attachment VI

Allergen search procedure

Allergen search was carried out against the database AllergenOnline of the University of Nebraska (version 16 released on January 27, 2016) using the recommended algorithm according to Codex Alimentarius 2003 [1] and the AllergenOnline website [2] as followed:

A sliding window of amino acid sequence 80mers of each phage protein was compared to the allergen database by local alignment search using FASTA (Version 36.3.8c Dec 2015, BL50 Blossum scoring matrix ktup:2 and gap open/ext: 20/10).

According to Codex Alimentarius, IgE cross-reactivity between phage proteins and known allergens was considered a possibility for more than 35% identity in a segment of 80 amino acids (80mer). All tested 80mers of phage proteins had identity to known allergens below 35% (see Table 1). Therefore no IgE cross-reactivity with phage proteins is to be expected according to the standards of the Codex Alimentarius and the AllergenOnline website. Detailed search results for all phages are provided below. Files show 80mer similarities from highest to lower values (see file names in Table 1).

Table 1. Highest similarity scores between phage protein 80mers and the AllergenOnline database. No similarity equal or higher than 35% has been found.

Phage name	Phage protein showing the highest similarity in 80mer	highest similarity in 80mer	detailed search result on page
ELB17	gp239	27.5%	2-5
MP82	gp42	30%	6-14
KAZ99a	gp73	28.8%	15-16
RMP11k	gp127	27.5%	17
RMS3b	gp78	28.8%	18-19
TAT2F	gp131	27.5%	20
DIN2	gp32	28.7%	21
MP75	gp35 and gp103	25%	22
FV7M4	gp17	26.2%	23
RMP9	gp23	27.5%	24-25
OBO18	gp42	27.5%	26-27

References:

[1] Codex Alimentarius Commission, 2003. Alinorm 03/34: Joint FAO/WHO Food Standard Programme, Codex Alimentarius Commission, Twenty-Fifth Session, Rome, Italy 30 June-5 July, 2003. Appendix III and Appendix IV Section 3.2: *Annex on the assessment of possible allergenicity*, pp. 47-60

[2] http://www.allergenonline.org/

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
ELB17_gp239	gi 18093971 emb CAD20405.1	30.14	73	51	0	1	73	30	102	0.53	26.2	27.5
ELB17_gp239	gi 2266625 emb CAB10765.1	27.85	79	57	0	1	79	29	107	0.42	26.6	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	29.73	74	52	0	7	80	29	102	0.53	26.2	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	29.73	74	52	0	6	79	29	102	0.53	26.2	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	29.73	74	52	0	5	78	29	102	0.53	26.2	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	29.73	74	52	0	4	77	29	102	0.53	26.2	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	29.73	74	52	0	3	76	29	102	0.53	26.2	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	29.73	74	52	0	2	75	29	102	0.53	26.2	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	29.73	74	52	0	1	74	29	102	0.53	26.2	27.5
ELB17_gp239	gi 2266625 emb CAB10765.1	27.5	80	58	0	1	80	28	107	0.26	27.2	27.5
ELB17_gp239	gi 18093971 emb CAD20405.1	28.77	73	52	0	8	80	29	101	0.53	26.2	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.77	73	52	0	1	73	55	127	1.5	24.9	26.3
ELB17_gp239	gi 15886861 emb CAC85911.1	28.38	74	53	0	7	80	30	103	1.1	25.5	26.3
ELB17_gp239	gi 15886861 emb CAC85911.1	28.38	74	53	0	6	79	30	103	1.1	25.5	26.3
ELB17_gp239	gi 15886861 emb CAC85911.1	28.38	74	53	0	5	78	30	103	1.1	25.5	26.3
ELB17_gp239	gi 15886861 emb CAC85911.1	28.38	74	53	0	4	77	30	103	1.1	25.5	26.3
ELB17_gp239	gi 15886861 emb CAC85911.1	28.38	74	53	0	3	76	30	103	1.1	25.5	26.3
ELB17_gp239	gi 15886861 emb CAC85911.1	28.38	74	53	0	2	75	30	103	1.1	25.5	26.3
ELB17_gp239	gi 15886861 emb CAC85911.1	28.38	74	53	0	1	74	30	103	1.1	25.5	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.38	74	53	0	7	80	54	127	1.5	24.9	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.38	74	53	0	6	79	54	127	1.5	24.9	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.38	74	53	0	5	78	54	127	1.5	24.9	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.38	74	53	0	4	77	54	127	1.5	24.9	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.38	74	53	0	3	76	54	127	1.5	24.9	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.38	74	53	0	2	75	54	127	1.5	24.9	26.3
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	28.38	74	53	0	1	74	54	127	1.5	24.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	11	80	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	11	80	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	10	79	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	10	79	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	9	78	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	9	78	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	8	77	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	8	77	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	7	76	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	7	76	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	6	75	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	6	75	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	5	74	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	5	74	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	4	73	169	238	0.0042	34.9	26.3

ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	4	73	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	3	72	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70	49	0	3	72	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 442577833 gb AGC60020.1	30	70	49	0	2	71	169	238	0.0042	34.9	26.3
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	26.58	79	58	0	2	80	150	228	0.0016	36.3	26.2
ELB17_gp166	gi 442577833 gb AGC60020.1	26.58	79	58	0	2	80	150	228	0.0016	36.3	26.2
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	26.58	79	58	0	1	79	150	228	0.0016	36.3	26.2
ELB17_gp166	gi 442577833 gb AGC60020.1	26.58	79	58	0	1	79	150	228	0.0016	36.3	26.2
ELB17_gp239	gi 2266625 emb CAB10765.1	26.92	78	57	0	3	80	28	105	0.33	26.9	26.2
ELB17_gp239	gi 2266625 emb CAB10765.1	26.92	78	57	0	2	79	28	105	0.33	26.9	26.2
ELB17_gp82	gi 2114497 gb AAB58417.1	25.32	79	59	0	2	80	27	105	0.0039	33.3	25.0
ELB17_gp82	gi 2114497 gb AAB58417.1	25.32	79	59	0	1	79	27	105	0.0039	33.3	25.0
ELB17_gp82	gi 2114497 gb AAB58417.1	25.32	79	59	0	2	80	29	107	0.0019	34.3	25.0
ELB17_gp82	gi 2114497 gb AAB58417.1	25.32	79	59	0	1	79	29	107	0.0019	34.3	25.0
ELB17_gp32	gi 332278195 sp Q40240.2 MPA5A_LOLPR	26.67	75	55	0	6	80	75	149	2	24.5	25.0
ELB17_gp32	gi 332278195 sp Q40240.2 MPA5A_LOLPR	26.67	75	55	0	5	79	75	149	2	24.5	25.0
ELB17_gp32	gi 332278195 sp Q40240.2 MPA5A_LOLPR	26.67	75	55	0	4	78	75	149	2	24.5	25.0
ELB17_gp32	gi 332278195 sp Q40240.2 MPA5A_LOLPR	26.67	75	55	0	3	77	75	149	2	24.5	25.0
ELB17_gp32	gi 332278195 sp Q40240.2 MPA5A_LOLPR	26.67	75	55	0	2	76	75	149	2	24.5	25.0
ELB17_gp32	gi 332278195 sp Q40240.2 MPA5A_LOLPR	26.67	75	55	0	1	75	75	149	2	24.5	25.0
ELB17_gp239	gi 2266625 emb CAB10765.1	27.03	74	54	0	7	80	28	101	1.1	25.2	25.0
ELB17_gp239	gi 2266625 emb CAB10765.1	27.03	74	54	0	6	79	28	101	1.1	25.2	25.0
ELB17_gp239	gi 2266625 emb CAB10765.1	27.03	74	54	0	5	78	28	101	1.1	25.2	25.0
ELB17_gp239	gi 2266625 emb CAB10765.1	27.03	74	54	0	4	77	28	101	1.1	25.2	25.0
ELB17_gp239	gi 15886861 emb CAC85911.1	27.4	73	53	0	1	73	31	103	3.6	23.9	25.0
ELB17_gp239	gi 14423124 gb AAK62278.1 AF325267_1	27.4	73	53	0	8	80	54	126	1.5	24.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	8	80	46	118	0.021	30.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	7	79	46	118	0.021	30.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	6	78	46	118	0.021	30.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	5	77	46	118	0.021	30.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	4	76	46	118	0.021	30.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	3	75	46	118	0.021	30.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	2	74	46	118	0.021	30.9	25.0
ELB17_gp82	gi 94468546 gb ABF18122.1	27.4	73	53	0	1	73	46	118	0.021	30.9	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	20	80	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	19	79	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	18	78	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	17	77	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	16	76	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	15	75	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	14	74	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	13	73	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	12	72	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	11	71	64	124	0.0079	31.3	25.0
ELB17_gp32	gi 291482310 emb CBK62695.1	32.79	61	41	0	10	70	64	124	0.0079	31.3	25.0
ELB17_gp239	gi 15886861 emb CAC85911.1	27.78	72	52	0	1	72	32	103	5.8	23.2	25.0
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ELB17_gp239	gi 113561 sp P22285.1 MPA92_POAPR	41.67	48	28	0	2	49	284	331	0.013	31.9	25.0
ELB17_gp239	gi 113561 sp P22285.1 MPA92_POAPR	41.67	48	28	0	1	48	284	331	0.013	31.9	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	27.78	72	52	0	7	78	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 442577833 gb AGC60020.1	27.78	72	52	0	7	78	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 442577833 gb AGC60020.1	27.78	72	52	0	6	77	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	27.78	72	52	0	6	77	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 442577833 gb AGC60020.1	27.78	72	52	0	5	76	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	27.78	72	52	0	5	76	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 442577833 gb AGC60020.1	27.78	72	52	0	4	75	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	27.78	72	52	0	4	75	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 442577833 gb AGC60020.1	27.78	72	52	0	3	74	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	27.78	72	52	0	3	74	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 442577833 gb AGC60020.1	27.78	72	52	0	2	73	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	27.78	72	52	0	2	73	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 442577833 gb AGC60020.1	27.78	72	52	0	1	72	157	228	0.0033	35.3	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	27.78	72	52	0	1	72	157	228	0.0033	35.3	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	24	80	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	24	80	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	23	79	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	23	79	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	22	78	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	22	78	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	21	77	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	21	77	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	20	76	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	20	76	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	19	75	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	19	75	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	18	74	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	18	74	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	17	73	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	17	73	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	16	72	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A LOLPR	35.09	57	37	0	16	72	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	15	71	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A LOLPR	35.09	57	37	0	15	71	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	14	70	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A LOLPR	35.09	57	37	0	14	70	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	13	69	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	13	69	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	12	68	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	12	68	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	11	67	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	11	67	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	10	66	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	10	66	19	75	0.0059	32.9	25.0
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ELB17 gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	9	65	19	75	0.0058	32.9	25.0
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ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	9	65	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	8	64	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	8	64	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	7	63	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	7	63	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	6	62	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	6	62	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	5	61	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	5	61	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	4	60	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	4	60	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	3	59	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	3	59	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	2	58	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	2	58	19	75	0.0059	32.9	25.0
ELB17_gp239	gi 4416516 gb AAD20386.1	35.09	57	37	0	1	57	19	75	0.0058	32.9	25.0
ELB17_gp239	gi 332278195 sp Q40240.2 MPA5A_LOLPR	35.09	57	37	0	1	57	19	75	0.0059	32.9	25.0
ELB17_gp166	gi 42559536 sp Q9NJA9.1 MYSP_ANISI	30	70									

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772 1	34.78	69	45	0	2	70	425	493	1.8	25.5	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	34.78	69	45	0	1	69	425	493	1.8	25.5	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	10	80	423	493	0.35	27.9	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	9	79	423	493	0.35	27.9	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	8	78	423	493	0.28	28.2	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	7	77	423	493	0.22	28.6	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	6	76	423	493	0.22	28.6	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	5	75	423	493	0.22	28.6	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	4	74	423	493	0.44	27.6	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	3	73	423	493	0.44	27.6	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	2	72	423	493	1.8	25.5	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.8	71	47	0	1	71	423	493	1.8	25.5	30.0
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	34.33	67	44	0	2	68	427	493	2.8	24.9	28.8
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	34.33	67	44	0	1	67	427	493	2.8	24.9	28.8
MP82_gp80	gi 3135499 gb AAC16526.1	31.08	74	51	0	7	80	183	256	0.068	29.2	28.7
MP82_gp80	gi 1684720 emb CAB05372.1	31.08	74	51	0	7	80	183	256	0.068	29.2	28.7
MP82_gp80	gi 3135501 gb AAC16527.1	31.08	74	51	0	7	80	183	256	0.068	29.2	28.7
MP82_gp80	gi 29500897 emb CAD87529.1	31.08	74	51	0	7	80	191	264	0.07	29.2	28.7
MP82_gp80	gi 345108717 emb CCD28287.1	31.08	74	51	0	7	80	216	289	0.077	29.2	28.7
MP82_gp80	gi 13430402 gb AAK25823.1	31.08	74	51	0	7	80	182	255	0.086	28.9	28.7
MP82_gp80	gi 3135503 gb AAC16528.1	31.08	74	51	0	7	80	183	256	0.086	28.9	28.7
MP82_gp80	gi 398830 emb CAA52753.1	31.08	74	51	0	7	80	219	292	0.098	28.9	28.7
MP82_gp80	gi 3309039 gb AAC25994.1	31.08	74	51	0	7	80	219	292	0.098	28.9	28.7
MP82_gp80	gi 3135499 gb AAC16526.1	31.08	74	51	0	6	79	183	256	0.068	29.2	28.7
MP82_gp80	gi 1684720 emb CAB05372.1	31.08	74	51	0	6	79	183	256	0.068	29.2	28.7
MP82_gp80	gi 3135501 gb AAC16527.1	31.08	74	51	0	6	79	183	256	0.068	29.2	28.7
MP82_gp80	gi 29500897 emb CAD87529.1	31.08	74	51	0	6	79	191	264	0.07	29.2	28.7
MP82_gp80	gi 345108717 emb CCD28287.1	31.08	74	51	0	6	79	216	289	0.077	29.2	28.7
MP82_gp80	gi 13430402 gb AAK25823.1	31.08	74	51	0	6	79	182	255	0.086	28.9	28.7
MP82_gp80	gi 3135503 gb AAC16528.1	31.08	74	51	0	6	79	183	256	0.086	28.9	28.7
MP82_gp80	gi 398830 emb CAA52753.1	31.08	74	51	0	6	79	219	292	0.098	28.9	28.7
MP82_gp80	gi 3309039 gb AAC25994.1	31.08	74	51	0	6	79	219	292	0.098	28.9	28.7
MP82_gp80	gi 3135499 gb AAC16526.1	31.08	74	51	0	5	78	183	256	0.068	29.2	28.7
MP82_gp80	gi 1684720 emb CAB05372.1	31.08	74	51	0	5	78	183	256	0.068	29.2	28.7
MP82_gp80	gi 3135501 gb AAC16527.1	31.08	74	51	0	5	78	183	256	0.068	29.2	28.7
MP82_gp80	gi 29500897 emb CAD87529.1	31.08	74	51	0	5	78	191	264	0.07	29.2	28.7
MP82_gp80	gi 345108717 emb CCD28287.1	31.08	74	51	0	5	78	216	289	0.077	29.2	28.7
MP82_gp80	gi 13430402 gb AAK25823.1	31.08	74	51	0	5	78	182	255	0.086	28.9	28.7
MP82_gp80	gi 3135503 gb AAC16528.1	31.08	74	51	0	5	78	183	256	0.086	28.9	28.7
MP82_gp80	gi 398830 emb CAA52753.1	31.08	74	51	0	5	78	219	292	0.098	28.9	28.7
MP82_gp80	gi 3309039 gb AAC25994.1	31.08	74	51	0	5	78	219	292	0.098	28.9	28.7

MD02 ~~00	a:1212E4001ab144C16E26.11	21.00	74	Г1	0	4	77	102	256	0.068	20.2	20.7
MP82_gp80	gi 3135499 gb AAC16526.1	31.08	74 74	51 51	0	4	77 77	183 183	256 256	0.068	29.2 29.2	28.7
MP82_gp80	gi 1684720 emb CAB05372.1	31.08	74 74	51 51	0	4			256	0.068		28.7
MP82_gp80	gi 3135501 gb AAC16527.1	31.08	74 74	51 51	0	4	77 77	183	256	0.068	29.2	28.7
MP82_gp80	gi 29500897 emb CAD87529.1	31.08	74	51	0	4	77 77	191	264	0.07	29.2	28.7
MP82_gp80	gi 345108717 emb CCD28287.1	31.08	74	51	0	4	77 77	216	289	0.077	29.2	28.7
MP82_gp80	gi 13430402 gb AAK25823.1	31.08	74	51	0	4	77 	182	255	0.086	28.9	28.7
MP82_gp80	gi 3135503 gb AAC16528.1	31.08	74	51	0	4	77 	183	256	0.086	28.9	28.7
MP82_gp80	gi 398830 emb CAA52753.1	31.08	74	51	0	4	77	219	292	0.098	28.9	28.7
MP82_gp80	gi 3309039 gb AAC25994.1	31.08	74	51	0	4	77	219	292	0.098	28.9	28.7
MP82_gp80	gi 3135499 gb AAC16526.1	31.08	74	51	0	3	76	183	256	0.068	29.2	28.7
MP82_gp80	gi 1684720 emb CAB05372.1	31.08	74	51	0	3	76	183	256	0.068	29.2	28.7
MP82_gp80	gi 3135501 gb AAC16527.1	31.08	74	51	0	3	76	183	256	0.068	29.2	28.7
MP82_gp80	gi 29500897 emb CAD87529.1	31.08	74	51	0	3	76	191	264	0.07	29.2	28.7
MP82_gp80	gi 345108717 emb CCD28287.1	31.08	74	51	0	3	76	216	289	0.077	29.2	28.7
MP82_gp80	gi 13430402 gb AAK25823.1	31.08	74	51	0	3	76	182	255	0.086	28.9	28.7
MP82_gp80	gi 3135503 gb AAC16528.1	31.08	74	51	0	3	76	183	256	0.086	28.9	28.7
MP82_gp80	gi 398830 emb CAA52753.1	31.08	74	51	0	3	76	219	292	0.098	28.9	28.7
MP82_gp80	gi 3309039 gb AAC25994.1	31.08	74	51	0	3	76	219	292	0.098	28.9	28.7
MP82_gp80	gi 3135499 gb AAC16526.1	31.08	74	51	0	2	75	183	256	0.068	29.2	28.7
MP82_gp80	gi 1684720 emb CAB05372.1	31.08	74	51	0	2	75	183	256	0.068	29.2	28.7
MP82_gp80	gi 3135501 gb AAC16527.1	31.08	74	51	0	2	75	183	256	0.068	29.2	28.7
MP82_gp80	gi 29500897 emb CAD87529.1	31.08	74	51	0	2	75	191	264	0.07	29.2	28.7
MP82_gp80	gi 345108717 emb CCD28287.1	31.08	74	51	0	2	75	216	289	0.077	29.2	28.7
MP82_gp80	gi 13430402 gb AAK25823.1	31.08	74	51	0	2	75	182	255	0.086	28.9	28.7
MP82_gp80	gi 3135503 gb AAC16528.1	31.08	74	51	0	2	75	183	256	0.086	28.9	28.7
MP82_gp80	gi 398830 emb CAA52753.1	31.08	74	51	0	2	75	219	292	0.098	28.9	28.7
MP82_gp80	gi 3309039 gb AAC25994.1	31.08	74	51	0	2	75	219	292	0.098	28.9	28.7
MP82_gp80	gi 3135499 gb AAC16526.1	31.08	74	51	0	1	74	183	256	0.068	29.2	28.7
MP82_gp80	gi 1684720 emb CAB05372.1	31.08	74	51	0	1	74	183	256	0.068	29.2	28.7
MP82_gp80	gi 3135501 gb AAC16527.1	31.08	74	51	0	1	74	183	256	0.068	29.2	28.7
MP82_gp80	gi 29500897 emb CAD87529.1	31.08	74	51	0	1	74	191	264	0.07	29.2	28.7
MP82_gp80	gi 345108717 emb CCD28287.1	31.08	74	51	0	1	74	216	289	0.077	29.2	28.7
MP82_gp80	gi 13430402 gb AAK25823.1	31.08	74	51	0	1	74	182	255	0.086	28.9	28.7
MP82_gp80	gi 3135503 gb AAC16528.1	31.08	74	51	0	1	74	183	256	0.086	28.9	28.7
MP82_gp80	gi 398830 emb CAA52753.1	31.08	74	51	0	1	74	219	292	0.098	28.9	28.7
MP82_gp80	gi 3309039 gb AAC25994.1	31.08	74	51	0	1	74	219	292	0.098	28.9	28.7
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.33	69	46	0	12	80	423	491	0.7	26.9	28.7
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.33	69	46	0	11	79	423	491	0.7	26.9	28.7
MP82_gp42	gi 5815436 gb AAD52672.1 AF178772_1	33.82	68	45	0	13	80	423	490	0.7	26.9	28.7
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	28.21	78	56	0	1	78	56	133	0.0033	33.6	27.5
MP82_gp80	gi 3135499 gb AAC16526.1	30.14	73	51	0	1	73	184	256	0.22	27.6	27.5
MP82_gp80	gi 1684720 emb CAB05372.1	30.14	73	51	0	1	73	184	256	0.22	27.6	27.5
MP82_gp80	gi 3135501 gb AAC16527.1	30.14	73 73	51	0	1	73	184	256	0.22	27.6	27.5
MP82_gp80	gi 29500897 emb CAD87529.1	30.14	73 73	51	0	1	73	192	264	0.22	27.6	27.5
MP82_gp80	gi 345108717 emb CCD28287.1	30.14	73 73	51	0	1	73	217	289	0.24	27.6	27.5
MP82_gp80	gi 13430402 gb AAK25823.1	30.14	73 73	51	0	1	73 73	183	255	0.24	27.0	27.5
1411 02_8P00	911-2-20405 20 10 10 20 20 11	50.14	, 5	J1	O	1	, 3	100	233	0.27	۷,۰۷	۷.5

MD02 an00	gi 3135503 gb AAC16528.1	20.14	73	51	0	1	73	184	256	0.20	27.2	27 E
MP82_gp80 MP82_gp80	gi 3133303 gb AAC10326.1 gi 398830 emb CAA52753.1	30.14 30.14	73 73	51	0 0	1	73 73	220	292	0.28 0.31	27.2	27.5 27.5
MP82_gp80	gi 3309039 gb AAC25994.1	30.14	73 73	51	0	1	73 73	220	292	0.31	27.2	27.5
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	27.85	73 79	57	0	2	80	55	133	0.0021	34.3	27.5
MP82_gp42	gi 267048 sp P29600.1 30B3_BACLE	27.85	79 79	57	0	1	79	55 55	133	0.0021	34.3	27.5
MP82_gp80	gi 207046 \$5 F25000.1 3083_BACLE gi 2398757 emb CAA50281.1	29.73	7 <i>9</i> 74	52	0	7	80	193	266	0.36	26.9	27.5
		29.73	74 74	52 52	0	6	79	193	266	0.36	26.9	27.5
MP82_gp80 MP82_gp80	gi 2398757 emb CAA50281.1 gi 2398757 emb CAA50281.1	29.73	74 74	52 52	0	5	7 <i>9</i> 78	193	266	0.36	26.9	27.5
MP82_gp80	gi 2398757 emb CAA50281.1 gi 2398757 emb CAA50281.1	29.73	74 74	52 52	0	4	78 77	193	266	0.36	26.9	27.5 27.5
	gi 2398757 emb CAA50281.1 gi 2398757 emb CAA50281.1	29.73	74 74	52 52	0	3	7 <i>7</i>	193	266	0.36	26.9	27.5 27.5
MP82_gp80 MP82_gp80	gi 2398757 emb CAA50281.1 gi 2398757 emb CAA50281.1	29.73	74 74	52 52	0	2	75	193	266	0.36	26.9	27.5 27.5
MP82_gp80	gi 2398757 emb CAA50281.1 gi 2398757 emb CAA50281.1	29.73	74 74	52 52	0	1	73 74	193	266	0.36	26.9	27.5 27.5
		29.73 35.48	62	40		1 19	80	181	242	0.0017	34.6	27.5 27.5
MP82_gp68	gi 219806592 dbj BAH10151.1		62		0			181		0.0017		
MP82_gp68	gi 219806592 dbj BAH10151.1	35.48 35.48	62 62	40 40	0 0	18 17	79 78	181	242 242	0.0017	34.6 34.6	27.5 27.5
MP82_gp68	gi 219806592 dbj BAH10151.1				_							
MP82_gp68	gi 219806592 dbj BAH10151.1	35.48	62	40	0	16	77 7 6	181	242	0.0017	34.6	27.5
MP82_gp68	gi 219806592 dbj BAH10151.1	35.48	62 63	40	0	15 14	76	181	242	0.0017	34.6	27.5
MP82_gp68	gi 219806592 dbj BAH10151.1	35.48	62	40	0	14	75 20	181	242	0.0017	34.6	27.5
MP82_gp68	gi 219806592 dbj BAH10151.1	34.43	61	40	0	20	80	181	241	0.0055	32.9	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.77	73 73	52	0	1	73 72	155	227	0.028	30.9	26.3
MP82_gp80	gi 2398757 emb CAA50281.1	28.77	73	52	0	1	73	194	266	1.1	25.2	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.38	74	53	0	7	80	154	227	0.022	31.2	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.38	74	53	0	6	79	154	227	0.022	31.2	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.38	74	53	0	5	78	154	227	0.022	31.2	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.38	74	53	0	4	77 76	154	227	0.022	31.2	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.38	74	53	0	3	76	154	227	0.022	31.2	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.38	74	53	0	2	75	154	227	0.022	31.2	26.3
MP82_gp42	gi 1225905 dbj BAA05540.1	28.38	74	53	0	1	74	154	227	0.022	31.2	26.3
MP82_gp143		60	35	14	0	46	80	158	192	2.10E-08	51	26.3
MP82_gp143		60	35	14	0	46	80	158	192	2.10E-08	51	26.3
MP82_gp80	gi 3135499 gb AAC16526.1	30	70	49	0	3	72	187	256	1.4	24.9	26.3
MP82_gp80	gi 1684720 emb CAB05372.1	30	70	49	0	3	72	187	256	1.4	24.9	26.3
MP82_gp80	gi 3135501 gb AAC16527.1	30	70	49	0	3	72	187	256	1.4	24.9	26.3
MP82_gp80	gi 29500897 emb CAD87529.1	30	70	49	0	3	72	195	264	1.4	24.9	26.3
MP82_gp80	gi 345108717 emb CCD28287.1	30	70	49	0	3	72	220	289	1.6	24.9	26.3
MP82_gp80	gi 398830 emb CAA52753.1	30	70	49	0	3	72	223	292	1.6	24.9	26.3
MP82_gp80	gi 3309039 gb AAC25994.1	30	70	49	0	3	72	223	292	1.6	24.9	26.3
MP82_gp80	gi 13430402 gb AAK25823.1	30	70	49	0	3	72	186	255	1.8	24.5	26.3
MP82_gp80	gi 3135503 gb AAC16528.1	30	70	49	0	3	72	187	256	1.8	24.5	26.3
MP82_gp80	gi 3135499 gb AAC16526.1	30	70	49	0	2	71	187	256	1.4	24.9	26.3
MP82_gp80	gi 1684720 emb CAB05372.1	30	70	49	0	2	71	187	256	1.4	24.9	26.3
MP82_gp80	gi 3135501 gb AAC16527.1	30	70	49	0	2	71	187	256	1.4	24.9	26.3
MP82_gp80	gi 29500897 emb CAD87529.1	30	70	49	0	2	71	195	264	1.4	24.9	26.3
MP82_gp80	gi 345108717 emb CCD28287.1	30	70	49	0	2	71	220	289	1.6	24.9	26.3
MP82_gp80	gi 398830 emb CAA52753.1	30	70	49	0	2	71	223	292	1.6	24.9	26.3
MP82_gp80	gi 3309039 gb AAC25994.1	30	70	49	0	2	71	223	292	1.6	24.9	26.3

MD02 an00	a: 12420402 ah 44K2E922 1	20	70	40	0	2	71	106	255	1.0	24 5	26.2
MP82_gp80	gi 13430402 gb AAK25823.1	30 30	70 70	49 49	0	2 2	71 71	186 187	255 256	1.8 1.8	24.5	26.3
MP82_gp80	gi 3135503 gb AAC16528.1 gi 3135499 gb AAC16526.1	30	70 70	49 49	0	1	71 70	187	256	1.6	24.5 24.9	26.3 26.3
MP82_gp80	gi 1684720 emb CAB05372.1	30	70 70	49 49	0 0	1	70 70	187	256 256	1.4	24.9 24.9	26.3
MP82_gp80		30	70 70	49 49		1	70 70	187	256	1.4	24.9	26.3
MP82_gp80	gi 3135501 gb AAC16527.1				0							
MP82_gp80	gi 29500897 emb CAD87529.1	30	70 70	49	0	1	70 70	195	264	1.4	24.9	26.3
MP82_gp80	gi 345108717 emb CCD28287.1	30	70 70	49	0	1	70 70	220	289	1.6	24.9	26.3
MP82_gp80	gi 398830 emb CAA52753.1	30	70 70	49	0	1	70 70	223	292	1.6	24.9	26.3
MP82_gp80	gi 3309039 gb AAC25994.1	30	70 70	49	0	1	70 70	223	292	1.6	24.9	26.3
MP82_gp80	gi 13430402 gb AAK25823.1	30	70 7 0	49	0	1	70	186	255	1.8	24.5	26.3
MP82_gp80	gi 3135503 gb AAC16528.1	30	70 26	49	0	1	70	187	256	1.8	24.5	26.3
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	45	80	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	45	80	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	44	79	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	44	79	158	193	1.60E-08	51.3	26.2
MP82_gp143	- · · · · · · · · · · · · · · · · · · ·	58.33	36	15	0	43	78	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	43	78	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	42	77	158	193	1.60E-08	51.3	26.2
MP82_gp143	- · · · · · · · · · · · · · · · · · · ·	58.33	36	15	0	42	77	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	41	76	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	41	76	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	40	75	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	40	75	158	193	1.60E-08	51.3	26.2
MP82_gp143	- · · · · · · · · · · · · · · · · · · ·	58.33	36	15	0	39	74	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	39	74	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	38	73	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	38	73	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	37	72	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	37	72	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	36	71	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	36	71	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	35	70	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	35	70	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	34	69	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	34	69	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 27526732 emb CAD24068.1	58.33	36	15	0	33	68	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	33	68	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	32	67	158	193	1.60E-08	51.3	26.2
MP82_gp143	gi 14575525 emb CAC42881.1	58.33	36	15	0	32	67	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	31	66	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	31	66	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	30	65	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	30	65	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	29	64	158	193	1.60E-08	51.3	26.2
MP82_gp143		58.33	36	15	0	29	64	158	193	1.60E-08	51.3	26.2
MP82_gp143	- · · · · · · · · · · · · · · · · · · ·	58.33	36	15	0	28	63	158	193	1.60E-08	51.3	26.2
0=_8P1 13	0.1	22.33		_5	•			_55		2.002 00	02.0	

11000 110 1110000011	=0.00	2.5	4=				4=0	400	4 605 00	=4.0	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	28	63	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	27	62	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	27	62	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	26	61	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	26	61	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	25	60	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	25	60	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	24	59	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	24	59	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	23	58	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	23	58	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	22	57	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	22	57	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	21	56	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	21	56	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	20	55	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	20	55	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	19	54	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	19	54	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	18	53	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	18	53	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	17	52	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	17	52	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	16	51	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	16	51	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	15	50	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	15	50	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	14	49	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	14	49	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	13	48	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	13	48	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	12	47	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	12	47	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	11	46	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	11	46	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	10	45	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	10	45	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	9	44	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	9	44	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	8	43	158	193	1.60E-08	51.3	26.2
									1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36 36	15 15	0	8	43	158	193			
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36 36	15 15	0	7	42	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36 36	15 15	0	7	42	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	6	41	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 14575525 emb CAC42881.1	58.33	36	15	0	6	41	158	193	1.60E-08	51.3	26.2
MP82_gp143 gi 27526732 emb CAD24068.1	58.33	36	15	0	5	40	158	193	1.60E-08	51.3	26.2

		=0.00	2.5	4-		_	40	4=0	400	4 605 00	=4.0	26.2
	5525 emb CAC42881.1	58.33	36	15	0	5	40	158	193	1.60E-08	51.3	26.2
	5732 emb CAD24068.1	58.33	36	15	0	4	39	158	193	1.60E-08	51.3	26.2
	5525 emb CAC42881.1	58.33	36	15 15	0	4	39	158	193	1.60E-08	51.3	26.2
	5732 emb CAD24068.1	58.33	36	15	0	3	38	158	193	1.60E-08	51.3	26.2
	5525 emb CAC42881.1	58.33	36	15	0	3	38	158	193	1.60E-08	51.3	26.2
	5732 emb CAD24068.1	58.33	36	15	0	2	37	158	193	1.60E-08	51.3	26.2
	5525 emb CAC42881.1	58.33	36	15	0	2	37	158	193	1.60E-08	51.3	26.2
	5732 emb CAD24068.1	58.33	36	15	0	1	36	158	193	1.60E-08	51.3	26.2
	5525 emb CAC42881.1	58.33	36	15	0	1	36	158	193	1.60E-08	51.3	26.2
	31137 gb KEY78748.1	26.58	79 7 0	58	0	2	80	63	141	0.21	27.6	26.2
	389 sp O42799.2 ALL7_ASPFU	26.58	79 7 0	58	0	2	80	63	141	0.27	27.2	26.2
	31137 gb KEY78748.1	26.58	79 7 0	58	0	1	79 7 0	63	141	0.21	27.6	26.2
	389 sp O42799.2 ALL7_ASPFU	26.58	79	58	0	1	79	63	141	0.27	27.2	26.2
	047 gb AAC25998.1	26.58	79 7 0	58	0	2	80	16	94	2.9	23.9	26.2
	045 gb AAC25997.1	26.58	79 7 0	58	0	2	80	16	94	2.9	23.9	26.2
	047 gb AAC25998.1	26.58	79	58	0	1	79	16	94	2.9	23.9	26.2
	045 gb AAC25997.1	26.58	79 	58	0	1	79	16	94	2.9	23.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	22	80	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	21	79	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	20	78	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	19	77	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	18	76	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	17	75	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	16	74	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	15	73	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	14	72	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	13	71	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	12	70	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	11	69	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	10	68	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	9	67	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	8	66	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	7	65	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	6	64	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	5	63	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	4	62	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	3	61	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	2	60	194	252	0.0014	34.9	26.2
	6630 emb CAD38396.1	35.59	59	38	0	1	59	194	252	0.0014	34.9	26.2
	8 sp P29600.1 SUBS_BACLE	27.27	77	56	0	1	77	57	133	0.01	31.9	26.2
	047 gb AAC25998.1	25.32	79	59	0	2	80	12	90	4.6	23.2	25.0
	045 gb AAC25997.1	25.32	79	59	0	2	80	12	90	4.7	23.2	25.0
	047 gb AAC25998.1	25.32	79	59	0	1	79	12	90	4.6	23.2	25.0
	045 gb AAC25997.1	25.32	79	59	0	1	79	12	90	4.7	23.2	25.0
	047 gb AAC25998.1	26.67	75	55	0	4	78	16	90	5.8	22.9	25.0
MP82_gp67 gi 33090	045 gb AAC25997.1	26.67	75	55	0	4	78	16	90	5.9	22.9	25.0

MD92 cn67	a: 2200047 ab 44C2F009.1	26.67	75		0	2	77	16	00	го	22.0	25.0
MP82_gp67 MP82_gp67	gi 3309047 gb AAC25998.1 gi 3309045 gb AAC25997.1	26.67 26.67	75 75	55 55	0 0	3 3	77 77	16 16	90 90	5.8 5.9	22.9 22.9	25.0 25.0
MP82_gp07		31.75	63	43	0	18	80	142	204	8.30E-05	38.9	25.0
MP82_gp143	gi 168419914 gb ACA23876.1	27.4	73	53	0	8	80	171	243	8.6	22.2	25.0
MP82_gp41	gi 168419914 gb ACA23876.1	27.4	73 73	53	0	7	79	171	243	8.6	22.2	25.0
MP82_gp41	gi 168419914 gb ACA23876.1	27.4	73 73	53	0	6	79 78	171	243	8.6	22.2	25.0
MP82_gp41		27.4	73 73	53	0	5	78 77	171	243	8.6	22.2	25.0 25.0
	gi 168419914 gb ACA23876.1	27.4 27.4	73 73	53	0	4	77 76	171 171	243 243	8.6	22.2	25.0 25.0
MP82_gp41	gi 168419914 gb ACA23876.1	27.4 27.4	73 73	53	0	3	76 75	171	243 243	8.6	22.2	25.0 25.0
MP82_gp41	gi 168419914 gb ACA23876.1		73 73	53	_		73 74					
MP82_gp41	gi 168419914 gb ACA23876.1	27.4			0	2		171	243	8.6	22.2	25.0
MP82_gp41	gi 168419914 gb ACA23876.1	27.4	73 72	53 53	0	1	73	171	243	8.6	22.2	25.0
MP82_gp42	gi 1225905 dbj BAA05540.1	27.78	72 72	52 53	0	9	80	154	225	0.057	29.9	25.0
MP82_gp42	gi 1225905 dbj BAA05540.1	27.78	72 72	52 53	0	8	79 76	154	225	0.057	29.9	25.0
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	27.78	72 72	52	0	5	76 75	62	133	0.013	31.6	25.0
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	27.78	72	52	0	4	75 74	62	133	0.013	31.6	25.0
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	27.78	72	52	0	3	74	62	133	0.013	31.6	25.0
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	27.78	72	52	0	2	73	62	133	0.013	31.6	25.0
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	27.78	72	52	0	1	72	62	133	0.013	31.6	25.0
MP82_gp143		60.61	33	13	0	48	80	158	190	1.00E-07	48.6	25.0
MP82_gp143		60.61	33	13	0	48	80	158	190	1.00E-07	48.6	25.0
MP82_gp68	gi 219806592 dbj BAH10151.1	33.9	59	39	0	22	80	181	239	0.018	31.2	25.0
MP82_gp68	gi 219806592 dbj BAH10151.1	33.9	59	39	0	21	79	181	239	0.018	31.2	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	22	80	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	22	80	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	22	80	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	22	80	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	21	79	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	21	79	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	21	79	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	21	79	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	20	78	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	20	78	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	20	78	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	20	78	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	19	77	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	19	77	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	19	77	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	19	77	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	18	76	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	18	76	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	18	76	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	18	76	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	17	75	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	17	75	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	17	75	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	17	75	194	252	0.014	31.6	25.0

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MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	16	74	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	16	74	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	16	74	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	16	74	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	15	73	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	15	73	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	15	73	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	15	73	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	14	72	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	14	72	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	14	72	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	14	72	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	13	71	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	13	71	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	13	71	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	13	71	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	12	70	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	12	70	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	12	70	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	12	70	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	11	69	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	11	69	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	11	69	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	11	69	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	10	68	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	10	68	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	10	68	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	10	68	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	9	67	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	9	67	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	9	67	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	9	67	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	8	66	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	8	66	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	8	66	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	8	66	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	7	65	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	7	65	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	7	65	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	7	65	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	6	64	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	6	64	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	6	64	194	252	0.0033	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	6	64	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	5	63	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725610 emb CAD38389.1 gi 21725632 emb CAD38397.1	33.9	59	39	0	5	63	194	252	0.0044	32.9	25.0
711 02_6p00	5.121723032 [CIND] CAD30337.1]	33.3	33	33	O	3	55	134	232	0.0033	52.5	23.0

MP82 gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	5	63	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	5	63	194	252	0.014	31.6	25.0
MP82 gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	4	62	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	4	62	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	4	62	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	4	62	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	3	61	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	3	61	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	3	61	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	3	61	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	2	60	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	2	60	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	2	60	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	2	60	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725616 emb CAD38389.1	33.9	59	39	0	1	59	194	252	0.0044	33.2	25.0
MP82_gp80	gi 21725632 emb CAD38397.1	33.9	59	39	0	1	59	194	252	0.0055	32.9	25.0
MP82_gp80	gi 21725618 emb CAD38390.1	33.9	59	39	0	1	59	194	252	0.014	31.6	25.0
MP82_gp80	gi 21725626 emb CAD38394.1	33.9	59	39	0	1	59	194	252	0.014	31.6	25.0
MP82_gp42	gi 267048 sp P29600.1 SUBS_BACLE	28.17	71	51	0	1	71	63	133	0.017	31.2	25.0
MP82_gp143	gi 56550550 dbj BAD77932.1	30.77	65	45	0	16	80	142	206	4.20E-05	39.9	25.0
MP82_gp143	gi 56550550 dbj BAD77932.1	30.77	65	45	0	15	79	142	206	4.20E-05	39.9	25.0
MP82_gp143	9	30.77	65	45	0	14	78	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	13	77	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	12	76	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	11	75	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	10	74	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	9	73	142	206	4.20E-05	39.9	25.0
MP82_gp143	• • • • • • • • • • • • • • • • • • • •	30.77	65	45	0	8	72	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	7	71	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	6	70	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	5	69	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	4	68	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	3	67	142	206	4.20E-05	39.9	25.0
MP82_gp143		30.77	65	45	0	2	66	142	206	4.20E-05	39.9	25.0
MP82_gp143	gi 56550550 dbj BAD77932.1	30.77	65	45	0	1	65	142	206	4.20E-05	39.9	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
KAZ99a_gp73	gi 25989482 gb AAM10779.1	28.75	80	57	0	1	80	38	117	0.33	26.9	28.8
KAZ99a_gp73	gi 25989482 gb AAM10779.1	28.21	78	56	0	3	80	37	114	0.84	25.6	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	9	80	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	8	79	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	8	79	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	7	78	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	7	78	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	6	77	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	6	77	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	5	76	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	5	76	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	4	75	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	4	75	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	3	74	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	3	74	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	2	73	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	2	73	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	30.56	72	50	0	1	72	46	117	0.53	26.2	27.5
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.56	72	50	0	1	72	46	117	0.67	25.9	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	27.85	79	57	0	2	80	37	115	0.53	26.2	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	27.85	79	57	0	1	79	37	115	0.53	26.2	27.5
KAZ99a_gp73	gi 25989482 gb AAM10779.1	31.82	66	45	0	6	71	52	117	1.1	25.2	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	31.82	66	45	0	6	71	52	117	1.3	24.9	26.3
KAZ99a_gp73	gi 25989482 gb AAM10779.1	31.82	66	45	0	5	70	52	117	1.1	25.2	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	31.82	66	45	0	5	70	52	117	1.3	24.9	26.3
KAZ99a_gp73	gi 25989482 gb AAM10779.1	31.82	66	45	0	4	69	52	117	1.1	25.2	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	31.82	66	45	0	4	69	52	117	1.3	24.9	26.3
KAZ99a_gp73	gi 25989482 gb AAM10779.1	31.82	66	45	0	3	68	52	117	1.1	25.2	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	31.82	66	45	0	3	68	52	117	1.3	24.9	26.3
KAZ99a_gp73	gi 25989482 gb AAM10779.1	31.82	66	45	0	2	67	52	117	1.1	25.2	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	31.82	66	45	0	2	67	52	117	1.3	24.9	26.3
KAZ99a_gp73	gi 25989482 gb AAM10779.1	31.82	66	45	0	1	66	52	117	1.1	25.2	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	31.82	66	45	0	1	66	52	117	1.3	24.9	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30	70	49	0	11	80	46	115	1.3	24.9	26.3
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30	70	49	0	10	79	46	115	1.3	24.9	26.3
KAZ99a_gp73	gi 25989482 gb AAM10779.1	27.27	77	56	0	4	80	37	113	2.7	23.9	26.2
KAZ99a_gp73	gi 33667930 gb AAQ24542.1	30.43	69	48	0	12	80	46	114	2.1	24.2	26.2
KAZ99a_gp52	gi 8453086 gb AAF75225.1 AF20898	26.32	76	56	0	5	80	41	116	0.24	28.2	25.0
KAZ99a_gp52	gi 8453086 gb AAF75225.1 AF20898	26.32	76	56	0	4	79	41	116	0.24	28.2	25.0
KAZ99a_gp52	gi 8453086 gb AAF75225.1 AF20898	26.32	76	56	0	3	78	41	116	0.24	28.2	25.0
KAZ99a_gp52	gi 8453086 gb AAF75225.1 AF20898	25.32	79	59	0	2	80	41	119	0.15	28.9	25.0
KAZ99a_gp52	gi 8453086 gb AAF75225.1 AF20898	25.32	79	59	0	1	79	41	119	0.15	28.9	25.0

gi|8453086|gb|AAF75225.1|AF20898 25.0 KAZ99a_gp52 27.03 74 54 0 7 80 41 114 0.47 27.2 27.03 74 54 KAZ99a_gp52 gi|8453086|gb|AAF75225.1|AF20898 0 6 79 41 114 0.47 27.2 25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
RMP11k_gp127	gi 1545895 emb CAB02216.1	27.5	80	58	0	1	80	35	114	0.31	26.3	27.5
RMP11k_gp127	gi 1545895 emb CAB02216.1	26.25	80	59	0	1	80	33	112	1.3	24.3	26.3
RMP11k_gp127	gi 1545895 emb CAB02216.1	28	75	54	0	1	75	40	114	0.63	25.3	26.3
RMP11k_gp127	gi 1545897 emb CAB02217.1	28	75	54	0	1	75	40	114	1	24.6	26.3
RMP11k_gp127	gi 1321731 emb CAA96548.1	28	75	54	0	1	75	40	114	1.3	24.3	26.3
RMP11k_gp127	gi 1545897 emb CAB02217.1	27.63	76	55	0	5	80	39	114	0.79	24.9	26.2
RMP11k_gp127	gi 1321731 emb CAA96548.1	27.63	76	55	0	5	80	39	114	0.99	24.6	26.2
RMP11k_gp127	gi 1545895 emb CAB02216.1	27.63	76	55	0	4	79	39	114	0.5	25.6	26.2
RMP11k_gp127	gi 1545897 emb CAB02217.1	27.63	76	55	0	4	79	39	114	0.79	24.9	26.2
RMP11k_gp127	gi 1321731 emb CAA96548.1	27.63	76	55	0	4	79	39	114	0.99	24.6	26.2
RMP11k_gp127	gi 1545895 emb CAB02216.1	27.63	76	55	0	3	78	39	114	0.5	25.6	26.2
RMP11k_gp127	gi 1545897 emb CAB02217.1	27.63	76	55	0	3	78	39	114	0.79	24.9	26.2
RMP11k_gp127	gi 1321731 emb CAA96548.1	27.63	76	55	0	3	78	39	114	0.99	24.6	26.2
RMP11k_gp127	gi 1545895 emb CAB02216.1	27.63	76	55	0	2	77	39	114	0.5	25.6	26.2
RMP11k_gp127	gi 1545897 emb CAB02217.1	27.63	76	55	0	2	77	39	114	0.79	24.9	26.2
RMP11k_gp127	gi 1321731 emb CAA96548.1	27.63	76	55	0	2	77	39	114	0.99	24.6	26.2
RMP11k_gp127	gi 1545895 emb CAB02216.1	27.63	76	55	0	1	76	39	114	0.5	25.6	26.2
RMP11k_gp127	gi 1545897 emb CAB02217.1	27.63	76	55	0	1	76	39	114	0.79	24.9	26.2
RMP11k_gp127	gi 1321731 emb CAA96548.1	27.63	76	55	0	1	76	39	114	0.99	24.6	26.2
RMP11k_gp127	gi 1545895 emb CAB02216.1	26.58	79	58	0	2	80	35	113	1	24.6	26.2
RMP11k_gp51	gi 8453086 gb AAF75225.1 AF208981_1	26.32	76	56	0	5	80	41	116	0.24	28.2	25.0
RMP11k_gp51	gi 8453086 gb AAF75225.1 AF208981_1	26.32	76	56	0	4	79	41	116	0.24	28.2	25.0
RMP11k_gp51	gi 8453086 gb AAF75225.1 AF208981_1	26.32	76	56	0	3	78	41	116	0.24	28.2	25.0
RMP11k_gp51	gi 8453086 gb AAF75225.1 AF208981_1	25.32	79	59	0	2	80	41	119	0.15	28.9	25.0
RMP11k_gp51	gi 8453086 gb AAF75225.1 AF208981_1	25.32	79	59	0	1	79	41	119	0.15	28.9	25.0
RMP11k_gp127	gi 1545897 emb CAB02217.1	26.67	75	55	0	6	80	39	113	2.5	23.3	25.0
RMP11k_gp127	gi 1321731 emb CAA96548.1	26.67	75	55	0	6	80	39	113	3.2	22.9	25.0
RMP11k_gp127	gi 1545897 emb CAB02217.1	27.03	74	54	0	7	80	39	112	4	22.6	25.0
RMP11k_gp127	gi 1321731 emb CAA96548.1	27.03	74	54	0	7	80	39	112	5	22.2	25.0
RMP11k_gp51	gi 8453086 gb AAF75225.1 AF208981_1	27.03	74	54	0	7	80	41	114	0.47	27.2	25.0
RMP11k_gp51	gi 8453086 gb AAF75225.1 AF208981_1	27.03	74	54	0	6	79	41	114	0.47	27.2	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
RMS3b_gp78	gi 25989482 gb AAM10779.1	28.75	80	57	0	1	80	38	117	0.33	26.9	28.8
RMS3b_gp78	gi 25989482 gb AAM10779.1	28.21	78	56	0	3	80	37	114	0.84	25.6	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	9	80	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	8	79	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	8	79	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	7	78	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	7	78	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	6	77	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	6	77	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	5	76	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	5	76	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	4	75	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	4	75	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	3	74	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	3	74	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	2	73	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	2	73	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	30.56	72	50	0	1	72	46	117	0.53	26.2	27.5
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.56	72	50	0	1	72	46	117	0.67	25.9	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	27.85	79	57	0	2	80	37	115	0.53	26.2	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	27.85	79	57	0	1	79	37	115	0.53	26.2	27.5
RMS3b_gp78	gi 25989482 gb AAM10779.1	31.82	66	45	0	6	71	52	117	1.1	25.2	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	31.82	66	45	0	6	71	52	117	1.3	24.9	26.3
RMS3b_gp78	gi 25989482 gb AAM10779.1	31.82	66	45	0	5	70	52	117	1.1	25.2	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	31.82	66	45	0	5	70	52	117	1.3	24.9	26.3
RMS3b_gp78	gi 25989482 gb AAM10779.1	31.82	66	45	0	4	69	52	117	1.1	25.2	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	31.82	66	45	0	4	69	52	117	1.3	24.9	26.3
RMS3b_gp78	gi 25989482 gb AAM10779.1	31.82	66	45	0	3	68	52	117	1.1	25.2	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	31.82	66	45	0	3	68	52	117	1.3	24.9	26.3
RMS3b_gp78	gi 25989482 gb AAM10779.1	31.82	66	45	0	2	67	52	117	1.1	25.2	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	31.82	66	45	0	2	67	52	117	1.3	24.9	26.3
RMS3b_gp78	gi 25989482 gb AAM10779.1	31.82	66	45	0	1	66	52	117	1.1	25.2	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	31.82	66	45	0	1	66	52	117	1.3	24.9	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30	70	49	0	11	80	46	115	1.3	24.9	26.3
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30	70	49	0	10	79	46	115	1.3	24.9	26.3
RMS3b_gp78	gi 25989482 gb AAM10779.1	27.27	77	56	0	4	80	37	113	2.7	23.9	26.2
RMS3b_gp78	gi 33667930 gb AAQ24542.1	30.43	69	48	0	12	80	46	114	2.1	24.2	26.2
RMS3b_gp57	gi 8453086 gb AAF75225.1 AF208981_	26.32	76	56	0	5	80	41	116	0.24	28.2	25.0
RMS3b_gp57	gi 8453086 gb AAF75225.1 AF208981_		76	56	0	4	79	41	116	0.24	28.2	25.0
RMS3b_gp57	gi 8453086 gb AAF75225.1 AF208981_		76	56	0	3	78	41	116	0.24	28.2	25.0
RMS3b_gp57	gi 8453086 gb AAF75225.1 AF208981_	25.32	79	59	0	2	80	41	119	0.15	28.9	25.0

RMS3b_gp57	gi 8453086 gb AAF75225.1 AF208981_	25.32	79	59	0	1	79	41	119	0.15	28.9	25.0
RMS3b_gp57	gi 8453086 gb AAF75225.1 AF208981_	27.03	74	54	0	7	80	41	114	0.47	27.2	25.0
RMS3b_gp57	gi 8453086 gb AAF75225.1 AF208981_	27.03	74	54	0	6	79	41	114	0.47	27.2	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
TAT2F_gp131	gi 1545895 emb CAB02216.1	27.5	80	58	0	1	80	35	114	0.31	26.3	27.5
TAT2F_gp131	gi 1545895 emb CAB02216.1	26.25	80	59	0	1	80	33	112	1.3	24.3	26.3
TAT2F_gp131	gi 1545895 emb CAB02216.1	28	75	54	0	1	75	40	114	0.63	25.3	26.3
TAT2F_gp131	gi 1545897 emb CAB02217.1	28	75	54	0	1	75	40	114	1	24.6	26.3
TAT2F_gp131	gi 1321731 emb CAA96548.1	28	75	54	0	1	75	40	114	1.3	24.3	26.3
TAT2F_gp131	gi 1545897 emb CAB02217.1	27.63	76	55	0	5	80	39	114	0.79	24.9	26.2
TAT2F_gp131	gi 1321731 emb CAA96548.1	27.63	76	55	0	5	80	39	114	0.99	24.6	26.2
TAT2F_gp131	gi 1545895 emb CAB02216.1	27.63	76	55	0	4	79	39	114	0.5	25.6	26.2
TAT2F_gp131	gi 1545897 emb CAB02217.1	27.63	76	55	0	4	79	39	114	0.79	24.9	26.2
TAT2F_gp131	gi 1321731 emb CAA96548.1	27.63	76	55	0	4	79	39	114	0.99	24.6	26.2
TAT2F_gp131	gi 1545895 emb CAB02216.1	27.63	76	55	0	3	78	39	114	0.5	25.6	26.2
TAT2F_gp131	gi 1545897 emb CAB02217.1	27.63	76	55	0	3	78	39	114	0.79	24.9	26.2
TAT2F_gp131	gi 1321731 emb CAA96548.1	27.63	76	55	0	3	78	39	114	0.99	24.6	26.2
TAT2F_gp131	gi 1545895 emb CAB02216.1	27.63	76	55	0	2	77	39	114	0.5	25.6	26.2
TAT2F_gp131	gi 1545897 emb CAB02217.1	27.63	76	55	0	2	77	39	114	0.79	24.9	26.2
TAT2F_gp131	gi 1321731 emb CAA96548.1	27.63	76	55	0	2	77	39	114	0.99	24.6	26.2
TAT2F_gp131	gi 1545895 emb CAB02216.1	27.63	76	55	0	1	76	39	114	0.5	25.6	26.2
TAT2F_gp131	gi 1545897 emb CAB02217.1	27.63	76	55	0	1	76	39	114	0.79	24.9	26.2
TAT2F_gp131	gi 1321731 emb CAA96548.1	27.63	76	55	0	1	76	39	114	0.99	24.6	26.2
TAT2F_gp131	gi 1545895 emb CAB02216.1	26.58	79	58	0	2	80	35	113	1	24.6	26.2
TAT2F_gp55	gi 8453086 gb AAF75225.1 AF208981_1	26.32	76	56	0	5	80	41	116	0.24	28.2	25.0
TAT2F_gp55	gi 8453086 gb AAF75225.1 AF208981_1	26.32	76	56	0	4	79	41	116	0.24	28.2	25.0
TAT2F_gp55	gi 8453086 gb AAF75225.1 AF208981_1	26.32	76	56	0	3	78	41	116	0.24	28.2	25.0
TAT2F_gp55	gi 8453086 gb AAF75225.1 AF208981_1	25.32	79	59	0	2	80	41	119	0.15	28.9	25.0
TAT2F_gp55	gi 8453086 gb AAF75225.1 AF208981_1	25.32	79	59	0	1	79	41	119	0.15	28.9	25.0
TAT2F_gp131	gi 1545897 emb CAB02217.1	26.67	75	55	0	6	80	39	113	2.5	23.3	25.0
TAT2F_gp131	gi 1321731 emb CAA96548.1	26.67	75	55	0	6	80	39	113	3.2	22.9	25.0
TAT2F_gp131	gi 1545897 emb CAB02217.1	27.03	74	54	0	7	80	39	112	4	22.6	25.0
TAT2F_gp131	gi 1321731 emb CAA96548.1	27.03	74	54	0	7	80	39	112	5	22.2	25.0
TAT2F_gp55	gi 8453086 gb AAF75225.1 AF208981_1	27.03	74	54	0	7	80	41	114	0.47	27.2	25.0
TAT2F_gp55	gi 8453086 gb AAF75225.1 AF208981_1	27.03	74	54	0	6	79	41	114	0.47	27.2	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
DIN2_gp32	gi 455288 gb AAA33405.1	30.26	76	53	0	5	80	247	322	0.27	27.6	28.7
DIN2_gp32	gi 455288 gb AAA33405.1	30.26	76	53	0	4	79	247	322	0.27	27.6	28.7
DIN2_gp60	gi 410060781 gb AFV53352.1	31.43	70	48	0	11	80	30	99	0.28	27.2	27.5
DIN2_gp60	gi 410060781 gb AFV53352.1	31.43	70	48	0	10	79	30	99	0.28	27.2	27.5
DIN2_gp60	gi 410060781 gb AFV53352.1	31.43	70	48	0	9	78	30	99	0.28	27.2	27.5
DIN2_gp32	gi 455288 gb AAA33405.1	29.33	75	53	0	6	80	247	321	0.86	25.9	27.5
DIN2_gp60	gi 410060781 gb AFV53352.1	31.88	69	47	0	12	80	30	98	0.28	27.2	27.5
DIN2_gp24	gi 6580762 gb AAF18269.1 AF066055_1	26.25	80	59	0	1	80	13	92	0.00035	37.9	26.3
DIN2_gp24	gi 6580762 gb AAF18269.1 AF066055_1	26.58	79	58	0	1	79	14	92	0.00056	37.3	26.2
DIN2_gp32	gi 455288 gb AAA33405.1	26.58	79	58	0	2	80	241	319	1.7	24.9	26.2
DIN2_gp32	gi 455288 gb AAA33405.1	26.58	79	58	0	1	79	241	319	1.7	24.9	26.2
DIN2_gp30	gi 113561 sp P22285.1 MPA92_POAPR	35.59	59	38	0	22	80	269	327	0.21	27.9	26.2
DIN2_gp30	gi 113561 sp P22285.1 MPA92_POAPR	35.59	59	38	0	21	79	269	327	0.21	27.9	26.2
DIN2_gp30	gi 113561 sp P22285.1 MPA92_POAPR	35.59	59	38	0	20	78	269	327	0.21	27.9	26.2
DIN2_gp30	gi 113561 sp P22285.1 MPA92_POAPR	35.59	59	38	0	19	77	269	327	0.21	27.9	26.2
DIN2_gp33	gi 60116876 gb AAX14379.1	25.32	79	59	0	2	80	237	315	0.83	26.5	25.0
DIN2_gp33	gi 148361511 gb ABQ59329.1	25.32	79	59	0	1	79	107	185	0.78	26.2	25.0
DIN2_gp33	gi 60116876 gb AAX14379.1	25.32	79	59	0	1	79	237	315	0.83	26.5	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	22	80	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	21	79	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	17	75	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	16	74	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	15	73	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	14	72	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	13	71	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	12	70	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	11	69	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	7	65	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	6	64	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	5	63	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	4	62	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	3	61	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	2	60	275	333	0.042	30.2	25.0
DIN2_gp32	gi 455288 gb AAA33405.1	33.9	59	39	0	1	59	275	333	0.042	30.2	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
MP75_gp35	gi 121584258 gb ABM60783.1	31.75	63	43	0	1	63	17	79	0.36	26.9	25.0
MP75_gp103	gi 442577833 gb AGC60020.1	26.32	76	56	0	1	76	430	505	0.11	30.2	25.0
MP75_gp103	gi 42559536 sp Q9NJA9.1 MYSP_A	26.32	76	56	0	1	76	430	505	0.11	30.2	25.0
MP75_gp103	gi 42559536 sp Q9NJA9.1 MYSP_A	27.03	74	54	0	2	75	432	505	0.17	29.6	25.0
MP75_gp103	gi 442577833 gb AGC60020.1	27.03	74	54	0	2	75	432	505	0.17	29.6	25.0
MP75_gp103	gi 442577833 gb AGC60020.1	27.03	74	54	0	1	74	432	505	0.17	29.6	25.0
MP75_gp103	gi 42559536 sp Q9NJA9.1 MYSP_A	27.03	74	54	0	1	74	432	505	0.17	29.6	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
FV7M4_gp17	gi 21954740 gb AAM83103.1	28	75	54	0	6	80	139	213	0.085	30.6	26.3
FV7M4_gp17	gi 21954740 gb AAM83103.1	28	75	54	0	5	79	139	213	0.085	30.6	26.3
FV7M4_gp17	gi 21954740 gb AAM83103.1	28	75	54	0	4	78	139	213	0.085	30.6	26.3
FV7M4_gp17	gi 21954740 gb AAM83103.1	28	75	54	0	3	77	139	213	0.085	30.6	26.3
FV7M4_gp17	gi 21954740 gb AAM83103.1	28	75	54	0	2	76	139	213	0.085	30.6	26.3
FV7M4_gp17	gi 21954740 gb AAM83103.1	28	75	54	0	1	75	139	213	0.085	30.6	26.3
FV7M4_gp17	gi 219806602 dbj BAH10156.1	26.32	76	56	0	1	76	5	80	0.36	26.9	25.0
FV7M4_gp8	gi 20796733 emb CAC83047.1	28.99	69	49	0	1	69	33	101	8.4	21	25.0
FV7M4_gp17	gi 219806602 dbj BAH10156.1	25.32	79	59	0	2	80	2	80	0.11	28.6	25.0
FV7M4_gp17	gi 219806602 dbj BAH10156.1	25.32	79	59	0	1	79	2	80	0.11	28.6	25.0
FV7M4_gp17	gi 21954740 gb AAM83103.1	27.03	74	54	0	1	74	140	213	0.43	28.2	25.0
FV7M4_gp17	gi 21954740 gb AAM83103.1	27.4	73	53	0	8	80	139	211	0.14	29.9	25.0
FV7M4_gp17	gi 21954740 gb AAM83103.1	27.4	73	53	0	7	79	139	211	0.14	29.9	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	9	80	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	8	79	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	7	78	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	6	77	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	5	76	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	4	75	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	3	74	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	2	73	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	27.78	72	52	0	1	72	67	138	0.69	27.6	25.0
FV7M4_gp22	gi 21954740 gb AAM83103.1	28.17	71	51	0	10	80	67	137	1.1	26.9	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	9	80	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	8	79	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	7	78	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	6	77	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	5	76	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	4	75	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	3	74	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	2	73	415	486	1.8	25.5	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	30.56	72	50	0	1	72	415	486	0.22	28.6	27.5
RMP9_gp23	gi 78128018 gb AAY84564.2	29.58	71	50	0	1	71	416	486	2.2	25.2	26.3
RMP9_gp23	gi 78128018 gb AAY84564.2	30	70	49	0	11	80	415	484	1.8	25.5	26.3
RMP9_gp23	gi 78128018 gb AAY84564.2	30	70	49	0	10	79	415	484	1.8	25.5	26.3
RMP9_gp23	gi 78128018 gb AAY84564.2	30	70	49	0	1	70	417	486	2.8	24.9	26.3
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	18	80	423	485	0.16	29	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	17	79	423	485	0.13	29.3	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	16	78	423	485	0.15	29.1	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	15	77	423	485	0.16	29	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	14	76	423	485	0.1	29.7	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	13	75	423	485	0.13	29.3	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	12	74	423	485	0.1	29.7	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	11	73	423	485	0.094	29.8	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	10	72	423	485	0.099	29.7	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	9	71	423	485	0.099	29.7	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	8	70	423	485	0.086	29.9	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	7	69	423	485	0.086	29.9	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	6	68	423	485	0.068	30.3	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	5	67	423	485	0.1	29.7	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	4	66	423	485	0.13	29.3	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	3	65	423	485	0.14	29.2	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	2	64	423	485	0.15	29.1	26.2
RMP9_gp31	gi 78128018 gb AAY84564.2	33.33	63	42	0	1	63	423	485	0.17	28.9	26.2
RMP9_gp23	gi 78128018 gb AAY84564.2	30.43	69	48	0	1	69	418	486	4.5	24.2	26.2
RMP9_gp54	gi 21514 emb CAA27588.1	26.32	76	56	0	5	80	261	336	10	22.5	25.0
RMP9_gp54	gi 158517845 sp P15476.2 PATB1_SOLTU	26.32	76	56	0	5	80	261	336	10	22.5	25.0
RMP9_gp54	gi 21514 emb CAA27588.1	26.32	76	56	0	4	79	261	336	10	22.5	25.0
RMP9_gp54	gi 158517845 sp P15476.2 PATB1_SOLTU	26.32	76	56	0	4	79	261	336	10	22.5	25.0
RMP9_gp54	gi 21514 emb CAA27588.1	26.32	76	56	0	3	78	261	336	10	22.5	25.0
RMP9_gp54	gi 158517845 sp P15476.2 PATB1_SOLTU	26.32	76	56	0	3	78	261	336	10	22.5	25.0
RMP9_gp54	gi 21514 emb CAA27588.1	26.32	76	56	0	2	77	261	336	10	22.5	25.0
RMP9_gp54	gi 158517845 sp P15476.2 PATB1_SOLTU	26.32	76 76	56 5.6	0	2	77 7 5	261	336	10	22.5	25.0
RMP9_gp54	gi 21514 emb CAA27588.1	26.32	76	56	0	1	76	261	336	10	22.5	25.0

RMP9_gp54	gi 158517845 sp P15476.2 PATB1_SOLTU	26.32	76	56	0	1	76	261	336	10	22.5	25.0
RMP9_gp31	gi 78128018 gb AAY84564.2	33.9	59	39	0	1	59	427	485	0.35	27.9	25.0

query ID	subject ID	% identity	alignment length	mismatch count	gap open count	query start	query end	subject start	subject end	e-Value	bitScore	% identity 80mer
OBO18_gp42	gi 219806598 dbj BAH10154.1	28.95	76	54	0	3	78	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806602 dbj BAH10156.1	28.95	76	54	0	3	78	116	191	0.28	27.2	27.5
OBO18_gp42	gi 125659386 dbj BAF46896.1	28.95	76	54	0	3	78	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806600 dbj BAH10155.1	28.95	76	54	0	3	78	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806573 dbj BAH10157.1	28.95	76	54	0	3	78	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806598 dbj BAH10154.1	28.95	76	54	0	2	77	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806602 dbj BAH10156.1	28.95	76	54	0	2	77	116	191	0.28	27.2	27.5
OBO18_gp42	gi 125659386 dbj BAF46896.1	28.95	76	54	0	2	77	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806600 dbj BAH10155.1	28.95	76	54	0	2	77	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806573 dbj BAH10157.1	28.95	76	54	0	2	77	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806598 dbj BAH10154.1	28.95	76	54	0	1	76	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806602 dbj BAH10156.1	28.95	76	54	0	1	76	116	191	0.28	27.2	27.5
OBO18_gp42	gi 125659386 dbj BAF46896.1	28.95	76	54	0	1	76	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806600 dbj BAH10155.1	28.95	76	54	0	1	76	116	191	0.28	27.2	27.5
OBO18_gp42	gi 219806573 dbj BAH10157.1	28.95	76	54	0	1	76	116	191	0.28	27.2	27.5
OBO18_gp42	gi 455288 gb AAA33405.1	27.5	80	58	0	1	80	247	326	1.1	25.5	27.5
OBO18_gp42	gi 11991227 gb AAG42254.1 AF306707_	27.5	80	58	0	1	80	218	297	0.3	27.2	27.5
OBO18_gp42	gi 219806596 dbj BAH10153.1	29.58	71	50	0	3	73	116	186	0.72	25.9	26.3
OBO18_gp42	gi 219806596 dbj BAH10153.1	29.58	71	50	0	2	72	116	186	0.72	25.9	26.3
OBO18_gp42	gi 219806596 dbj BAH10153.1	29.58	71	50	0	1	71	116	186	0.72	25.9	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	15	80	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	15	80	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	14	79	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	14	79	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	13	78	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	13	78	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	12	77	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	12	77	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	11	76	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	11	76	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	10	75	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	10	75	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	9	74	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	9	74	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	8	73	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	8	73	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	7	72	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	7	72	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	6	71	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	6	71	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	5	70	216	281	0.14	28.2	26.3

OBO18 gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	5	70	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	4	69	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	4	69	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	3	68	216	281	0.14	28.2	26.3
OBO18 gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	3	68	241	306	0.15	28.2	26.3
OBO18 gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	2	67	216	281	0.14	28.2	26.3
OBO18_gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	2	67	241	306	0.15	28.2	26.3
OBO18_gp42	gi 29500897 emb CAD87529.1	31.82	66	45	0	1	66	216	281	0.14	28.2	26.3
OBO18 gp42	gi 345108717 emb CCD28287.1	31.82	66	45	0	1	66	241	306	0.15	28.2	26.3
OBO18 gp42	gi 156145810 gb ABU53681.1	27.63	76	55	0	3	78	116	191	0.9	25.6	26.2
OBO18 gp42	gi 156145810 gb ABU53681.1	27.63	76	55	0	2	77	116	191	0.9	25.6	26.2
OBO18 gp42	gi 156145810 gb ABU53681.1	27.63	76	55	0	1	76	116	191	0.9	25.6	26.2
OBO18_gp50	gi 8453086 gb AAF75225.1 AF208981_1	26.92	78	57	0	3	80	137	214	0.19	28.6	26.2
OBO18_gp50	gi 8453086 gb AAF75225.1 AF208981_1	26.92	78	57	0	2	79	137	214	0.19	28.6	26.2
OBO18_gp50	gi 8453086 gb AAF75225.1 AF208981_1	26.92	78	57	0	1	78	137	214	0.19	28.6	26.2
OBO18_gp15	gi 85701160 sp Q00002.2 PDI_ALTAL	26.67	75	55	0	6	80	168	242	1.4	25.5	25.0
OBO18_gp15	gi 85701160 sp Q00002.2 PDI_ALTAL	26.67	75	55	0	5	79	168	242	1.4	25.5	25.0
OBO18_gp15	gi 85701160 sp Q00002.2 PDI_ALTAL	26.67	75	55	0	4	78	168	242	1.4	25.5	25.0
OBO18_gp15	gi 85701160 sp Q00002.2 PDI_ALTAL	26.67	75	55	0	3	77	168	242	1.4	25.5	25.0
OBO18_gp15	gi 85701160 sp Q00002.2 PDI_ALTAL	26.67	75	55	0	2	76	168	242	1.4	25.5	25.0
OBO18_gp15	gi 85701160 sp Q00002.2 PDI_ALTAL	26.67	75	55	0	1	75	168	242	1.4	25.5	25.0
OBO18_gp42	gi 29500897 emb CAD87529.1	32.79	61	41	0	4	64	221	281	0.57	26.2	25.0
OBO18_gp42	gi 345108717 emb CCD28287.1	32.79	61	41	0	4	64	246	306	0.62	26.2	25.0
OBO18_gp42	gi 29500897 emb CAD87529.1	32.79	61	41	0	3	63	221	281	0.57	26.2	25.0
OBO18_gp42	gi 345108717 emb CCD28287.1	32.79	61	41	0	3	63	246	306	0.62	26.2	25.0
OBO18_gp42	gi 29500897 emb CAD87529.1	32.79	61	41	0	2	62	221	281	0.57	26.2	25.0
OBO18_gp42	gi 345108717 emb CCD28287.1	32.79	61	41	0	2	62	246	306	0.62	26.2	25.0
OBO18_gp42	gi 29500897 emb CAD87529.1	32.79	61	41	0	1	61	221	281	0.57	26.2	25.0
OBO18_gp42	gi 345108717 emb CCD28287.1	32.79	61	41	0	1	61	246	306	0.62	26.2	25.0
OBO18_gp42	gi 4468224 emb CAB38044.1	28.17	71	51	0	3	73	116	186	4.6	23.2	25.0
OBO18_gp42	gi 4468224 emb CAB38044.1	28.17	71	51	0	2	72	116	186	4.6	23.2	25.0
OBO18_gp42	gi 4468224 emb CAB38044.1	28.17	71	51	0	1	71	116	186	4.6	23.2	25.0
OBO18_gp42	gi 29500897 emb CAD87529.1	30.77	65	45	0	1	65	217	281	0.45	26.6	25.0
OBO18_gp42	gi 345108717 emb CCD28287.1	30.77	65	45	0	1	65	242	306	0.49	26.6	25.0

Two hundred and eighty-one pages have been removed in accordance with copyright laws. The removed reference citations can be found at Part VII. References

FDA questions for FinkTec in connection with GRN 1038

1. On pg. 27 (section VI.2), you provide a number of references to support your conclusion that there are no adverse effects in various safety studies in humans and animals (i.e., Carlton et al., 2005; Chibani-Chennoufi et al., 2004; Bruttin and Brussow, 2005; Weber-Dabrowska, Mulczyk and Gorski, 2003; Gorski et al., 2009; Kutter et al., 2010; Kutateladze, 2015). For the completeness of your safety narrative, please provide a short discussion comparing the levels/doses that showed no adverse effects in these studies to the dietary exposure of your article of commerce from the intended uses.

FinkTec answer:

Carlton et al 2005 fed rats with a daily dose of 5 x 10^{11} PFU (1 mL of a 5 x 10^{11} PFU/mL solution) over eight days (EDI = $100 \mu g/animal/day$).

Chibani-Chennoufi et al. 2004 force fed mice with a single dose of 1 x 10^9 PFU (EDI = $0.2 \mu g/animal/day$).

Bruttin and Brüssow, 2005 allowed healthy volunteers to drink 1.5 x 10^7 PFU (150 mL of a 1 x 10^5 PFU/mL solution) (EDI = 3.0 ng/person/day).

Weber-Dabrowska, Mulczyk and Gorski 2003 do not provide the titers of their various bacteriophage solutions used in their clinical study.

Kutter et al. 2010 in their review indicate that the standard Georgian bacteriophage product contains 10^5 - 10^6 PFU/mL, but no information is provided about how much of the product is applied in a single treatment.

Kutateladze, 2015 does not provide any experimental information.

Sarker et al. 2017 (Oral application of *Escherichia coli* bacteriophage: safety tests in healthy and diarrheal children from Bangladesh. Environmental Microbiology 19, 237-250) treated children with up to 1.4×10^9 PFU (EDI = $0.28 \mu g/person/day$).

The calculated incremental EDI for "Applied Phage Meat S2" is $0.70 \,\mu\text{g/person/day}$ and would thus lie in the same range as in the studies of Chibani-Chennoufi and Sarker and more than a 100 fold lower than in the study of Carlton. Thus, supporting the conclusion that no adverse effects could be expected. Bruttin and Brüssow used a very low dose for their initial small scale safety study, with a 100-fold lower EDI. However, the same research team used that initial study to then run a larger scale safety trial in Bangladesh with a 100-fold higher EDI (Sarker et al. 2017).

2. We note that Table 3 you listed on pg. 18 is not included in your GRAS notice. Please confirm that this is a typographical error and that the correct Table you refer to is Table 2.

FinkTec answer:

We confirm that the "Table 3" on page 18 is a typographical error and should read "Table 2"

3. You state on pg. 7 (section I.5) that your GRAS conclusion is partly based on "a comprehensive search of the scientific literature" but you do not provide any details of your literature search. Please provide the details of your literature search(es), including date (month and year), search engine(s) used, and search terms. If an updated literature search from initial search date to the present is needed, please discuss if any new information was found that would contradict your current GRAS conclusion.

FinkTec answer:

We regularly search the pubmed database for relevant publications:

https://pubmed.ncbi.nlm.nih.gov

Using a combination of search terms:

"clinical trial" as Publication Type and

"bacteriophage" as a MeSH term.

A search performed in June 2022 resulted in 81 publications that were then manually screened for their relevance (oral application and human health or animal health). Seven publications that could be considered relevant but were not initially included in our GRAS application (submitted in September 2021) are listed below. No recent relevant publications in between September 2021 and the present were found.

- 1. "Bacteriophage for Gastrointestinal Health (PHAGE) Study: Evaluating the Safety and Tolerability of Supplemental Bacteriophage Consumption". Gindin M, Febvre HP, Rao S, Wallace TC, Weir TL. J Am Coll Nutr. 2019 Jan;38(1):68-75. doi: 10.1080/07315724.2018.1483783
- 2. "Metagenome analysis of Russian and Georgian Pyophage cocktails and a placebo-controlled safety trial of single phage versus phage cocktail in healthy Staphylococcus aureus carriers". McCallin S, Sarker SA, Sultana S, Oechslin F, Brüssow H. Environ Microbiol. 2018 Sep;20(9):3278-3293.

doi: 10.1111/1462-2920.14310

3. "Oral application of Escherichia coli bacteriophage: safety tests in healthy and diarrheal children from Bangladesh".

Sarker SA, Berger B, Deng Y, Kieser S, Foata F, Moine D, Descombes P, Sultana S, Huq S, Bardhan PK, Vuillet V, Praplan F, Brüssow H. Environ Microbiol. 2017 Jan;19(1):237-250. doi: 10.1111/1462-2920.13574.

4. "Oral Phage Therapy of Acute Bacterial Diarrhea With Two Coliphage Preparations: A Randomized Trial in Children From Bangladesh".

Sarker SA, Sultana S, Reuteler G, Moine D, Descombes P, Charton F, Bourdin G, McCallin S, Ngom-Bru C, Neville T, Akter M, Huq S, Qadri F, Talukdar K, Kassam M, Delley M, Loiseau C, Deng Y, El Aidy S, Berger B, Brüssow H. EBioMedicine. 2016 Jan 5;4:124-37.

doi: 10.1016/j.ebiom.2015.12.023

5. "Safety analysis of a Russian phage cocktail: from metagenomic analysis to oral application in healthy human subjects".

McCallin S, Alam Sarker S, Barretto C, Sultana S, Berger B, Huq S, Krause L, Bibiloni R, Schmitt B, Reuteler G, Brüssow H. Virology. 2013 Sep 1;443(2):187-96.

doi: 10.1016/j.virol.2013.05.022

- 6. "Oral T4-like phage cocktail application to healthy adult volunteers from Bangladesh". Sarker SA, McCallin S, Barretto C, Berger B, Pittet AC, Sultana S, Krause L, Huq S, Bibiloni R, Bruttin A, Reuteler G, Brüssow H. Virology. 2012 Dec 20;434(2):222-32. doi: 10.1016/j.virol.2012.09.002
- 7. "PHAGE Study: Effects of Supplemental Bacteriophage Intake on Inflammation and Gut Microbiota in Healthy Adults".

Febvre HP, Rao S, Gindin M, Goodwin NDM, Finer E, Vivanco JS, Lu S, Manter DK, Wallace TC, Weir TL. Nutrients. 2019 Mar 20;11(3):666. doi: 10.3390/nu11030666.

The results presented in these seven publications also support the current GRAS conclusion, no contradicting information was found.

Overbey, Katie

From: Kristi Smedley <smedley@cfr-services.com>
Sent: Tuesday, November 22, 2022 3:34 PM

To: Overbey, Katie

Cc: h.lehnherr@ptc-phage.com

Subject: [EXTERNAL] RE: Additional Questions for GRN 1038

Attachments: GRN 1038 - FinkTec answers to FDA guestions.docx; Att1 specification growth

medium.pdf; Att2 specification monopotassium phosphate.pdf; Att3 Certificate ISI FOOD.pdf; R1 Ashton et al 2016 Salmonella identification.pdf; R2 Joensen et al 2014 Virulence finder.pdf; R3 Kennedy et al 1984 Coliphages in food.pdf; att4 ERS USDA data

sheet MeatSDRecent.xlsx

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dr. Overbey:

As we have previously corresponded (11/17/2022); Fink Tech is providing an amendment to GRN 1038 based on your additional questions (email of November 7, 2022). There were two sets of questions, one from FDA reviewers and one from the FSIS reviewers.

Attached to this email is the response of the FDA questions (with the exception of number 18 and 19). We are working with Exponent for this data, and will respond as soon as we have received the eaters-only mean and 90th percentile dietary exposure for the intended uses of the ingredient for the U.S. population aged 2 years and older based on U.S. food consumption data.

In addition, as we noted in our email of November 17, 2022, we will be responding to the FFSIS questions, once the additional studies are completed.

Please let us know if you have any problems receiving this information or have additional concerns.

Kristi O. Smedley, Ph.D.

Center for Regulatory Services, Inc. 5200 Wolf Run Shoals Rd. Woodbridge, VA 22192

Ph. 703-590-7337 Cell 703-786-7674 Fax 703-580-8637

From: Overbey, Katie [mailto:Katie.Overbey@fda.hhs.gov]

Sent: Monday, November 07, 2022 11:58 AM

To: Kristi Smedley

Subject: Additional Questions for GRN 1038

Dear Dr. Smedley,

During our review of GRAS Notice No. 1038 we noted additional questions that need to be addressed. Further, USDA FSIS has also identified questions that they would like the notifier to address. Please find both the FDA and USDA questions attached.

Please format your response such that each answer immediately follows the stated question. Please ensure that your responses do not contain confidential business information and please do not submit a revised version of the GRAS notice.

We respectfully request a response to these questions within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

Thank you in advance for your attention to our comments, Katie

Katie Overbey, Ph.D., M.S (she/her/hers)

Regulatory Review Scientist

Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
Tel: 240-402-7536
katie.overbey@fda.hhs.gov



The scientists of FinkTec provide the following answers to the questions raised by the FDA:

FDA Questions/Comments Regarding GRN 001038:

1. Throughout the notice, and in several of the appendices, the notifier states that the target of the phage preparations is "Salmonella enterica spp." As "enterica" is a species of Salmonella (as well as a subspecies of S. enterica), please clarify if the phage preparations are specific for Salmonella enterica only, or for Salmonella spp. in general. For example, on page 8 of the notice, the notifier identifies the substance as "Salmonella-specific phage preparation".

The phage preparations were developed to combat the serovars of *Salmonella enterica* subsp. *enterica* that are relevant for meat and meat processing. However, as some of the bacteriophages also show activity against *Salmonella bongori*, the second *Salmonella* species, it would be correct to say that the bacteriophages are active against *Salmonella* spp. in general.

2. Throughout the notice, and in several of the appendices, the notifier italicizes serovars of *Salmonella* (e.g., Typhimurium, Paratyphi). As serovars are not italicized, for the administrative record, please provide a statement clarifying these discrepancies. Please note, we are not requesting that the notifier correct these instances as they appear in the notice and its appendices, but that they provide a statement of affirmation.

We acknowledge our mistake, in the current nomenclature the *Salmonella* serovars are not italicized and the serovar names are capitalized.

3. Throughout the notice, and in several of the appendices, the notifier describes the host range of the phage preparations. For example, in Table 2 (page 18), the notifier includes various serovars of *Salmonella*, but refers to them as strains. As serovars and strains are not the same, for the administrative record, please clarify this discrepancy.

We acknowledge our mistake, serovars and strains are not equivalent. The header in Table 2 (page 18) should read: *Salmonella* serovars covered by "*Applied Phage Vegetable S2*", and also Table 2 in Attachment I should mention serovars not strains.

4. On page 11 of the notice, the notifier states "For each bacteriophage, a specific host strain, either *E. coli* or *Salmonella* is grown to a target optical density ... and infected with the bacteriophage". In addition to the strain of *E. coli*, page 10 further identifies two *Salmonella* host strains, including a strain of *Salmonella bongori* and a strain of *Salmonella* Paratyphi B var. Java. On pages 9 and 17, and elsewhere in the notice, the notifier identifies the host as "*Salmonella enterica* spp." Please clarify this discrepancy. Further, please explain why *E. coli* was used to propagate some of the phages in the phage preparations (described in the notice as a "*Salmonella*-specific phage preparation").

Salmonella bongori used to be classified as Salmonella enterica subspecies V, we thus wrongly grouped it with the Salmonella enterica subsp. enterica serotype Paratyphi B var Java host. As Salmonella bongori is currently classified as a separate Salmonella species, the two hosts should be named separately.

E. coli and *Salmonella* are two closely related members of the Enterobacteriaceae family. The differences between them, that result in the taxonomic distinction, are not always relevant for a bacteriophage infection. For example, both bacteria express a porin protein called OmpC. A bacteriophage that recognizes OmpC as a surface receptor will thus be able to infect and grow on both bacterial species. Wherever possible we used the non-pathogenic *E. coli* K-12 host for the propagation of *Salmonella*-specific bacteriophages as an additional safety measure.

5. On page 19 of the notice, the notifier states "In addition, *E. coli* K1 derivatives have been used repeatedly in the production of GRAS notified food additives." For the administrative record, please clarify if *E. coli* "K1" should be written as *E. coli* K-12.

The K1 is a mistake, it should read *E. coli* K-12.

- 6. When describing the host strains used to propagate the different phages, the notifier states "The two non-human pathogenic *Salmonella enterica* strains are known to produce no enterotoxins that could compromise the final product and have been considered safe for the production of salmonella-specific bacteriophages (GRAS Notice 000435)" (page 19).
- a. The notifier states that two strains of *S. enterica* are used as host strains; however, on page 10 of the notice, and in paragraph one on page 19, the notifier states that (in addition to the strain of *E. coli* used), *S. bongori* strain ATCC 43975 and *Salmonella* Paratyphi B var. Java strain ATCC BAA-1584 are used to propagate some of the phages. *S. bongori* is a species distinct from *S. enterica*. For the administrative record, please clarify this discrepancy.

As mentioned above in the answer to question 4, *Salmonella bongori* used to be classified as *Salmonella enterica* subspecies V, we thus wrongly still grouped it with *Salmonella enterica* subsp. *enterica* serotype Paratyphi B var Java. As *Salmonella bongori* is currently classified as a separate *Salmonella* species, the two hosts should be named separately.

b. The notifier cites GRN 000435 in the quoted passage; however, it is unclear what the relevance of GRN 000435 is in this context as the notifier has not summarized this information. For the administrative record, and as each GRAS notice stands on its own, please summarize the information from GRN 000435 that is relevant to the above quoted passage.

The notifier of GRN 000435 produces bacteriophages on the *Salmonella* serovars *S*. Hadar, *S*. Kentucky, *S*. Enteritidis, *S*. Agona and *S*. Typhimurium. Their safety argument was, that these *Salmonella enterica* host strains are not known to produce any enterotoxins that could compromise the safety of the final bacteriophage product.

c. Please clarify how the notifier confirmed that the strains of *Salmonella* used to propagate some of the phages were non-pathogenic. Please include citations to relevant peer-reviewed publications, as appropriate.

We agree with the safety argument of the notifier of GRN 000435, but chose an even more careful approach, when selecting *Salmonella* hosts for the propagation of the bacteriophages. Whenever possible we used a non-pathogenic *E. coli* K-12 host. Where that was not possible, we used strains of *Salmonella* that are known to cause the fewest infections in humans, i.e. *Salmonella bongori* and *Salmonella* Paratyphi B var Java (Ashton et al. 2016)

7. For the administrative record, please briefly specify how the purity of the host culture is ensured, and state whether the fermentation process is conducted in a contained, sterile environment.

The bacterial host strains are maintained in a two-tiered master cell stock – working cell stock system. The characterized strains are cryopreserved at -80°C, in a 20% glycerol buffered growth medium to eliminate contamination, biological degradation and genetic variation. The ability to support the growth of high-titer bacteriophage stocks is the quality criterium that is examined every time a new working cell stock is derived from the master cell stock. A contaminated working cell stock would result in a loss of titer.

The fermentation process is conducted in a stainless steel, stirred tank bioreactor (INFORS) that guarantees a contained and sterile environment.

8. Please state whether any of the raw materials used in the fermentation are major allergens or are derived from major allergens. If any of the raw materials used are major allergens or are derived from major allergens, please discuss why these materials do not pose a safety concern. For example, on page 15 of the notice, the notifier identifies "soy peptone" as a component of the fermentation media. Per the Food Allergen Labeling and Consumer Protection Act, soybeans are one of the major food allergens.

Our GRAS conclusion stated that we would be using animal product free growth media and listed ingredients that may be valuable. However, the growth media FinkTec uses (see attachment 1) does not contain any soy products. In general, it can be argued that already during the peptone production the proteins of the raw material are degraded to peptides, including any potential allergenic proteins. During the fermentation process, producing the bacteriophages, the peptones are further degraded to amino acids and then turned into bacterial and bacteriophage proteins. At the end of the fermentation process the bacteriophages are purified, removing all components of the growth medium and bacterial debris. Thus, there should be no traces of potential allergens in the final bacteriophage product. But as noted above, the FinkTec growth media do not contain soy peptones or any soy product (attachment 1).

9. On page 15, the notifier lists the Code of Federal Regulations (CFR) citation for monopotassium phosphate as 21 CFR 582.4521. We note that 21 CFR 582 corresponds to substances that are generally recognized as safe (GRAS) for use in animal drugs, feeds, and related products. As such, this is not an appropriate CFR citation for substances used in human conventional foods. For the administrative record, please make a statement that corrects this reference.

Yes, the citation to the monopotassium phosphate (21 CFR 582.4521) is specific for use in animal feed. The reference for use in human foods would be 21 CFR 160.110; although the regulation is specific for standardized egg products; the exposure would be far lower when used in a bacteriophage product than when used as a direct addition to frozen eggs. We have provided the food grade specification for the monopotassium phosphate product used by FinkTec (attachment 2).

10. On page 14 of the notice, the notifier lists the analytical method used to enumerate *Enterobacteriaceae* as ISO 6888-1, which corresponds to "Microbiology of the Food Chain - Horizontal Method for the Enumeration of Coagulase-Positive Staphylococci (*Staphylococcus aureus* and other species) - Part 1: Method Using Baird-Parker Agar Medium". For the administrative record, please clarify this discrepancy.

The citation on phage 14 is a mistake, the correct method is described in ISO 21528

11. The notifier lists "Table 2" on page 16 of the notice, however, the table included on the corresponding page is Table 1. For the administrative record, please clarify this discrepancy.

The numbering in the text is correct, the numbering of the tables is incorrect. "Table 1" is found on page 12. The table on page 16 should be marked as "Table 2" and the table on page 18 should be marked as "Table 3".

12. We note the following questions for the specifications listed on page 16 of the notice (Table 1): a. We note that the concentration is expressed as "bacteriophages/mL". Please confirm that it should be "plaque forming units" (PFU)/mL".

The concentration should correctly be expressed in (PFU)/mL.

b. The microbial specifications in Table 1 are listed as colony forming units (CFU)/g (as well as the critical limits presented on page 14); however, the product is characterized as a liquid product. Please clarify this discrepancy.

For water-based solutions with a density of 1, one gram equals one mL. The external, accredited laboratory (see attachment 3) delivers their analyses results in (CFU)/g even when analysing our liquid products.

c. ISO 48833 is listed as the analytical method used to assess total plate count. This citation does not correspond to an ISO method. Please clarify if the analytical method used to assess total plate count is ISO 4833. Further, please clarify whether Part 1 or Part 2 of the method is used.

The analytical method used is ISO 4833-1.

d. The provided specifications for total plate count, yeast and mold, and Enterobacteriaceae on page 16 of the notice differ from those listed as critical limits for CCP2 in the summary of the HACCP plan (page 14). CCP2 corresponds to the final sterile filtration step prior to shipping the final product. The critical limit set at this manufacturing step for each of the three identified hazards is > 10 CFU/g, with the corrective action identified as "redo sterile filtration" if the CFU/g count exceeds the critical limit. Therefore, the provided specifications for total plate count, yeast and mold, and Enterobacteriaceae on page 16 of the notice exceed the critical limits set on page 14. Please clarify this discrepancy.

Thank you for pointing out this discrepancy. We modified our internal HACCP plan summary, see below, to correct the critical limits for total plate count, yeast and mold and Enterobacteriaceae.

I.1.1 HACCP plan summary

Subject	ISSUE DATE	PRODUCT
CCP HACCP Plan Summary	2.03.2016 modified 14.11.2022	Applied Phage Vegetable S2
FinkTec GmbH		Page 1 of 1
Oberster Kamp 23		
59069 Hamm		
Germany		

Critical			Monitoring	Monitoring					
Control									
Points		Critical					Corrective		
ССР	Hazard(s)	Limit	what	how	Frequency	who	Action(s)	CCP Verification	Records
			Total						
			aerobic						
	bacterial		germ				Redo sterile		
CCP 1	contamination	>50 CFU/g	count	ISO 4833-1	each batch	QC	filtration	positive control	
			Yeast and				Redo sterile		
		>100 CFU/g	moulds	NMKL 98	each batch	QC	filtration	positive control	
			Total						
			aerobic						
	bacterial		germ				Redo sterile		
CCP 2	contamination	>50 CFU/g	count	ISO 4833-1	each batch	QC	filtration	positive control	
			Yeast and				Redo sterile		
		>100 CFU/g	moulds	NMKL 98	each batch	QC	filtration	positive control	
			Enterobac-						
			teriaceae				Redo sterile		
		>100 CFU/g		ISO 21528	each batch	QC	filtration	positive control	

e. Several of the footnotes included on page 16 do not correspond with the referenced analytical methods in Table 1. Further, some of the footnotes reference analytical methods that have since been revised (e.g., ISO 6888-1:1999 has been revised by ISO 6888-1:2021). For the administrative record, please provide a revised list of relevant footnotes to accompany Table 1.

We updated the footnotes to the table. A revised table is provided below in the answer to question 14.

13. Please state whether all analytical methods used to analyze the batches for conformance with the stated specifications have been validated for that particular purpose.

The analyses are performed by an external, accredited laboratory and the methods have been validated for that purpose (attachment 3).

14. We note that the specifications do not include a limit for lead that we typically request for ingredients produced by fermentation. Please include a specification limit for lead in Table 1 on page 16 and provide a reference for the corresponding analytical method.

Revised Table 2:

Table 2: Product specifications of "Applied Phage Vegetable S2"

Description Standardized bacteriophage cockts					
	based on naturally occurring				
		bacteriophages, stabilized			
Concentration	Approx. $> 1 \times 10^9 P$	FU/mL ¹			
Packaging	Stainless steel KEG	barrels, flat fitting			
Storage	Cool and dry (recon	nmended 4-8°C), do			
-	not store in direct su	n light			
Shelf life	6 months, process in	nmediately after			
	opening				
Appearance	Colorless to light ye	llowish liquid			
Texture	Liquid				
рН	7.0-7.4				
odor/taste	characteristic				
Micro	Microbiological Parameters				
Total plate count	ISO 4833-1 ²	< 50 CFU/g			
Yeast and Mould	NMKL 98 ³	< 100 CFU/g			
Staphylococcus	ISO 6888 ²	< 10 CFU/g			
Salmonella	NMKL 71 ³	not detectable in 25 g			
Enterobacteriacea	ISO 21528 ²	< 100 CFU/g			
Sulfite-reducing Clostridia	ISO 15213 ²	< 1000 CFU/g			
	Heavy metals				
Lead	DIN EN ISO	< 10 μg/L			
	11885:2009-09 ⁴				
	Identity	I == ,			
PCR Verification ⁵	Complies	Yes/no (for single			
		phage)			

¹Clokie and Kropinski 2009

²https://www.iso.org/standard/76672.html

³http://www.nmkl.org/index.php/en/

⁴https://www.beuth.de/en/standard/din-en-iso-11885/118931490

⁵Mullis et al. 1987

15. Please provide results from a minimum of three (preferably five) non-consecutive batches to demonstrate that the phage preparations can be manufactured to meet the provided specifications listed in Table 1 (page 16), including the limit for lead.

The analytical method to determine the lead concentration is DIN EN ISO 11885:2009-09 Water quality - Determination of selected elements by inductively coupled plasma optical emission spectrometry (ICP-OES). The limit for lead < 10 μ g/L follows the regulation for potable water in Germany. The analyses results of three non-consecutive batches are provided below, showing that in all three production batches the lead concentration is below 5 μ g/L, in the uncritical range.

Lead analysis as completed by Raiffeisen LaborServices (November 18, 2022)

Batch number	Lead analysis*
29032021	< 5 ug/L
18012022	< 5 ug/L
7092022	< 5 ug/L

^{*}Limit of quantification 5 microgram/liter (approximately 5 ppb)

https://www.raiffeisen-laborservice.de/service/Analysemethoden

16. On page 17 of the notice, the notifier lists the phage names and classifications for the phages that may be included in the phage preparations. Bacteriophage DSM 26158 ("ELB17") is missing from the list of phages. For the administrative record, please clarify this discrepancy.

That is an omission, bacteriophage DSM 26158 (ELB17) should be included in this list.

17. On page 23, the notifier states that the average disappearance in 2020 was 281.3 pounds of red meat and poultry, per capita, per year. As a reference, the notifier provides a link to the USDA Livestock and Meat Domestic Data (https://www.ers.usda.gov/dataproducts/livestock-meat-domestic-data/). We note that we were not able to confirm average disappearance in 2020 of 281.3 pounds of red meat and poultry, per capita. Please specify which data set was used to obtain this value.

We checked the https://www.ers.usda.gov/data-products/livestock-and-meat-domestic-data/ webpage on 11/22/22. The data set "all meat statistics"; "meat statistics tables recent" was last updated on 10/26/2022. The excel sheet (attachment 4) shows a per capita disappearance of 279.9 pounds (carcass weight) of red meat and poultry for the year 2020.

18. We note that in order to provide a conservative estimate, an eaters-only dietary exposure, not a per capita dietary exposure, should be provided. Please provide an eaters-only mean and 90th percentile dietary exposure for the intended uses of the ingredient for the U.S. population aged 2 years and older based on U.S. food consumption data.

We are in the process of organizing the necessary food consumption data to calculate the requested eaters-only dietary exposure.

19. On page 23, the notifier explains how the estimate of dietary exposure was calculated. In the revised dietary exposure, the notifier should reference any data sets used in their estimation and ensure that the correct units are provided.

The revised calculation will include the data sets and will pay specific attention to the units provided.

20. On page 25 of the notice, the notifier states that Part 4: Self-Limiting Levels of Use is not applicable. Based on the intended conditions of use of the phage preparations presented in the notice, we do not believe that the notifier's statement is accurate. We recommend that the notifier review the statements provided by other notifiers of phage preparations that have been submitted to and evaluated by FDA and received "no questions" response letters (e.g., GRN 000917), and provide a revised statement (in their own words) to Part 4. These GRAS notices may be accessed using our online GRAS inventory.

We would like to amend the section "Part 4: Self-Limited Levels of use" with the following statement:

The bacteriophage cocktail, formulated as "Applied Phage Meat S2", is intended for use as antimicrobial to control Salmonella spp. in red meat and poultry. The purpose to use "Applied Phage Meat S2" as a processing aid for fruits and vegetables that are at risk to be contaminated with Salmonella is to reduce or eliminate the bacterial contamination in the final food product, thus making it safer for human consumption.

The self-limiting levels of use are:

- The handler/processor would use the minimum required dose to achieve the desired effect of eliminating the *Salmonella* contamination, due to the cost of the product.
- Bacteriophages are inert physical particles without metabolic activity of their own. After depleting their host organism from food or food contact surfaces, the concentration of bacteriophage particles would stagnate and eventually dwindle or reach the natural concentration of bacteriophages found in all foods (Kennedy, Oblinger, and Bitton 1984).
- The biological activity of bacteriophages is sensitive to a number of environmental factors including heat and UV light. Exposure to these factors will reduce the number of active bacteriophages in food. Most effective is thereby the standard process of cooking.

21. On pages 28-31 of the notice, the notifier summarizes other phage preparations that have been previously evaluated by various regulatory bodies. Several of the summaries are either incomplete (e.g., missing the food categories covered by the notice), incorrect (e.g., include food categories that were removed by a notifier during evaluation), or are missing (e.g., supplements to an existing GRAS notice, GRAS notices with response letters issued prior to the submission of GRN 001038). Examples are provided below. For the administrative record, please make a statement that corrects these references. For future submissions, we recommend that the notifier please refer to the response letters when summarizing the intended uses of previously submitted GRAS notices, as the information displayed in the online GRAS inventory may not be entirely accurate. a. GRN 000752 is missing the food categories included in the response letter.

- b. GRNs 000827, 000834, and 000966 include food categories that were removed by the notifier during evaluation of the notice, and therefore were not included in the response letters and/or the supplement response letters.
- c. The notifier of GRN 000888 requested that we cease our evaluation of the notice for administrative reasons.
- d. GRNs 000198, 000603, and 000672 are missing from the notifier's summary. Further, some of the listed GRAS notices had supplements that were evaluated prior to the submission of GRN 001038 (including, but not limited to, GRN 000435).

We acknowledge that our list of GRAS notices was incomplete and inaccurate and will strive to follow the recommendations of the reviewer for future submissions.

22. Page 4 of Appendix 1 lists the various serovars of *Salmonella* that were analyzed to determine the host range of the phage preparations; however, a negative control (e.g., *E. coli*) is not listed. How was specificity of the phage preparations for *Salmonella enterica* determined? Is there cross reactivity with other genera of bacteria?

As *Salmonella* and *E. coli* are very closely related bacterial genera, all bacteriophages were also tested for their ability to grow on *E. coli*. No experiments to detect cross reactivity against distantly related genera were performed.

23. The notifier states that Appendix 2 contains confidential business information. We do not believe that the information presented in Appendix 2 meets the definition of trade secret information or commercial or financial information, which is privileged or confidential, per 21 CFR 20.61. Please clarify how and why the information presented in Appendix 2 is confidential. Further, Appendix 2 contains summaries of Appendices 4-6, which are not identified by the notifier as containing confidential business information. For the administrative record, please provide the summaries of Appendices 4-6 as presented in Appendix 2.

FinkTec considers Attachment II, Paragraphs 2-7 to contain confidential business information as the genetic relationships between our bacteriophages and bacteriophages described in the public databases, in this bioinformatical detail, could be used by a skilled competitor to retro-engineer our product and then produce a product with equivalent efficiency. Paragraphs 1, 8 and 9 of Attachment II are not considered to be Confidential Business information.

Paragraph 8:

The search engine "Virulence Finder" and a curated database of *E. coli* toxins and virulence factors provided by the Center for Genomic Epidemiology of Danish Technical University (Lyngby, Denmark) were employed for the analysis of the eleven bacteriophage genomes for presence of known *E. coli* toxins and virulence factors. Initially, the database contained sequence variants for 76 genes (Joensen et al. 2014); at the moment of the search the Database version 2018-10-12 was used and it had 957 sequence variants of 102 *E. coli* genes associated with virulence (gene names are listed in the attached table). The search was performed using the lowest possible stringency provided by the search engine (85% identity and 40% minimum length of the match) and resulted in no hits, demonstrating the absence of *E. coli* virulence genes in the genomes of the eleven bacteriophages studied (the search output for every investigated genome is included as **Attachment IV**).

Paragraph 9:

These analyses confirmed not only the lytic nature of all bacteriophages but also demonstrated that no toxin genes (as listed in EPA 40 CFR Ch. (7-1-11 Edition) § 725.421-725.422) (**Attachment V**), no antibiotic resistance markers, no genes coding for proteins with allergenic properties (**Attachment VI**) nor any other detrimental genes were present.

List of attachments:

- 1. Specification for the yeast-based growth medium
- 2. Specification for monopotassium phosphate
- 3. Certificate ISI Food laboratory
- 4. ERS USDA Excel data sheet "MeatSDRecent"

References:

Ashton, Philip M., Satheesh Nair, Tansy M. Peters, Janet A. Bale, David G. Powell, Anaïs Painset, Rediat Tewolde, et al. 2016. "Identification of Salmonella for Public Health Surveillance Using Whole Genome Sequencing." *PeerJ* 2016 (4): 1–18. https://doi.org/10.7717/peerj.1752.

Joensen, Katrine Grimstrup, Flemming Scheutz, Ole Lund, Henrik Hasman, Rolf S. Kaas, Eva M. Nielsen, and Frank M. Aarestrup. 2014. "Real-Time Whole-Genome Sequencing for Routine Typing, Surveillance, and Outbreak Detection of Verotoxigenic Escherichia Coli." *Journal of Clinical Microbiology* 52 (5): 1501–10. https://doi.org/10.1128/JCM.03617-13.

Kennedy, J. E., J. L. Oblinger, and G. Bitton. 1984. "Recovery of Coliphages from Chicken, Pork Sausage and Delicatessen Meats." *J Food Protection* 47: 623–26. http://www.ingentaconnect.com/contentone/iafp/jfp/1984/00000047/0000008/ar t00009?crawler=true.



Product range:

NuCel® **YEAST PEPTONE**

NuCel® 581 PW - Powder



APPLICATION

Suitable for a broad range of mesophilic and thermophilic lactic bacteria, NuCel® 581 PW associated with yeast extract promotes microorganisms growth and can be used during the strain conservation as viability protective agent.

DESCRIPTION

NuCel® 581 PW is a primary yeast peptone obtained by the autolysis of a selected strain of yeast, especially grown on a molasses-based media.

STATEMENTS

NuCel® 581 PW is guaranteed to be Non-GM, free of animal origin ingredient, halal and kosher.

COMPOSITION

NuCel® 581 PW is a high quality source of readily available soluble, amino acids, medium-sized peptides, vitamins and essential elements.

PHYSICO-CHEMICAL **SPECIFICATIONS**

Expressed on product as is

Dry matter	Min.	94,0	g / 100 g
Total nitrogen	Min.	10,00	g / 100 g
Amino nitrogen	Min.	1,60	g / 100 g
Proteins	Min.	62,5	g / 100 g
рН		6,2-7,2	

MICROBIOLOGICAL SPECIFICATIONS

Total mesophilic bacteria	Max.	5000	CFU/g
Total coliforms	Max.	5	CFU/g
Spores of clostridium perfringens	Max.	10	CFU/g
Yeasts	Max.	50	CFU/g
Moulds	Max.	50	CFU/g
Bacillus cereus	Max.	100	CFU/g
Enterobacteria	Max.	10	CFU/g
Salmonella		Neg.	CFU/25g
E.coli		Neg.	CFU/g
Pathogenic Staphylococcus		Neg.	CFU/g
Listeria		Neg.	CFU/25g

PACKAGING & PALLET

20 kg (44 lbs) sealed paper bags with polyethylene liner/ pallets of 600 kg (1,322 lbs)

SHELF LIFE & STORAGE 3 years in their original packaging, stored in a dry place at a cool to ambient temperature and protected from direct sunlight.

©Procelvs. NuCel® is a registered trademarks of Procelvs. Use and/or sale of these products may be covered by one or more patents as well as patent applications in EU. US and other countries. Product registration requirements apply in selected regions and countries; counsult Process on product any office of the best of our knowledge at the indicated date and remains our property. It is the user's responsibility to ensure that the conditions and possible uses of the product conform in particular to current laws and regulations.



Order N° Delivery note : 206225 OP : 10359202

Vendor Code

Letter of crédit Invoice CERTIFICATE OF ANALYSIS / CONFORMITY

Customer

IMCD DEUTSCHLAND GmbH

Consignee

ALFRED TALK GMBH & CO. KG

F.A.O Poltner

sandra.bender@imcd.de

Page: 1 / 1

Item

: NuCel 581 PW

Your reference

Batch N°

erence : /

: AD22A00450

Use by : 22.01.2025

Production date: 23.01.2022

Bio Springer is a ISO 9001, FSSC22000 certified company

Characteristic	Value	Unit
DRY MATTER	97,5	g%g
TOTAL NITROGEN	11,88	g%g
AMINO NITROGEN	2,71	g%g
PH	6,8	
PROTEINS (N X 6.25)	74,3	g%g
TOTAL MESO BACTERIA	< 5	/g
TOTAL COLIFORMS	0	/g
SPORES CLOS PERF.	< 5	/g
YEASTS	< 5	/g
MOULDS	< 5	/g
BACILLUS CEREUS	< 20	/g
ENTEROBACTERIA	< 5	/g
SALMONELLA	0	/25g
E. COLI	0	/g
PATHOGENIC STAPH	0	/g
LISTERIA	0	/25g

Maisons-Alfort, le 04.04.2022

Département Qualité/ Mme Armelle BOULANGER



Distribueras av IMCD Sweden AB

24-timmars nödtelefonnummer:

+44 1235 239670 (flerspråkig service)

Giftinformationscentralen 112 -begär Giftinformation

Carechem International, UK:

Hyllie Boulevard 53 215 37 MALMÖ sds@imcdaroup.com

Product: NuCel® 581 PW **Product Number: 581 PW**

SECTION 1: IDENTIFICATION

Product Identifiers

NuCel® 581 PW is a primary Yeast peptone obtained by the autolysis of a selected strain of yeast, especially grown on a molasses-

: NuCel® 581 PW Product name

: 581 PW Product Code(s)

Application of the Substance or Mixture

Product Use : Fermentation Aid

Product Restrictions : No relevant information available.

Details of the Supplier of the Safety Data Sheet

Company Identification : Procelys, a Business Unit of Bio Springer France

> 103 Rue Jean Jaurès 94704 Maisons Alfort

France

Emergency Telephone Number

Emergency : +33 (0) 1 49 77 18 45 / 46

SECTION 2: HAZARD(S) IDENTIFICATION

Classification of the Substance or Mixture

GHS Classification in accordance with European Regulations and 29 CFR 1910 (OSHA HCS)

Not a hazardous substance or mixture.

GHS Label Elements

Not a hazardous substance or mixture.

Hazard(s) Not Otherwise Classified

(HNOC) or not covered by GHS : Material may cause slight irritation on prolonged or repeated contact. Do not handle this

material if you have known allergies or otherwise physical reaction to yeast.

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

Yeast extracts are natural ingredients containing:

Proteins, Peptides and Amino-acids; Carbohydrates, Minerals and lipids Common Name/ Synonyms : Saccharomyces Cerevisiae : 84604-16-0 and/or 8013-01-2 CAS Number EC Number : 238-294-5 and/or 232-387-9

Hazardous Components

No ingredients are hazardous according to European Standards criteria No components need to be disclosed according to the applicable regulations.

SDS Issue Date : January 6th, 2020 SDS Revision Number : V 02-2020

Procelys, a Business Unit of Bio Springer France 103 Rue Jean Jaurès – 94704 Maisons Alfort - France



Product: NuCel® 581 PW **Product Number:** 581 PW

SECTION 4: FIRST-AID MEASURES

Description of First Aid Measures

Eye Contact : Remove contact lenses at once. Flush eyes with plenty of water for at least 15 minutes,

occasionally lifting the upper and lower eyelids. Get medical help if needed.

Skin Contact : Flush skin with plenty of water; If irritation or adverse symptoms develop, seek medical

attention.

Ingestion : If victim is conscious and alert, rinse mouth with water as a precaution. Never give

anything to an unconscious person; get medical assistance.

Inhalation : Remove from exposure and move to fresh air immediately. If not breathing, give

artificial respiration. If breathing is difficult, give oxygen and get medical help

immediately.

Most Importance Symptoms and Effects, Both Acute and Delayed

No further relevant information available.

Indication of Any Immediate Medical Attention and Special Treatment Needed

No further relevant information available.

SECTION 5: FIRE-FIGHTING MEASURES

Extinguishing Media

Suitable Extinguishing Agents : Use dry chemical, carbon dioxide, water spray, or alcohol-resistant foam. Use agent most

appropriate to extinguish fire.

Contra-indicated extinction medium: None. **Particular risks**: None.

Special Hazards Arising From the Substance or Mixture

Carbon oxides

Advice for Firefighters

Protective Equipment : Wear self-contained breathing apparatus for firefighting if necessary.

Additional Information : No data available

SECTION 6: ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures

Avoid dust formation. Avoid breathing vapors, mist or gas. Use proper personal protective equipment as indicated in Section 8.

Environmental Precautions

Prevent further leakage or spillage if safe to do so. Do not let product enter drains.

Avoid discharging directly into the sewers (organic pollution).

Methods and Materials for Containment and Clean Up

Sweep up and shovel. Keep in suitable, closed containers for disposal.

SDS Issue Date : January 6th, 2020 Procelys, a Business Unit of Bio Springer France SDS Revision Number : V 02-2020 Procelys, a Business Unit of Bio Springer France 103 Rue Jean Jaurès – 94704 Maisons Alfort - France



Product: NuCel® 581 PW **Product Number:** 581 PW

Easily eliminate by a simple washing with water. Avoid high pressure rinsing.

Reference to Other Sections

See Section 7 for information on safe handling.

See Section 8 for information on personal protection equipment.

See Section 13 for disposal information.

SECTION 7: HANDLING AND STORAGE

Precautions For Safe Handling

Handle in accordance with good industrial hygiene and safety practices. These practices include avoiding unnecessary exposure and removal of the material from eyes, skin and clothing. Provide appropriate exhaust ventilation at places where dust is formed. Normal measures for preventative fire protection. For precautions, see section 2.

Conditions for Safe Storage, Including Any Incompatibilities

Keep container tightly closed in a cool, dry and well-ventilated place.

Specific End Use(s)

Apart from the use(s) mentioned in Section 1, no other specific uses are stipulated.

SECTION 8: EXPOSURE CONTROL/ PERSONAL PROTECTION

Control Parameters

Exposure Limits : European Agency for Safety and Health have not established specific exposure limits for

this material.

Respiratory protection: Safety mask to prevent from dust inhalation.

Ventilation: Use adequate ventilation.Hand protection: Use adequate ventilation.Eye protection: Protective goggles.

Appropriate Engineering Controls

Provide natural or mechanical ventilation to minimize exposure. The use of local mechanical exhaust ventilation is preferred at sources of air contamination such as open process equipment.

Personal Protective Equipment

Eyes : Wear appropriate protective eyeglasses or chemical safety goggles as described by

OSHA's eye and face protection regulations in 29 CFR 1910.133 or European Standard

EN166.

Skin : Wear appropriate protective gloves to prevent skin exposure. Dispose of contaminated

gloves after use in accordance with applicable laws and good laboratory practices. Wash

and dry hands.

Clothing : Wear appropriate protective clothing to prevent skin exposure.

Respirators : Follow the OSHA respirator regulations found in 29 CFR 1910.134 or European

Standard EN 149. Use a NIOSH/MSHA or European Standard EN 149 approved

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Product: NuCel® 581 PW **Product Number: 581 PW**

> respirator if exposure limits are exceeded or if irritation or other symptoms are experienced.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

Information on Basic Physical and Chemical Properties

Appearance:

Odor

Form : Highly hygroscopic powder Color : Yellow to dark brown : Typical of yeast

pH (8.33% solution)

Breakdown temperature :>100°C Self-ignition temperature $: > 250^{\circ}C$ Danger of explosion : Class 1 dust Minimal ignition temperature in 5 mm layer $: > 400^{\circ}C$ Minimal ignition temperature in cloud $: > 500^{\circ}C$ Minimal Ignition Energy (MIE) : 1000 mJ < ME

Solubility : Very soluble in water but not applicable in organic solvent

Violence of explosion

- Pmax (bar) : 7.1 - (dP/dt) max (bar/s) : 199 - Kst (bar.m/s) : 54 - Class : 1

Density (g/cm3) : 0.3 - 0.6

Other Safety Information

No further relevant information available.

NOTE: These physical data are typical values based on material tested but may vary from sample to sample. Typical values should not be construed as a guaranteed analysis of any specific lot or as specifications for the product.

SECTION 10: STABILITY AND REACTIVITY

Yeast peptone have bacteriological stability when kept in their original packaging, stored in a cool and dry place protected from direct sunlight.

Reactivity

No Data Available

Chemical Stability

Stable under normal temperatures and pressures.

Possibility of Hazardous Reactions

No dangerous reactions known.

Conditions to Avoid

No further relevant information available, however Prevent dust dispersion.

Procelys, a Business Unit of Bio Springer France SDS Issue Date : January 6th, 2020 SDS Revision Number : V 02-2020 103 Rue Jean Jaurès – 94704 Maisons Alfort - France



Product: NuCel® 581 PW **Product Number:** 581 PW

Incompatible Materials

No further relevant information available.

Hazardous Decomposition Products

No dangerous decomposition products known.

SECTION 11: TOXICOLOGICAL INFORMATION

Information on Toxicological Effects

Acute toxicity

No Data Available

Skin Corrosion/Irritation

No Data Available

Serious Eye Damage/Eye Irritation

No Data Available

Respiratory or Skin Sensitization

Repeated inhalations of dust may cause sensitization and will cause allergic type reaction in sensitized individual.

Germ Cell Mutagenicity

No Data Available

Carcinogenicity

No Data Available

SECTION 12: ECOLOGICAL INFORMATION

Toxicity

Toxicity to Fish : No Information Found Toxicity to Other Aquatic Invertebrates : No Information Found

Persistence and Degradability

Biodegradability : Yeast peptone are highly biodegradable.

Results of PBT and vPvB Assessment

PBT : Not Applicable vPcB : Not Applicable

Other Adverse Effects

No further relevant information available.

SECTION 13: DISPOSAL CONSIDERATIONS

Product and Contaminated Packaging must be disposing of in accordance with local requirements.

SDS Issue Date : January 6th, 2020 SDS Revision Number : V 02-2020 Procelys, a Business Unit of Bio Springer France 103 Rue Jean Jaurès – 94704 Maisons Alfort - France



Product: NuCel® 581 PW **Product Number:** 581 PW

SECTION 14: TRANSPORTATION INFORMATION

This product is not a dangerous good according to international transport regulations.

The data provided in this section is for information only. Please apply the appropriate regulations to properly classify your shipment for transportation.

Road Transport ADR : Not Regulated Rail Transport RID : Not Regulated Sea and Inland waterway Transport AND : Not Regulated IMDG : Not Regulated

Air Transport ICAO/IATA : Not Regulated

SECTION 15: REGULATORY INFORMATION

Yeast peptone are not classified under EC 1272/2008 Regulation (CLP).

SECTION 16: OTHER INFORMATION

Yeast peptone are intended for industrial use only.

SDS Issue Date : January 6th, 2020

SDS Revision Number : V 02-2020 **Supersedes Issue Date** : V 00 - 2010

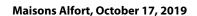
Summary of Changes

Revision No.	Changes		
V 01-2017	New presentation		
V02-2020	Logo Change		
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Disclaimer

The information in this SDS was obtained from current and reliable sources. However, the data is provided without any warrant, expressed or implied, regarding its correctness or accuracy. Since the use, handling, storage and disposal of this product are beyond Lesaffre Yeast Corporation's control, it is the responsibility of the user both to determine safe conditions for the use of this product and to assume liability of loss, damage, or expense arising out of the product's improper use. No warranty expressed or implied regarding the product described herein shall be created by or inferred from any statement or omission in this SDS. Various Federal, State or Provincial agencies may have specific regulations concerning the transportation, handling, storage, use, or disposal of this product which may not be reflected in this SDS. The user should review these regulations to ensure full compliance.

SDS Issue Date : January 6th, 2020 Procelys, a Business Unit of Bio Springer France SDS Revision Number : V 02-2020 103 Rue Jean Jaurès – 94704 Maisons Alfort - France





Allergens Statement - NuCel® 581 PW

-Version 2.0_102019 -Allergens

Allergens as defined by previous EU Directives 2003/89/EC - 2006/142/EC - 2007/68/EC		Presence in the recipe		Presence On the same production line		Presence On the production site	
		Yes	No	Yes	No	Yes	No
CEREALS containing gluten, and products thereof	i.e.wheat, rye, barley, oats, spelt, kamut or Hybrids		Х	Х		Х	
i.e. almond , hazelnut, wallnut, NUTS and products thereof cashew nut, pecan nut, pistachio nut,			X		x		Х
EGGS and products thereof			Х		X		Х
MUSTARD and products thereof			Х		Χ		Х
PEANUTS and products thereof			Х		Χ		Х
FISH and products thereof			Х		Х		Х
SOY and products thereof			Х		Х		Х
SESAME seeds and products t	hereof		Х		Χ		Х
CELERY and products thereof			Х		Х		Х
CRUSTACEANS and products t	hereof		Х		Х		Х
MILK and products thereof			Х		Х		Х
SULPHITES added E220 / E227			Х		Х		Х
LUPIN and products thereof			Х		Х		Х
MOLLUSC and products thereof			Х		Х		Х

 $Use of a processing aid from barley on the line. Cross contamination under control. \ NuCel § 581 PW powders are guaranteed gluten < 10 ppm (detection limit).$

Quality DepartmentArmelle Boulanger, Quality Director

BIO SPRINGER

BIO SPIKINGER,
Département Qualité
S.A. sa repital de 1375 000 euros
CS. Chein 544 00196 - SBET 542 00196 00026
NAF 10827. TVA FR 93 543 001 996
103, rue Jean Jaurès - 94704 Maisons-Alfort
Tél. : 01 49 771 18 4574
Fax : 01 43 75 69 00

Valid until the further notice

PRODUCT SPECIFICATION DATA SHEET







DESCRIPTION

General Description Potassium monophosphate for Hygroscopic white crystals with the crystal	ood grade thout foreign matters. Risk of caking	Date effective – edition December, 2012-02
Grade Food grade	E number(s)	Formula KH ₂ PO ₄
Molecular weight	EINECS	CAS number
136	231-913-4	7778-77-0

PRODUCT CHARACTERISTICS

Chemical properties	Unit	Typical analysis	Specifications	Methods
Total P ₂ O ₅ (anhydrous)	%	52.1	51.6 – 53.0	PLC 20
Assay on dried basis	%	> 99.0	99.0 Min.	Calculation
pH solution 1%		4.5	4.3 – 4.7	PLC 07
pH solution 5 %		4.3	4.2 – 4.5	PLC 07
Insoluble matters	%	< 0.20	0.20 Max.	PLC 03
Loss on desiccation @ 105℃	%	< 0.05	0.50 Max.	PLC 13
Impurities content				
Pb	ppm	< 0.5	1.0 Max.	PICP 05
As	ppm	0.2	1.0 Max.	PICP 04
F	ppm	2.7	10.0 Max.	PLC 14
Cd	ppm	< 0.1	1.0 Max.	PICP 05
Hg	ppm	< 0.1	0.1 Max.	PICP 04
Heavy metals (as Pb)	ppm	< 10	10 Max.	PLC 08
Physical properties				
Tapped density	g/cm ³ lbs/ft ³	1.54 96	1.43 – 1.63 89 - 102	Calculation
<u>Granulometry</u>				
Cumulated retain on :				
1000 µm	%	1	4 Max.	PLC 09
420 μm (40 mesh)	%	27	0 - 50	PLC 09
150 μm (100 mesh)	%	87	55 - 98	PLC 09
75 μm (200 mesh)	%	94	80 - 100	PLC 09
45 μm (325 mesh)	%	97	85 - 100	PLC 09

THEORETICAL VALUES

Solubility	22 g/100 g water @ 20 ℃
K₂O	34.6 %

IDENTIFICATION TEST

Positive tests for potassium and phosphate

PRODUCT SPECIFICATION DATA SHEET







STORAGE & SHELF LIFE

Store in a cool, dry and odorless place. Protect from humidity. Keep in the packaging of origin, shrink-wrapped. Best before: 2 years after production date.

KEY PROPERTIES

Buffering agent, mineral enrichment.

APPLICATIONS

- Buffering agent.
- Mineral supply.
- Water treatment.

Plant location Packaging types Handling precautions Puurs - Belgium

Polyethylene bags of 25 kg net

See MSDS

CERTIFICATIONS

ISO 9001 (Quality) - OHSAS 18001 (Security) - ISO 14001 (Environment) - FSSC 22000 (Food Safety) - Kosher Pareve Passover - Halal - Responsible Care

REGULATIONS & STATEMENTS

Meets the requirements of current European Community regulations for Food additives (Council Regulation 2012/231/EC), as well as the current edition of the Food Chemical Codex (FCC). Are subject to a quantitative limitation fixed by the consolidated edition of the European Community Regulation 2008/1333/EC – Annex II.

Meets the requirements of Regulation 767/2009/EC on the placing on the market and use of feed and Regulation 2011/575/EC on the Catalogue of Feed Materials. Directive 2002/32/EC on undesirable substances in animal feed.

GMO free - Allergen free - BSE/TSE free - Mineral origin

PrayphosTM MKP FG complies with the specifications of the current European Pharmacopoeia and US Pharmacopoeia

MISCELLANEOUS

Although the information and recommendations set forth herein are presented in good faith and believed to be correct as of the date hereof, Prayon makes no representations or warranties as to the completeness or accuracy. Information is supplied upon the condition that the persons receiving the same will make their own determination as to its suitability for their purposes prior to use. Additionally, it is the user's responsibility to verify, in every case, the local legislation related to the use of the product. In no event will Prayon be responsible for damages of any nature resulting from the use of or reliance upon information or the product to which information refers. Nothing contained herein is to be construed as a recommendation to use any product, process, equipment or formulation in conflict with any patent and Prayon makes no representation or warranty, express or implied, that the use thereof will not infringe any patent. The typical data set forth herein are based on samples tested and are not guaranteed for all samples or applications. The product specification limits are subject to change. Please contact Prayon for the most current data sheet. Deliveries are governed by the general sale conditions defined by Prayon.







Accreditation to testing



Company:

ISI Food Protection ApS

Brendstrupgaardsvej 102

DK-8200 Aarhus N

Registration number:

543

Valid:

03-06-2013 to 31-07-2017

Scope:

Testing

Product

- Food

Test Type

- Chemical testing
- Microbiological testing

Testing is performed according to the current list of test methods approved by DANAK.

The company complies with the criteria in EN ISO/IEC 17025:2005 – General requirements for the competence of testing and calibration laboratories and demonstrates technical competence for the defined scope and the operation of a quality management system (refer joint ISO-ILAC-IAF Communiqué dated January 2009, www.danak.dk).

Jesper Høy

Kirsten Marie Rosenberg

In case of any disputes, the Document in Danish language shall have priority.

Meat Supply and Disappearance Created Tuesday, October 25, 2022

Created Tuesday, March 31, 2020

Updates of this data can be found at the USDA, ERS Livestock and Meat Domestic Data page. Jump to a table in this workbook by selecting its worksheet tab or by clicking its link below.

Table 1—Beef

Table 2—Veal

Table 3—Pork

Table 4—Lamb and mutton

Table 5—Total red meat

Table 6—Broiler

Table 7—Other chicken

Table 8—Turkey

Table 9—Total poultry

Table 10—Total red meat and poultry

Table 11---Egg and egg products

Contact: Russell Knight at USDA, Economic Research Service.

Beef: Supply and disappearance (carcass weight, million pounds) and per capita disappearance (pounds)

Year and	qtr 1/		Production 2/									Per capita	disappearance	e (pounds)
		Commercial	Farm	Total	Beginning stocks	Imports 3/	Total supply 4/	Exports 3/	Ending stocks		U.S. population 6/ (1,000 persons)	Carcass weight	Retail weight	Boneless retail weight
2018	Q1 Jan-Mar	6,466	25	6,491	649	721	7,861	731	617	6,513	326,325	20.0	14.0	13.4
	Q2 Apr-Jun	6,726	8	6,734	617	805	8,156	801	595	6,760	326,703	20.7	14.5	13.8
	Q3 Jul-Sep	6,819	8	6,827	595	807	8,229	828	672	6,729	327,167	20.6	14.4	13.8
	Q4 Oct-Dec	6,862	25	6,886	672	664	8,223	799	662	6,761	327,602	20.6	14.4	13.8
	Yr Jan-Dec	26,872	66	26,938	649	2,998	30,585	3,160	662	26,763	326,949	81.9	57.3	54.8
2019	Q1 Jan-Mar	6,414	26	6,440	662	739	7,841	700	604	6,537	329,868	19.8	13.9	13.3
	Q2 Apr-Jun	6,817	9	6,825	604	836	8,266	790	540	6,936	330,245	21.0	14.7	14.1
	Q3 Jul-Sep	6,923	9	6,931	540	771	8,242	788	625	6,828	330,729	20.6	14.5	13.8
	Q4 Oct-Dec	7,001	26	7,027	625	712	8,365	749	642	6,974	331,208	21.1	14.7	14.1
	Yr Jan-Dec	27,155	69	27,224	662	3,058	30,944	3,026	642	27,276	330,513	82.5	57.8	55.2
2020	Q1 Jan-Mar	6,931	26	6,957	642	774	8,373	769	670	6,934	331,534	20.9	14.6	14.0
	Q2 Apr-Jun	6,059	9	6,067	670	848	7,585	605	573	6,408	331,693	19.3	13.5	12.9
	Q3 Jul-Sep	7,115	9	7,124	573	1,025	8,722	759	617	7,346	331,841	22.1	15.5	14.8
	Q4 Oct-Dec	7,069	26	7,095	617	693	8,405	819	716	6,870	331,978	20.7	14.5	13.8
	Yr Jan-Dec	27,174	70	27,244	642	3,339	31,225	2,951	716	27,559	331,761	83.1	58.1	55.6
2021	Q1 Jan-Mar	6,900	26	6,925	716	696	8,337	798	645	6,894	331,950	20.8	14.5	13.9
	Q2 Apr-Jun	6,963	8	6,972	645	865	8,482	875	535	7,072	332,021	21.3	14.9	14.2
	Q3 Jul-Sep	6,979	8	6,988	535	923	8,446	912	585	6,949	332,297	20.9	14.6	14.0
	Q4 Oct-Dec	7,106	25	7,131	585	863	8,579	856	676	7,048	332,583	21.2	14.8	14.2
	Yr Jan-Dec	27,948	68	28,016	716	3,346	32,078	3,441	676	27,962	332,213	84.2	58.9	56.3

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates" and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:44:55 AM

^{2/} Cold storage data converted to carcass-weight-equivalent basis.

^{3/} Includes veal beginning in 1989.

^{4/} Totals may not add due to rounding.

^{5/} Includes shipments to U.S. territories.

^{6/} Includes Armed Forces overseas. Estimate is calendar-year average.

Veal: Supply and disappearance (carcass weight, million pounds) and per capita disappearance (pounds)

Year and qtr 1/		Production 2/										Per capita	disappearance	e (pounds)
		Commercial	Farm	Total	Beginning stocks	Imports 3/	Total supply 4/	Exports 3/	Ending stocks	Total dis- appearance 4/ 5/	U.S. population 6/ (1,000 persons)	Carcass weight	Retail weight	Boneless retail weight
2018	Q1 Jan-Mar	19	1	20	16		36		21	15	326,325	.0	.0	.0
	Q2 Apr-Jun	18	1	20	21		40		15	25	326,703	.1	.1	.1
	Q3 Jul-Sep	19	1	20	15		35		14	21	327,167	.1	.1	.0
	Q4 Oct-Dec	20	1	22	14		35		8	27	327,602	.1	.1	.1
	Yr Jan-Dec	76	5	81	16		97		8	89	326,949	.3	.2	.2
2019	Q1 Jan-Mar	18	1	20	8		28		5	23	329,868	.1	.1	.0
	Q2 Apr-Jun	18	1	19	5		24		4	19	330,245	.1	.0	.0
	Q3 Jul-Sep	18	1	20	4		24		6	18	330,729	.1	.0	.0
	Q4 Oct-Dec	20	1	21	6		27		6	20	331,208	.1	.1	.0
	Yr Jan-Dec	75	5	79	8		87		6	81	330,513	.2	.2	.2
2020	Q1 Jan-Mar	17	1	19	6		25		5	20	331,534	.1	.0	.0
	Q2 Apr-Jun	16	1	17	5		22		3	18	331,693	.1	.0	.0
	Q3 Jul-Sep	16	1	17	3		20		9	11	331,841	.0	.0	.0
	Q4 Oct-Dec	16	1	17	9		26		9	17	331,978	.1	.0	.0
	Yr Jan-Dec	64	5	69	6		75		9	66	331,761	.2	.2	.1
2021	Q1 Jan-Mar	14	1	16	9		25		9	16	331,950	.0	.0	.0
	Q2 Apr-Jun	12	1	13	9		22		6	16	332,021	.0	.0	.0
	Q3 Jul-Sep	13	1	14	6		20		5	14	332,297	.0	.0	.0
	Q4 Oct-Dec	15	1	16	5		21		4	17	332,583	.1	.0	.0
	Yr Jan-Dec	53	5	58	9		68		4	64	332,213	.2	.2	.1

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates" and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:45:10 AM

^{2/} Cold storage data converted to carcass-weight-equivalent basis.

^{3/} Reported with beef beginning in 1989.

^{4/} Totals may not add due to rounding.

^{5/} Includes shipments to U.S. territories.

^{6/} Includes Armed Forces overseas. Estimate is calendar-year average.

Pork: Supply and disappearance (carcass weight, million pounds) and per capita disappearance (pounds)

Year and	l qtr 1/	Production 2/										Per capita	disappearance	e (pounds)
		Commercial	Farm	Total	Beginning stocks	Imports	Total supply 3/	Exports	Ending stocks		U.S. population 5/ (1,000 persons)	Carcass weight	Retail weight	Boneless retail weight
2018	Q1 Jan-Mar	6,645	4	6,649	554	279	7,483	1,515	680	5,288	326,325	16.2	12.6	11.8
	Q2 Apr-Jun	6,325	3	6,328	680	270	7,278	1,521	627	5,130	326,703	15.7	12.2	11.4
	Q3 Jul-Sep	6,315	3	6,318	627	245	7,190	1,298	656	5,236	327,167	16.0	12.4	11.7
	Q4 Oct-Dec	7,031	4	7,035	656	248	7,938	1,542	559	5,837	327,602	17.8	13.8	13.0
	Yr Jan-Dec	26,315	14	26,329	554	1,042	27,926	5,877	559	21,490	326,949	65.7	51.0	47.9
2019	Q1 Jan-Mar	6,838	4	6,843	559	259	7,660	1,445	676	5,539	329,868	16.8	13.0	12.2
	Q2 Apr-Jun	6,615	3	6,618	676	227	7,522	1,535	696	5,291	330,245	16.0	12.4	11.7
	Q3 Jul-Sep	6,706	3	6,709	696	232	7,636	1,515	667	5,454	330,729	16.5	12.8	12.0
	Q4 Oct-Dec	7,478	4	7,483	667	227	8,377	1,826	646	5,905	331,208	17.8	13.8	13.0
	Yr Jan-Dec	27,638	15	27,652	559	945	29,156	6,321	646	22,189	330,513	67.1	52.1	48.9
2020	Q1 Jan-Mar	7,426	4	7,431	646	206	8,283	2,021	675	5,588	331,534	16.9	13.1	12.3
	Q2 Apr-Jun	6,313	3	6,316	675	220	7,211	1,773	512	4,926	331,693	14.9	11.5	10.8
	Q3 Jul-Sep	7,048	3	7,051	512	226	7,789	1,627	521	5,641	331,841	17.0	13.2	12.4
	Q4 Oct-Dec	7,515	4	7,520	521	252	8,292	1,858	467	5,967	331,978	18.0	13.9	13.1
	Yr Jan-Dec	28,303	15	28,318	646	904	29,869	7,279	467	22,122	331,761	66.7	51.7	48.6
2021	Q1 Jan-Mar	7,292	4	7,296	467	247	8,011	1,922	502	5,587	331,950	16.8	13.1	12.3
	Q2 Apr-Jun	6,668	3	6,671	502	260	7,434	1,903	494	5,036	332,021	15.2	11.8	11.1
	Q3 Jul-Sep	6,530	3	6,533	494	308	7,336	1,550	530	5,256	332,297	15.8	12.3	11.5
	Q4 Oct-Dec	7,185	5	7,189	530	364	8,083	1,652	446	5,986	332,583	18.0	14.0	13.1
	Yr Jan-Dec	27,675	15	27,690	467	1,180	29,337	7,026	446	21,865	332,213	65.8	51.1	48.0

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates"

and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:45:02 AM

^{2/} Cold storage data converted to carcass-weight-equivalent basis.

^{3/} Totals may not add due to rounding.

^{4/} Includes shipments to U.S. territories.

^{5/} Includes Armed Forces overseas. Estimate is calendar-year average.

Lamb and mutton: Supply and disappearance (carcass weight, million pounds) and per capita disappearance (pounds)

Year and	qtr 1/	Р	roduction 2/									Per capita	disappearance	e (pounds)
		Commercial	Farm	Total	Beginning stocks	Imports	Total supply 3/	Exports	Ending stocks		U.S. population 5/	Carcass weight	5	Boneless retail weight
										3/ 4/	(1,000 persons)			
2018	Q1 Jan-Mar	39	1	40	27	80	146	1	29	117	326,325	.4	.3	.2
	Q2 Apr-Jun	39	1	40	29	66	135	2	39	94	326,703	.3	.3	.2
	Q3 Jul-Sep	37	1	38	39	70	146	1	40	105	327,167	.3	.3	.2
	Q4 Oct-Dec	39	1	40	40	57	138	1	36	100	327,602	.3	.3	.2
	Yr Jan-Dec	153	5	158	27	273	458	6	36	415	326,949	1.3	1.1	.8
2019	Q1 Jan-Mar	37	1	38	36	80	155	2	31	122	329,868	.4	.3	.2
	Q2 Apr-Jun	40	1	41	31	73	145	1	40	104	330,245	.3	.3	.2
	Q3 Jul-Sep	36	1	37	40	53	130	1	42	87	330,729	.3	.2	.2
	Q4 Oct-Dec	36	1	37	42	66	145	2	35	109	331,208	.3	.3	.2
	Yr Jan-Dec	149	5	153	36	272	462	6	35	422	330,513	1.3	1.1	.8
2020	Q1 Jan-Mar	35	1	36	35	102	173	1	38	134	331,534	.4	.4	.3
	Q2 Apr-Jun	36	1	37	38	67	142	1	47	95	331,693	.3	.3	.2
	Q3 Jul-Sep		1	35	47	62	144	1	31	112	331,841	.3	.3	.2
	Q4 Oct-Dec	33	1	34	31	70	135	1	25	109	331,978	.3	.3	.2
	Yr Jan-Dec	138	5	143	35	302	479	3	25	451	331,761	1.4	1.2	.9
2021	Q1 Jan-Mar	35	1	36	25	69	130	1	25	104	331,950	.3	.3	.2
	Q2 Apr-Jun	36	1	37	25	93	155	1	21	133	332,021	.4	.4	.3
	Q3 Jul-Sep	32	1	33	21	100	154	1	26	128	332,297	.4	.3	.3
	Q4 Oct-Dec	35	1	36	26	103	164	1	22	141	332,583	.4	.4	.3
	Yr Jan-Dec	138	5	143	25	364	532	3	22	506	332,213	1.5	1.4	1.0

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates"

and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:45:00 AM

^{2/} Cold storage data converted to carcass-weight-equivalent basis.

^{3/} Totals may not add due to rounding.

^{4/} Includes shipments to U.S. territories.

^{5/} Includes Armed Forces overseas. Estimate is calendar-year average.

Total red meat: Supply and disappearance (carcass weight, million pounds) and per capita disappearance (pounds)

Year and qtr 1/		Production 2/										Per capita	disappearance	e (pounds)
		Commercial	Farm	Total	Beginning stocks	Imports	Total supply 3/	Exports	Ending stocks	Total dis- appearance 3/ 4/		Carcass weight	Retail weight	Boneless retail weight
2018	Q1 Jan-Mar	13,168	32	13,200	1,246	1,080	15,526	2,248	1,346	11,932	326,325	36.6	26.9	25.4
	Q2 Apr-Jun	13,107	13	13,121	1,346	1,141	15,608	2,323	1,276	12,009	326,703	36.8	27.0	25.5
	Q3 Jul-Sep	13,189	13	13,202	1,276	1,122	15,601	2,128	1,382	12,091	327,167	37.0	27.2	25.7
	Q4 Oct-Dec	13,952	31	13,983	1,382	969	16,334	2,343	1,266	12,726	327,602	38.8	28.6	27.1
	Yr Jan-Dec	53,417	90	53,507	1,246	4,313	59,065	9,042	1,266	48,758	326,949	149.1	109.7	103.7
2019	Q1 Jan-Mar	13,307	33	13,340	1,266	1,078	15,683	2,147	1,315	12,221	329,868	37.0	27.3	25.8
	Q2 Apr-Jun	13,490	14	13,504	1,315	1,136	15,956	2,326	1,280	12,350	330,245	37.4	27.5	26.0
	Q3 Jul-Sep	13,683	14	13,696	1,280	1,056	16,032	2,305	1,340	12,387	330,729	37.5	27.5	26.0
	Q4 Oct-Dec	14,535	33	14,568	1,340	1,005	16,914	2,576	1,330	13,008	331,208	39.3	28.9	27.3
	Yr Jan-Dec	55,015	93	55,108	1,266	4,276	60,650	9,353	1,330	49,968	330,513	151.2	111.2	105.2
2020	Q1 Jan-Mar	14,409	33	14,443	1,330	1,082	16,854	2,791	1,388	12,676	331,534	38.2	28.1	26.6
	Q2 Apr-Jun	12,424	14	12,438	1,388	1,135	14,960	2,378	1,135	11,448	331,693	34.5	25.3	24.0
	Q3 Jul-Sep	14,213	14	14,227	1,135	1,313	16,675	2,386	1,178	13,111	331,841	39.5	29.0	27.4
	Q4 Oct-Dec	14,633	33	14,666	1,178	1,015	16,859	2,678	1,217	12,963	331,978	39.0	28.8	27.2
	Yr Jan-Dec	55,680	94	55,774	1,330	4,545	61,648	10,233	1,217	50,198	331,761	151.3	111.3	105.2
2021	Q1 Jan-Mar	14,241	32	14,273	1,217	1,012	16,503	2,720	1,181	12,601	331,950	38.0	27.9	26.4
	Q2 Apr-Jun	13,679	14	13,693	1,181	1,218	16,093	2,779	1,057	12,256	332,021	36.9	27.1	25.6
	Q3 Jul-Sep	13,554	14	13,567	1,057	1,331	15,955	2,462	1,146	12,347	332,297	37.2	27.3	25.8
	Q4 Oct-Dec	14,341	32	14,373	1,146	1,329	16,848	2,509	1,147	13,192	332,583	39.7	29.2	27.6
	Yr Jan-Dec	55,815	92	55,906	1,217	4,890	62,014	10,470	1,147	50,397	332,213	151.7	111.5	105.4

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates"

and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:45:07 AM

^{2/} Cold storage data converted to carcass-weight-equivalent basis.

^{3/} Totals may not add due to rounding.

^{4/} Includes shipments to U.S. territories.

^{5/} Includes Armed Forces overseas. Estimate is calendar-year average.

Broilers: Supply and disappearance (million pounds) and per capita disappearance (pounds)

Year and	qtr 1/		Production 2/									Per capita	disappearance	e (pounds)
		Federally inspected	Condemn- ation 3/	,	Beginning stocks	Imports	Total supply 5/	Exports	Ending stocks		U.S. population 7/ (1,000 persons)	Carcass weight	Retail weight	Boneless retail weight
2018	Q1 Jan-Mar	10,385	111	10,274	856	34	11,165	1,709	841	8,614	326,325	26.4	22.7	15.9
	Q2 Apr-Jun	10,687	114	10,573	841	31	11,444	1,704	848	8,893	326,703	27.2	23.4	16.4
	Q3 Jul-Sep	10,940	117	10,823	848	37	11,707	1,785	924	8,999	327,168	27.5	23.6	16.6
	Q4 Oct-Dec	10,588	113	10,475	924	37	11,436	1,871	845	8,720	327,602	26.6	22.9	16.0
	Yr Jan-Dec	42,601	456	42,145	856	139	43,140	7,069	845	35,226	326,949	107.7	92.6	64.9
2019	Q1 Jan-Mar	10,384	111	10,273	845	31	11,149	1,721	835	8,593	329,868	26.0	22.4	15.7
	Q2 Apr-Jun	10,945	117	10,827	835	32	11,694	1,722	803	9,169	330,245	27.8	23.8	16.7
	Q3 Jul-Sep	11,402	122	11,280	803	36	12,120	1,773	876	9,471	330,729	28.6	24.6	17.2
	Q4 Oct-Dec	11,175	120	11,055	876	32	11,963	1,888	937	9,138	331,208	27.6	23.7	16.6
	Yr Jan-Dec	43,905	470	43,435	845	131	44,411	7,103	937	36,371	330,513	110.0	94.5	66.2
2020	Q1 Jan-Mar	11,238	120	11,117	937	37	12,092	1,860	880	9,352	331,534	28.2	24.2	17.0
	Q2 Apr-Jun	10,940	117	10,823	880	32	11,735	1,729	836	9,169	331,692	27.6	23.7	16.6
	Q3 Jul-Sep	11,358	122	11,237	836	42	12,115	1,821	851	9,443	331,841	28.5	24.4	17.1
	Q4 Oct-Dec	11,047	118	10,929	851	34	11,814	1,959	830	9,025	331,978	27.2	23.4	16.4
	Yr Jan-Dec	44,583	477	44,106	937	145	45,188	7,368	830	36,989	331,761	111.5	95.8	67.1
2021	Q1 Jan-Mar	10,893	117	10,777	830	32	11,639	1,851	700	9,089	331,949	27.4	23.5	16.5
	Q2 Apr-Jun	11,232	120	11,112	700	41	11,852	1,772	700	9,380	332,021	28.3	24.3	17.0
	Q3 Jul-Sep	11,581	124	11,457	700	38	12,195	1,835	700	9,660	332,298	29.1	25.0	17.5
	Q4 Oct-Dec	11,193	120	11,073	700	43	11,817	1,898	705	9,214	332,584	27.7	23.8	16.7
	Yr Jan-Dec	44,899	480	44,419	830	155	45,403	7,355	705	37,343	332,213	112.4	96.6	67.7

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates" and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

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^{2/} Includes other production (not federally inspected) prior to 2001.

^{3/} Condemnations are 0 prior to 1973 because total ready-to-cook (RTC) production already accounted for condemnations.

^{4/} Total RTC production (federally inspected and other production) less further-processed and cut-up meat condemned under Federal inspection.

^{5/} Totals may not add due to rounding.

^{6/} Includes shipments to U.S. territories.

^{7/} Includes Armed Forces overseas. Estimate is calendar-year average.

Total poultry: Supply and disappearance (million pounds) and per capita disappearance (pounds)

Year and	qtr 1/		Production 2/									Per capita	disappearance	e (pounds)
	-	Federally inspected	Condemn- ation 3/	Net ready-to- cook (RTC) 4/	Beginning stocks	Imports	Total supply 5/	Exports	Ending stocks		population 7/	Carcass weight	Retail weight	Boneless retail weight
2018	Q1 Jan-Mar	11,961	111	11,850	1,170	40	13,060	1,885	1,308	9,868	326,325	30.2	26.5	18.9
	Q2 Apr-Jun	12,303	115	12,189	1,308	37	13,533	1,872	1,413	10,248	326,703	31.4	27.5	19.6
	Q3 Jul-Sep	12,515	117	12,397	1,413	42	13,853	1,948	1,495	10,410	327,168	31.8	27.9	19.9
	Q4 Oct-Dec	12,239	113	12,126	1,495	41	13,661	2,058	1,153	10,450	327,602	31.9	28.1	20.1
	Yr Jan-Dec	49,018	456	48,562	1,170	160	49,892	7,763	1,153	40,976	326,949	125.3	110.1	78.5
2019	Q1 Jan-Mar	11,957	111	11,846	1,153	35	13,034	1,887	1,312	9,835	329,868	29.8	26.1	18.6
	Q2 Apr-Jun	12,529	117	12,412	1,312	35	13,759	1,907	1,349	10,503	330,245	31.8	27.9	19.8
	Q3 Jul-Sep	12,992	122	12,870	1,349	40	14,260	1,957	1,412	10,890	330,729	32.9	28.9	20.6
	Q4 Oct-Dec	12,773	120	12,653	1,412	35	14,100	2,072	1,175	10,853	331,208	32.8	28.9	20.6
	Yr Jan-Dec	50,251	470	49,781	1,153	146	51,080	7,824	1,175	42,081	330,513	127.3	111.8	79.6
2020	Q1 Jan-Mar	12,842	120	12,721	1,175	42	13,938	2,019	1,274	10,645	331,534	32.1	28.1	20.0
	Q2 Apr-Jun	12,446	117	12,329	1,274	37	13,640	1,878	1,316	10,446	331,692	31.5	27.6	19.6
	Q3 Jul-Sep	12,958	122	12,837	1,316	49	14,201	1,981	1,361	10,860	331,841	32.7	28.7	20.4
	Q4 Oct-Dec	12,630	118	12,512	1,361	40	13,912	2,137	1,057	10,718	331,978	32.3	28.5	20.3
	Yr Jan-Dec	50,876	478	50,398	1,175	167	51,740	8,015	1,057	42,669	331,761	128.6	112.9	80.4
2021	Q1 Jan-Mar	12,410	117	12,293	1,057	37	13,387	1,995	1,056	10,336	331,949	31.1	27.3	19.4
	Q2 Apr-Jun	12,771	120	12,651	1,056	48	13,754	1,922	1,111	10,721	332,021	32.3	28.3	20.1
	Q3 Jul-Sep	13,125	124	13,001	1,111	45	14,157	1,985	1,122	11,050	332,298	33.3	29.2	20.7
	Q4 Oct-Dec	12,689	120	12,569	1,122	51	13,742	2,045	874	10,823	332,584	32.5	28.6	20.4
	Yr Jan-Dec	50,995	481	50,514	1,057	180	51,751	7,947	874	42,930	332,213	129.2	113.4	80.7

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates" and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:45:05 AM

^{2/} Includes other production (not federally inspected) prior to 2001.

^{3/} Condemnations are 0 prior to 1973 because total ready-to-cook (RTC) production already accounted for condemnations.

^{4/} Total RTC production (federally inspected and other production) less further-processed and cut-up meat condemned under Federal inspection.

^{5/} Totals may not add due to rounding.

^{6/} Includes shipments to U.S. territories.

^{7/} Includes Armed Forces overseas. Estimate is calendar-year average.

Other chicken: Supply and disappearance (million pounds) and per capita disappearance (pounds)

Year and	qtr 1/		Production 2/									Per capita	disappearance	e (pounds)
	ľ	Federally	Condemn-	Net ready-to-	Beginning	Imports	Total	Exports	Ending	Total dis-	U.S.	Carcass	Retail weight	Boneless
		inspected	ation 3/	cook (RTC)	stocks		supply 5/		stocks		population 7/	weight		retail weight
				4/						5/ 6/	(1,000			
											persons)			
2018	Q1 Jan-Mar	125		124	5	1	130	23	4	103	326,325	.3	.3	.2
	Q2 Apr-Jun	139		139	4	1	143	22	4	118	326,703	.4	.4	.2
	Q3 Jul-Sep	144		144	4	1	148	22	6	120	327,168	.4	.4	.2
	Q4 Oct-Dec	132		132	6		139	17	6	116	327,602	.4	.4	.2
	Yr Jan-Dec	539	1	539	5	2	546	84	6	456	326,949	1.4	1.4	.8
2019	Q1 Jan-Mar	127		127	6	1	133	19	7	107	329,868	.3	.3	.2
	Q2 Apr-Jun	134		134	7	1	141	20	7	114	330,245	.3	.3	.2
	Q3 Jul-Sep	137		137	7	1	145	26	8	112	330,729	.3	.3	.2
	Q4 Oct-Dec	131		131	8	1	139	17	5	116	331,208	.4	.4	.2
	Yr Jan-Dec	529	1	528	6	2	536	81	5	449	330,513	1.4	1.4	.8
2020	Q1 Jan-Mar	135		135	5		141	21	6	114	331,534	.3	.3	.2
	Q2 Apr-Jun	136		136	6		143	23	5	115	331,692	.3	.3	.2
	Q3 Jul-Sep	146		146	5	1	152	17	9	126	331,841	.4	.4	.2
	Q4 Oct-Dec	131		131	9		140	14	4	122	331,978	.4	.4	.2
	Yr Jan-Dec	549	1	549	5	2	556	75	4	477	331,761	1.4	1.4	.9
2021	Q1 Jan-Mar	127		127	4	1	132	14	6	112	331,949	.3	.3	.2
	Q2 Apr-Jun	140		140	6	1	146	10	5	131	332,021	.4	.4	.2
	Q3 Jul-Sep	141		141	5	1	146	12	8	126	332,298	.4	.4	.2
	Q4 Oct-Dec	130		129	8	1	138	8	3	127	332,584	.4	.4	.2
	Yr Jan-Dec	537	1	537	4	3	544	44	3	497	332,213	1.5	1.5	.9

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates" and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:45:01 AM

^{2/} Includes other production (not federally inspected) prior to 2001.

^{3/} Condemnations are 0 prior to 1973 because total ready-to-cook (RTC) production already accounted for condemnations.

^{4/} Total RTC production (federally inspected and other production) less further-processed and cut-up meat condemned under Federal inspection.

^{5/} Totals may not add due to rounding.

^{6/} Includes shipments to U.S. territories.

^{7/} Includes Armed Forces overseas. Estimate is calendar-year average.

Turkeys: Supply and disappearance (million pounds) and per capita disappearance (pounds)

Year and	qtr 1/		Production 2/									Per capita	disappearance	(pounds)
	-	Federally inspected	Condemn- ation 3/	Net ready-to- cook (RTC)	Beginning stocks	Imports	Total supply 5/	Exports	Ending stocks		U.S. population 7/ (1,000	Carcass weight	Retail weight	Boneless retail weight
				.,						<i>3</i> , <i>3</i> ,	persons)			
2018	Q1 Jan-Mar	1,452		1,452	310	5	1,766	153	463	1,150	326,325	3.5	3.5	2.8
	Q2 Apr-Jun	1,477		1,477	463	6	1,946	147	562	1,237	326,703	3.8	3.8	3.0
	Q3 Jul-Sep	1,431		1,431	562	5	1,997	141	565	1,292	327,168	3.9	3.9	3.1
	Q4 Oct-Dec	1,518		1,518	565	3	2,087	170	303	1,614	327,602	4.9	4.9	3.9
	Yr Jan-Dec	5,878		5,878	310	19	6,206	611	303	5,293	326,949	16.2	16.2	12.8
2019	Q1 Jan-Mar	1,446		1,446	303	4	1,753	147	470	1,135	329,868	3.4	3.4	2.7
	Q2 Apr-Jun	1,451		1,451	470	3	1,924	166	539	1,220	330,245	3.7	3.7	2.9
	Q3 Jul-Sep	1,453		1,453	539	3	1,995	159	528	1,308	330,729	4.0	4.0	3.1
	Q4 Oct-Dec	1,467		1,467	528	2	1,998	167	233	1,598	331,208	4.8	4.8	3.8
	Yr Jan-Dec	5,818		5,818	303	12	6,133	639	233	5,261	330,513	15.9	15.9	12.6
2020	Q1 Jan-Mar	1,469		1,469	233	4	1,706	139	388	1,179	331,534	3.6	3.6	2.8
	Q2 Apr-Jun	1,369		1,369	388	5	1,762	126	475	1,161	331,692	3.5	3.5	2.8
	Q3 Jul-Sep	1,454		1,454	475	6	1,935	143	501	1,291	331,841	3.9	3.9	3.1
	Q4 Oct-Dec	1,451		1,451	501	6	1,958	164	223	1,571	331,978	4.7	4.7	3.7
	Yr Jan-Dec	5,743		5,743	233	21	5,997	571	223	5,203	331,761	15.7	15.7	12.4
2021	Q1 Jan-Mar	1,390		1,390	223	3	1,616	130	351	1,136	331,949	3.4	3.4	2.7
	Q2 Apr-Jun	1,399		1,399	351	6	1,756	140	406	1,210	332,021	3.6	3.6	2.9
	Q3 Jul-Sep	1,403		1,403	406	6	1,815	138	414	1,263	332,298	3.8	3.8	3.0
	Q4 Oct-Dec	1,366		1,366	414	7	1,787	140	166	1,481	332,584	4.5	4.5	3.5
	Yr Jan-Dec	5,558		5,558	223	22	5,804	548	166	5,090	332,213	15.3	15.3	12.1

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates"

and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

Date run: 10/25/2022 10:45:08 AM

^{2/} Includes other production (not federally inspected) prior to 2001.

^{3/} Condemnations are 0 prior to 1973 because total ready-to-cook (RTC) production already accounted for condemnations. Condemnations were dropped after 2013.

^{4/} Total RTC production (federally inspected and other production) less further-processed and cut-up meat condemned under Federal inspection.

^{5/} Totals may not add due to rounding.

^{6/} Includes shipments to U.S. territories.

^{7/} Includes Armed Forces overseas. Estimate is calendar-year average.

Total red meat and poultry: Supply and disappearance (carcass weight, million pounds) and per capita disappearance (pounds)

Year and	qtr 1/		Production 2/									Per capita	disappearance	e (pounds)
		Commercial	Other 3/	Total 4/	Beginning stocks	Imports	Total supply 5/	Exports	Ending stocks		U.S. population 7/ (1,000 persons)	Carcass weight	Retail weight	Boneless retail weight
2018	Q1 Jan-Mar	25,019	32	25,050	2,416	1,120	28,587	4,133	2,654	21,800	326,325	66.8	53.4	44.3
	Q2 Apr-Jun	25,296	13	25,309	2,654	1,178	29,142	4,196	2,689	22,256	326,703	68.1	54.5	45.1
	Q3 Jul-Sep	25,586	13	25,600	2,689	1,164	29,453	4,076	2,877	22,501	327,167	68.8	55.1	45.6
	Q4 Oct-Dec	26,077	31	26,109	2,877	1,010	29,996	4,401	2,419	23,176	327,602	70.7	56.8	47.2
	Yr Jan-Dec	101,978	90	102,068	2,416	4,473	108,957	16,805	2,419	89,733	326,949	274.5	219.8	182.2
2019	Q1 Jan-Mar	25,153	33	25,186	2,419	1,113	28,717	4,033	2,627	22,057	329,868	66.9	53.4	44.4
	Q2 Apr-Jun	25,902	14	25,916	2,627	1,172	29,715	4,233	2,629	22,853	330,245	69.2	55.4	45.8
	Q3 Jul-Sep	26,553	14	26,567	2,629	1,096	30,292	4,262	2,752	23,278	330,729	70.4	56.4	46.6
	Q4 Oct-Dec	27,188	33	27,221	2,752	1,040	31,013	4,648	2,504	23,861	331,208	72.0	57.8	48.0
	Yr Jan-Dec	104,796	93	104,889	2,419	4,421	111,729	17,176	2,504	92,048	330,513	278.5	223.0	184.8
2020	Q1 Jan-Mar	27,131	33	27,164	2,504	1,124	30,792	4,810	2,662	23,321	331,534	70.3	56.3	46.6
	Q2 Apr-Jun	24,753	14	24,767	2,662	1,172	28,600	4,256	2,451	21,893	331,693	66.0	52.9	43.6
	Q3 Jul-Sep	27,050	14	27,064	2,451	1,362	30,876	4,367	2,539	23,971	331,841	72.2	57.7	47.9
	Q4 Oct-Dec	27,145	33	27,178	2,539	1,055	30,771	4,815	2,274	23,681	331,978	71.3	57.2	47.5
	Yr Jan-Dec	106,078	94	106,172	2,504	4,713	113,389	18,248	2,274	92,866	331,761	279.9	224.2	185.6
2021	Q1 Jan-Mar	26,534	32	26,566	2,274	1,048	29,889	4,715	2,237	22,938	331,950	69.1	55.2	45.8
	Q2 Apr-Jun	26,330	14	26,343	2,237	1,266	29,847	4,701	2,168	22,977	332,021	69.2	55.4	45.7
	Q3 Jul-Sep	26,555	14	26,568	2,168	1,376	30,112	4,447	2,267	23,397	332,297	70.4	56.4	46.5
	Q4 Oct-Dec	26,910	32	26,942	2,267	1,380	30,590	4,554	2,021	24,015	332,583	72.2	57.9	48.0
	Yr Jan-Dec	106,328	92	106,420	2,274	5,070	113,765	18,418	2,021	93,327	332,213	280.9	224.9	186.1

^{1/} Latest data may be preliminary.

Red meat cold storage data converted to carcass-weight-equivalent basis.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates"

and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

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^{2/} Commercial red meat production and federally inspected poultry production.

^{3/} Farm red meat production and, prior to 2001, other poultry production.

^{4/} Total red meat production and net ready-to-cook (RTC) poultry production. Includes other poultry production beginning in 2001.

^{5/} Totals may not add due to rounding.

^{6/} Includes shipments to U.S. territories.

^{7/} Includes Armed Forces overseas. Estimate is calendar-year average.

Eggs and egg products: Supply and disappearance (shell-egg equivalent, million dozen) and per capita disappearance (shell-egg equivalent, number)

Year and	qtr 1/		Production											
		Table	Hatching	Total	Beginning stocks 2/	Imports	Total supply 3/	Exports	Ending stocks 2/	Hatching use	Total dis- appearance 3/ 4/	population 5/	`	Federally inspected eggs broken 6/
2018	Q1 Jan-Mar	1,952	281	2,233	23	4	2,261	84	22	262	1,893	326,325	70	558
	Q2 Apr-Jun	1,987	293	2,280	22	5	2,306	85	24	269	1,929	326,703	71	607
	Q3 Jul-Sep	2,024	297	2,321	24	5	2,349	82	22	264	1,981	327,168	73	620
	Q4 Oct-Dec	2,079	292	2,371	22	4	2,398	83	23	263	2,029	327,602	74	615
	Yr Jan-Dec	8,043	1,163	9,205	23	18	9,246	333	23	1,058	7,833	326,949	287	2,400
2019	Q1 Jan-Mar	2,047	289	2,336	23	4	2,363	69	29	267	1,999	329,868	73	607
	Q2 Apr-Jun	2,056	297	2,352	29	3	2,385	85	29		1,998	330,245	73	630
	Q3 Jul-Sep	2,046	298	2,344	29	4	2,376	84	28	270	1,994	330,729	72	623
	Q4 Oct-Dec	2,111	298	2,409	28	4	2,441	95	32	272	2,042	331,208	74	628
	Yr Jan-Dec	8,260	1,182	9,442	23	15	9,479	334	32	1,081	8,032	330,513	292	2,488
2020	Q1 Jan-Mar	2,050	301	2,351	32	4	2,386	86	31	276	1,993	331,534	72	605
	Q2 Apr-Jun	1,957	304	2,261	31	4	2,296	83	30	266	1,916	331,692	69	484
	Q3 Jul-Sep	2,008	311	2,319	30	4	2,353	89	29	267	1,967	331,841	71	564
	Q4 Oct-Dec	2,051	310	2,361	29	4	2,395	85	25	270	2,015	331,978	73	563
	Yr Jan-Dec	8,066	1,226	9,292	32	15	9,339	344	25	1,079	7,892	331,761	285	2,215
2021	Q1 Jan-Mar	1,982	308	2,290	25	4	2,319	95	21	273	1,930	331,949	70	537
	Q2 Apr-Jun	1,957	321	2,277	21	5	2,303	103	20	278	1,902	332,021	69	571
	Q3 Jul-Sep	1,982	318	2,299	20	4	2,323	109	19	276	1,920	332,298	69	593
	Q4 Oct-Dec	2,050	321	2,371	19	5	2,395	85	19	277	2,014	332,584	73	602
	Yr Jan-Dec	7,971	1,267	9,238	25	18	9,280	392	19	1,104	7,765	332,213	280	2,303

^{1/} Latest data may be preliminary.

Source: USDA, World Agricultural Outlook Board, "World Agricultural Supply and Demand Estimates" and supporting materials and USDA, Economic Research Service estimates of per capita disappearance.

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^{2/} Eggs stocks include only frozen egg products.

^{3/} Totals may not add due to rounding.

^{4/} Includes shipments to U.S. territories.

^{5/} Includes Armed Forces overseas. Estimate is calendar-year average.

^{6/} Commercially broken eggs used for egg products.

Eighteen pages have been removed in accordance with copyright laws. The removed reference citation is:

P. M. Ashton, S. Nair, T. M. Peters, et al., "Identification of Salmonella for public health surveillance using whole genome sequencing", PeerJ, 4:e1752; DOI 10.7717/peerj.1752

Ten pages have been removed in accordance with copyright laws. The removed reference citation is:

K. G. Joensen, F. Scheutz, O. Lund, et al., "Real-Time Whole-Genome Sequencing for Routine Typing, Surveillance, and Outbreak Detection of Verotoxigenic Escherichia coli", Journal of Clinical Microbiology, vol. 52, no. 5, pp. 1501-1510, 2014.

Four pages have been removed in accordance with copyright laws. The removed reference citation is:

J. E. Kennedy, Jr., J. L. Oblinger, and G. Bitton, "Recovery of Coliphages from Chicken, Pork Sausage and Delicatessen Meats", Journal of Food Protection, vol. 47, no. 8, pp. 623-626, 1984.

The scientists of FinkTec provide the following answers to the questions raised by the FSIS:

GRN 1038 FSIS Questions 11/07/2022

1. The notifier lists the expected final phage concentration to range from 10_5 to 10_7 PFU/g. A use level of 10_5 PFU/g is relatively low as we generally would like to see a minimum multiplicity of infection (MOI) of 10 and preferably higher. *Salmonella* could easily be present in meat products at 10_5 CFU/g which would drop the MOI to 1. Please clarify for what application would you suggest a usage titer after dilution of 10_5 PFU/g and if you expect the MOI in these applications to be of concern.

The concept of MOI, unfortunately, is not optimally suited to describe a practical application of a bacteriophage product. In the laboratory, when both bacteria and bacteriophages are present in excess, an MOI of 5, for example 1 x 108 CFU/mL and 5 x 108 PFU/mL, tells us, using Poisson distribution, that over 99% of the bacterial cells will be infected by at least one bacteriophage. However, this is not the case when you look at an example where there is 1 CFU/mL and 5 PFU/mL. Even though the MOI in this case is also 5, it is unlikely that the single bacterial cell will be found and infected by a bacteriophage (passive diffusion). The question we had to ask was just how many bacteriophages do we have to add to a single cell per mL in order to guarantee that this single cell is infected by at least one bacteriophage (no passive diffusion required). Our experimental evidence is that 10⁵ PFU/mL are sufficient for this in a liquid environment. Thus, to keep with the MOI nomenclature, we use an MOI of 105. Even when the contamination level is not 1 CFU/g, but 10 CFU/g or 100 CFU/g, the number of bacteriophages applied would still guarantee that all target bacterial cells are potentially infected. Thus, if the contamination level on the meat is low, spraying a carcass with a bacteriophage solution or dipping a piece of meat in a bacteriophage solution with a concentration of 1 x 10⁵ PFU/mL could be sufficient to see a significant reduction or elimination. However, if the contamination level is higher and reaches 10⁵ CFU/g, then of course, as suggested by the reviewer, a higher concentration of the phage product would need to be applied.

2. Please indicate how you plan to provide different products to users to ensure that there is a rotation of phages used in order to prevent resistance.

The rotation of bacteriophages in the "Applied Phage Meat S2" product will be a quality service provided by the FinkTec laboratory in coordination with the quality control body of a meat processing plant. Salmonella strains isolated at the entry level of a processing plant will be analysed for their sensitivity to the eleven bacteriophages described by FinkTec and a tailored cocktail will be designed for a specific plant. The goal is that every Salmonella strain should be covered by at least two genetically independent bacteriophages. Such a tailored cocktail can then be further adapted over time as the Salmonella strains detected at the entry level might vary. A development of resistance during the application in a meat processing plant is unlikely, as the bacteria are present in low concentrations and do not show significant growth under the in-plant conditions.

3. For the administrative record, please confirm that all 11 phages in this submission have been characterized. For the included stability and efficacy studies, please indicate which phage mixture(s) were used.

All eleven bacteriophages have been characterized in dept. Their genomes have been sequenced and the sequences were analysed using bioinformatics tools. The eleven bacteriophages are genetically independent (no duplicates) and their host range on a relevant set of *Salmonella* serovars has been determined.

The two batches of the *Applied Phage Meat S2* product (batch Nr. 15032021 und batch Nr. 7062022) that were used for the efficacy studies had an identical composition, containing the bacteriophages:

MP82 (DSM 26173) RMS3b (DSM 33043) TAT2F (DSM 33044) DIN2 (DSM 33045) RMP9 (DSM 26157) and OBO18 (DSM33041).

4. For the efficacy studies described in Appendices 7-9, the initial incubation period and incubation temperature for phage after application was 4 h at room temperature (21°C). This is not consistent with expected in-plant conditions. Please provide updated data where the initial application and reduction of bacteria from the phage solution is measured at 4°C, which is more consistent with expected conditions of use.

Updated data is provided in the attachments I-III to this document. The three studies on pork, beef and chicken meat show, that the efficacy of the Applied Phage Meat S2 product was not affected by the lower temperature and thus would also work under in-plant conditions. This can be rationalized with the fact that the energy required for adsorption and injection are stored within the structure of the bacteriophage particle, and their release is not temperature dependent. Using an appropriately high concentration of bacteriophages guarantees that no temperature depending passive diffusion step is required for the bacteriophages to find their target bacteria.

5. The notifier includes ground products in the intended uses for the phage preparations. However, the included efficacy studies do not include ground product. In order to include ground meat uses, the notifier should provide efficacy studies for ground products using the phage preparations. Additionally, please note that FSIS will require descriptive labeling for the use of this ingredient in ground product that indicates the addition of the phage preparation.

In the process of producing ground meat products, the *Applied Phage Meat S2* product has to be applied before the grinding step in order for the product to work. During the grinding process the surface to weight ratio of the meat is dramatically increased. Contaminating bacteria that originally resided on the surface of the meat are distributed over this enlarged surface. To apply the bacteriophage product after the grinding step would require an additional processing step to homogenously distribute the bacteriophages. It would also require much higher concentrations of the bacteriophage product due to the increased surface to weight ratio and in hand with this the addition of significant amounts of liquid to the ground meat. For ground meat that is not further processed, this is not an option. In attachment IV to this document, we provide a study that shows that reduced amounts of *Salmonella* can be detected in ground meat when the bacteriophage product is applied before the grinding step.

The requirement for descriptive labelling is duly noted.

List of attachments:

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I Study_#R022-001_4°C_Salmonella_pork
II Study_#R022-002_4°C_Salmonella_beef
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III Study_#R022-003_4°C_Salmonella_chicken

IV Study_#R022-004_4°C_Salmonella_ground meat

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw pork at 4°C.

Study Number # R022-001

PTC Phage Technology Center GmbH

Siemensstraße 42

D- 59199 Bönen

Tel.: 49 (0) 2383 919 175

Fax: 49 (0) 2383 919 179

Dr. Michael Fink

FINK TEC GmbH

Oberster Kamp 23

D-59069 Hamm

Tel.: 49 (0) 2385 730

1. STUDY TITLE

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw pork at 4°C.

2. STUDY DIRECTOR

Hansjörg Lehnherr, Ph.D.

3. STUDY PERSONNEL

The following personnel contributed to the conduct and reporting of the studies reported herein:

Name:Title:Role:Hansjörg Lehnherr, Ph.D.Chief scientistStudy directorAndrea Kroj, Ph.D.Research scientistHands-on-research

4. PERFORMING LABORATORY

PTC Phage Technology Center GmbH Siemensstraße 42 D- 59199 Bönen

Tel.: 49 (0) 2383 919 174 Fax: 49 (0) 2383 919 179

5. STUDY OBJECTIVE

Determine the bacterial load reduction of a *S.* Typhimurium strain on raw pork, resulting from the application of *Applied Phage Meat S2* after 4 h to evaluate the efficacy of the bacteriophage product at 4°C.

6. TEST MATRIX

The used raw pork was obtained from a supermarket in Hamm, NRW, Germany. Samples were not washed or pre-treated prior to the studies.

7. COCKTAIL LOT AND APPLICATION

Applied Phage Meat S2 lot # 6072022Applied Phage Meat S2 titer: 5×10^9 PFU/mL per phage component.

The application titer was 2×10^9 PFU/mL per phage component.

8. BACTERIAL STRAINS USED TO EVALUATE COCKTAIL EFFICIENCY

Each pork sample was challenged with 1×10^3 bacterial cells of the *S.* Typhimurium strain indicated below. The total reduction in *Salmonella* bacterial load was measured.

• A chloramphenicol resistant *Salmonella* Typhimurium isolate was used for the experiments.

9. MEDIA AND REAGENTS

- LB broth Lennox (Roth, Karlsruhe, Germany; catalog # X964.4) with 34 µg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- LB agar Lennox (Roth, Karlsruhe, Germany; catalog # X965.2)
 with 34 μg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- PBS (8 g/L NaCl, 0.2 g/L KCl, 1.15 g/L Na₂HPO₄, 0.2 g/L KH₂PO₄; pH 7.5)

10. GENERAL OUTLINE OF THE STUDY

- Original pork pieces were cut into 21 samples (10.00 cm²/sample).
- Applied Phage Meat S2 was diluted with PBS buffer to an application titer of 2×10^9 PFU/mL.
- 20 samples were homogenously contaminated with 1×10^3 cells/cm² of an overnight culture of the test strain. One sample was not treated with bacteria and served as the uncontaminated, untreated control.
- All samples were incubated for 30 min at 4°C (±1°C).
- 10 contaminated pork samples were treated with 50 μ L of *Applied Phage Meat S2* with a titer of 2 x 10⁹ PFU/mL, resulting in an application concentration of 1 x 10⁷ PFU/cm².

 $50\,\mu L$ of PBS buffer was applied to the remaining 10 samples as the contaminated, untreated controls.

- Incubation period was 4 h at 4°C (±1°C).
- The numbers of viable Salmonella were determined after 4 h.
- To each meat piece 5 mL of PBS were added and then the pieces were treated for 5 min in a stomacher.
- The supernatant was plated on LB agar plates containing chloramphenicol.
- LB agar plates were incubated at 37°C overnight and the numbers of viable *Salmonella* cells were determined by counting colonies.
- The tests were performed with ten (n = 10) replicates.

11. RESULTS

1. Raw Data

Table 1: Salmonella plate counts for Study #R022-001 After 4 h at 4°C

Time	Treatment	Surface	Temperature	Bacteria	Number of	Total
		(cm²)	(cm²) (°C)		samples	CFU/cm ²
	PBS	10.00	4	Yes	10	200
						400
						380
						375
						405
						300
						345
						300
						365
4 hours						305
4 hours	1 x 10 ⁷ PFU/cm ²	10.00	4	Yes	10	65
						55
						75
						35
						65
						50
						25
						25
						15
						10

2. Tabular presentation of results

Table 2: Reduction of *Salmonella* counts on pork samples treated with *Applied Phage Meat S2* phage solution $(1 \times 10^7 \text{ PFU/cm}^2)$ at 4°C .

*** highest significant with p < 0.001

Time	Treatment	Replicates	Mean CFU/sample	% Reduction	Significance
4 hours	PBS	10	338	87.56	Yes***
	1 x 10 ⁷	10	42		
	PFU/cm ²				

3. Graphical presentation of results

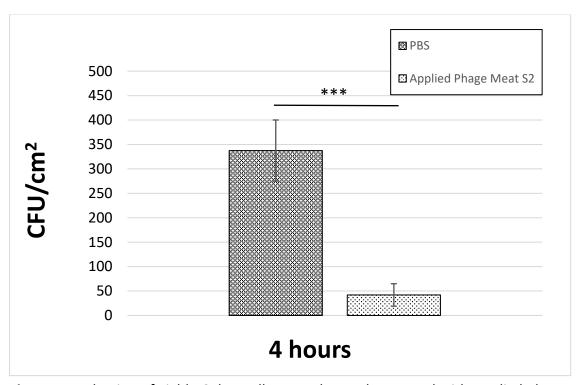


Figure 1: Reduction of viable *Salmonella* on pork samples treated with *Applied Phage Meat S2* phage solution $(1 \times 10^7 \text{ CFU/cm}^2)$ at 4°C.

^{***} highest significant with p < 0.001

4. Statistical analysis

Statistical analysis was performed using Office 2013 Excel for Windows (Microsoft Corporation, Redmond, WA).

The efficacy of the *Applied Phage Meat S2* treatment in reducing the number of viable *Salmonella* Typhimurium on experimentally contaminated pork samples was evaluated by comparing the data obtained for PBS control samples and for *Applied Phage Meat S2* treated samples.

Table 3: Analysis of *Applied Phage Meat S2* induced *Salmonella* reduction on pork samples by independent samples t-test.

T-test	Adjusted p value	Significance level	Significance	Summary
PBS vs. Applied Phage Meat S2	0,00000002	$\alpha = 0.001$	Yes	***

Applying 1.0 x 10^7 PFU/cm² Applied Phage Meat S2 to pork samples (A = 10.0 cm²) reduced the number of viable Salmonella by 87.6% after 4 h of incubation at 4°C. The observed reduction was highest statistically significant (p < 0.001).

PTC Phage Technology Center GmbH

12. SUMMARY CONCLUSION OF THE STUDY

13.

SIGNATURES

Applied Phage Meat S2 can significantly reduce viable Salmonella Typhimurium levels on experimentally contaminated pork samples by 87,6% in 4 h contact time at 4° C, when used at 1.0×10^{7} PFU/cm².

	23.11.2022
Andrea Kroj, Ph.D.	Date
Research scientist	
	23.M. 2022
Hansjörg Lehnherr, Ph.D.	Date
Study director	

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw beef at 4°C.

Study Number # R022-002

PTC Phage Technology Center GmbH

Siemensstraße 42

D- 59199 Bönen

Tel.: 49 (0) 2383 919 175

Fax: 49 (0) 2383 919 179

Dr. Michael Fink

FINK TEC GmbH

Oberster Kamp 23

D-59069 Hamm

Tel.: 49 (0) 2385 730

1. STUDY TITLE

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw beef at 4°C.

2. STUDY DIRECTOR

Hansjörg Lehnherr, Ph.D.

3. STUDY PERSONNEL

The following personnel contributed to the conduct and reporting of the studies reported herein:

Name:	Title:	Role:
Hansjörg Lehnherr, Ph.D.	Chief scientist	Study director
Andrea Kroj, Ph.D.	Research scientist	Hands-on-research

4. PERFORMING LABORATORY

PTC Phage Technology Center GmbH Siemensstraße 42 D- 59199 Bönen

Tel.: 49 (0) 2383 919 174 Fax: 49 (0) 2383 919 179

5. STUDY OBJECTIVE

Determine the bacterial load reduction of a *S.* Typhimurium strain on raw beef, resulting from the application of *Applied Phage Meat S2* after 4 h to evaluate the efficacy of the bacteriophage product at 4°C.

6. TEST MATRIX

The used raw beef was obtained from a supermarket in Hamm, NRW, Germany. Samples were not washed or pre-treated prior to the studies.

7. COCKTAIL LOT AND APPLICATION

Applied Phage Meat S2 lot # 6072022Applied Phage Meat S2 titer: 5×10^9 PFU/mL per phage component.

The application titer was 2×10^9 PFU/mL per phage component.

8. BACTERIAL STRAINS USED TO EVALUATE COCKTAIL EFFICIENCY

Each beef meat sample was challenged with 1×10^3 bacterial cells of the *S.* Typhimurium strain indicated below. The total reduction in *Salmonella* bacterial load was measured.

• A chloramphenicol resistant *Salmonella* Typhimurium isolate was used for the experiments.

9. MEDIA AND REAGENTS

- LB broth Lennox (Roth, Karlsruhe, Germany; catalog # X964.4) with 34 µg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- LB agar Lennox (Roth, Karlsruhe, Germany; catalog # X965.2)
 with 34 μg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- PBS (8 g/L NaCl, 0.2 g/L KCl, 1.15 g/L Na₂HPO₄, 0.2 g/L KH₂PO₄; pH 7.5)

10. GENERAL OUTLINE OF THE STUDY

- Original beef pieces were cut into 21 samples (10.00 cm²/sample).
- Applied Phage Meat S2 was diluted with PBS buffer to an application titer of 2×10^9 PFU/mL.
- 20 samples were homogenously contaminated with 1×10^3 cells/cm² of an overnight culture of the test strain. One sample was not treated with bacteria and served as the uncontaminated, untreated control.
- All samples were incubated for 30 min at 4°C (±1°C).
- 10 contaminated beef samples were treated with 50 μ L of *Applied Phage Meat S2* with a titer of 2 x 10⁹ PFU/mL, resulting in an application concentration of 1 x 10⁷ PFU/cm².

 $50\,\mu L$ of PBS buffer was applied to the remaining 10 samples as the contaminated, untreated controls.

- Incubation period was 4 h at 4°C (±1°C).
- The numbers of viable Salmonella were determined after 4 h.
- To each meat piece 5 mL of PBS were added and then the pieces were treated for 5 min in a stomacher.
- The supernatant was plated on LB agar plates containing chloramphenicol.
- LB agar plates were incubated at 37°C overnight and the numbers of viable *Salmonella* cells were determined by counting colonies.
- The tests were performed with ten (n = 10) replicates.

11. RESULTS

1. Raw Data

Table 1: Salmonella plate counts for Study #R022-002 After 4 h at 4°C

Time	Treatment	Surface (cm²)	Temperature (°C)	Bacteria	Number of samples	Total CFU/cm ²
	PBS	10.00	4	Yes	10	345
						355
						400
						310
						410
						425
						450
						365
						375
4 hours						375
4 110013	1 x 10 ⁷ PFU/cm ²	10.00	4	Yes	10	15
						20
						20
						15
						10
						10
						5
						15
						25
						10

2. Tabular presentation of results

Table 2: Reduction of *Salmonella* counts on beef samples treated with *Applied Phage Meat S2* phage solution $(1 \times 10^7 \text{ PFU/cm}^2)$ at 4°C .

*** highest significant with p < 0.001

Time	Treatment	Replicates	Mean CFU/sample	% Reduction	Significance
4 hours	PBS	10	381	96.19	Yes***
	1 x 10 ⁷ PFU/cm ²	10	15		

3. Graphical presentation of results

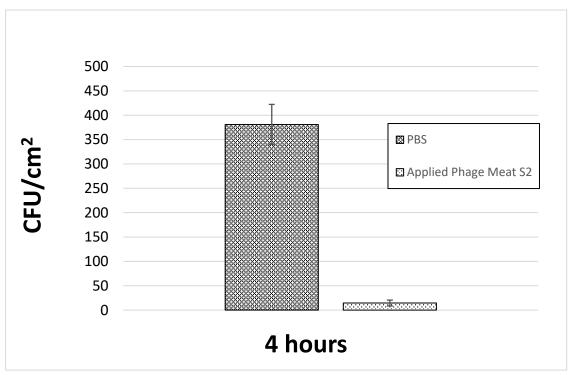


Figure 1: Reduction of viable Salmonella on beef samples treated with Applied Phage Meat S2 phage solution (1 x 10^7 CFU/cm²) at 4°C (4 h).

*** highest significant with p < 0.001

4. Statistical analysis

Statistical analysis was performed using Office 2013 Excel for Windows (Microsoft Corporation, Redmond, WA) and the online ANOVA/Tukey HSD calculation tool of Navendu Vasavada (28.05.2021: http://astatsa.com/OneWay_Anova_with_TukeyHSD/).

The efficacy of the *Applied Phage Meat S2* treatment in reducing the number of viable *Salmonella* Typhimurium on experimentally contaminated beef samples was evaluated by comparing the data obtained for PBS control samples and for *Applied Phage Meat S2* treated samples.

Table 3: Analysis of *Applied Phage Meat S2* induced *Salmonella* reduction on beef samples by independent samples t-test.

T-test	Adjusted p value	Significance level	Significance	Summary
PBS vs. Applied Phage Meat S2	0,0000000002	$\alpha = 0.001$	Yes	***

Applying 1.0 x 10^7 PFU/cm² Applied Phage Meat S2 to beef samples (A = 10.0 cm²) reduced the number of viable Salmonella by 96.2% after 4 h of incubation at 4°C. The observed reduction was highest statistically significant (p < 0.001).

12. SUMMARY CONCLUSION OF THE STUDY

13. SIGNATURES

Applied Phage Meat S2 can significantly reduce viable Salmonella Typhimurium levels on experimentally contaminated beef samples by 96.2% in 4 h contact time at 4°C, when used at 1.0×10^7 PFU/cm².

	24.11.2022
Andrea Kroj, Ph.D.	Date
Research scientist	
	24.M. 2022
Hansjörg Lehnherr, Ph.D.	Date
Study director	

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw chicken at 4°C.

Study Number # R022-003

PTC Phage Technology Center GmbH

Siemensstraße 42

D- 59199 Bönen

Tel.: 49 (0) 2383 919 175

Fax: 49 (0) 2383 919 179

Dr. Michael Fink

FINK TEC GmbH

Oberster Kamp 23

D-59069 Hamm

Tel.: 49 (0) 2385 730

1. STUDY TITLE

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw chicken at 4°C.

2. STUDY DIRECTOR

Hansjörg Lehnherr, Ph.D.

3. STUDY PERSONNEL

The following personnel contributed to the conduct and reporting of the studies reported herein:

Name:Title:Role:Hansjörg Lehnherr, Ph.D.Chief scientistStudy directorAndrea Kroj, Ph.D.Research scientistHands-on-research

4. PERFORMING LABORATORY

PTC Phage Technology Center GmbH Siemensstraße 42 D- 59199 Bönen

Tel.: 49 (0) 2383 919 174 Fax: 49 (0) 2383 919 179

5. STUDY OBJECTIVE

Determine the bacterial load reduction of a *S.* Typhimurium strain on raw chicken, resulting from the application of *Applied Phage Meat S2* after 4 h to evaluate the efficacy of the bacteriophage product at 4°C.

6. TEST MATRIX

The used raw chicken was obtained from a supermarket in Hamm, NRW, Germany. Samples were not washed or pre-treated prior to the studies.

7. COCKTAIL LOT AND APPLICATION

Applied Phage Meat S2 lot # 6072022Applied Phage Meat S2 titer: 5×10^9 PFU/mL per phage component.

The application titer was 2×10^9 PFU/mL per phage component.

8. BACTERIAL STRAINS USED TO EVALUATE COCKTAIL EFFICIENCY

Each chicken meat sample was challenged with 1×10^3 bacterial cells of the *S.* Typhimurium strain indicated below. The total reduction in *Salmonella* bacterial load was measured.

• A chloramphenicol resistant *Salmonella* Typhimurium isolate was used for the experiments.

9. MEDIA AND REAGENTS

- LB broth Lennox (Roth, Karlsruhe, Germany; catalog # X964.4) with 34 µg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- LB agar Lennox (Roth, Karlsruhe, Germany; catalog # X965.2)
 with 34 μg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- PBS (8 g/L NaCl, 0.2 g/L KCl, 1.15 g/L Na₂HPO₄, 0.2 g/L KH₂PO₄; pH 7.5)

10. GENERAL OUTLINE OF THE STUDY

- Original chicken pieces were cut into 21 samples (10.00 cm²/sample).
- Applied Phage Meat S2 was diluted with PBS buffer to an application titer of 2×10^9 PFU/mL.
- 20 samples were homogenously contaminated with 1×10^3 cells/cm² of an overnight culture of the test strain. One sample was not treated with bacteria and served as the uncontaminated, untreated control.
- All samples were incubated for 30 min at 4°C (±1°C).
- 10 contaminated chicken samples were treated with 50 μ L of *Applied Phage Meat S2* with a titer of 2 x 10⁹ PFU/mL, resulting in an application concentration of

1 x 10^7 PFU/cm². 50 μ L of PBS buffer was applied to the remaining 10 samples as the contaminated, untreated controls.

- Incubation period was 4 h at 4°C (±1°C).
- The numbers of viable Salmonella were determined after 4 h.
- To each meat piece 5 mL of PBS were added and then the pieces were treated for 5 min in a stomacher.
- The supernatant was plated on LB agar plates containing chloramphenicol.
- LB agar plates were incubated at 37°C overnight and the numbers of viable *Salmonella* cells were determined by counting colonies.
- The tests were performed with ten (n = 10) replicates.

11. RESULTS

1. Raw Data

Table 1: Salmonella plate counts for Study #R022-003 After 4 h at 4°C

	Ci 4 ii at 4 C	- ·				
Time	Treatment	Surface	Temperature	Bacteria	Number of	Total
		(cm²)) (°C)		samples	CFU/cm ²
	PBS	10.00	4	Yes	10	330
						290
						340
						255
						320
						285
						380
						410
						270
4 hours						375
4 110013	1 x 10 ⁷ PFU/cm ²	10.00	4	Yes	10	40
						20
						10
						25
						15
						15
						5
						10
						15
						10

2. Tabular presentation of results

Table 2: Reduction of *Salmonella* counts on chicken samples treated with *Applied Phage Meat S2* phage solution $(1 \times 10^7 \text{ PFU/cm}^2)$.

*** highest significant with p < 0.001

Time	Treatment	Replicates	Mean CFU/sample	% Reduction	Significance
4 hours	PBS	10	326	94.93	Yes***
	1 x 10 ⁷ PFU/cm ²	10	17		

3. Graphical presentation of results

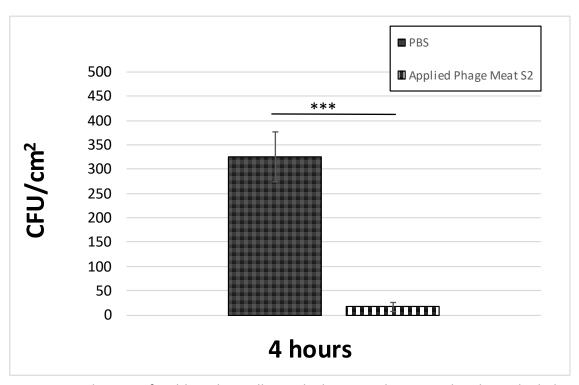


Figure 1: Reduction of viable *Salmonella* on chicken samples treated with *Applied Phage Meat S2* phage solution $(1 \times 10^7 \text{ CFU/cm}^2)$ at 4°C (4 h).

*** highest significant with p < 0.001

4. Statistical analysis

Statistical analysis was performed using Office 2013 Excel for Windows (Microsoft Corporation, Redmond, WA) and the online ANOVA/Tukey HSD calculation tool of Navendu Vasavada (28.05.2021: http://astatsa.com/OneWay Anova with TukeyHSD/).

The efficacy of the *Applied Phage Meat S2* treatment in reducing the number of viable *Salmonella* Typhimurium on experimentally contaminated chicken samples was evaluated by comparing the data obtained for PBS control samples and for *Applied Phage Meat S2* treated samples.

Table 3: Analysis of *Applied Phage Meat S2* induced *Salmonella* reduction on chicken samples by independent samples t-test.

T-test	Adjusted p value	Significance level	Significance	Summary
PBS vs. Applied Phage Meat S2	0,0000000065	$\alpha = 0.001$	Yes	***

Applying 1.0×10^7 PFU/cm² Applied Phage Meat S2 to chicken samples (A = 10.0 cm^2) reduced the number of viable Salmonella by 94.9 % after 4 h of incubation at 4°C. The observed reduction was highest statistically significant (p < 0.001).

12. SUMMARY CONCLUSION OF THE STUDY

Applied Phage Meat S2 can significantly reduce viable Salmonella Typhimurium levels on experimentally contaminated chicken samples by 94.9 % in 4 h contact time at 4° C, when used at 1.0×10^{7} PFU/cm².

13. SIGNATURES	
	25. M. 2022
Andrea Kroj, Ph.D. Research scientist	Date
	25. M. 2022
Hansjörg Lehnherr, Ph.D. Study director	Date

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw turkey breast processed to ground meat at 4°C.

Study Number # R022-004

PTC Phage Technology Center GmbH

Siemensstraße 42

D- 59199 Bönen

Tel.: 49 (0) 2383 919 175

Fax: 49 (0) 2383 919 179

Dr. Michael Fink

FINK TEC GmbH

Oberster Kamp 23

D-59069 Hamm

Tel.: 49 (0) 2385 730

1. STUDY TITLE

Evaluation of the ability of "Applied Phage Meat S2" to reduce Salmonella Typhimurium contaminations on experimentally contaminated raw turkey breast processed to ground meat at 4°C.

2. STUDY DIRECTOR

Hansjörg Lehnherr, Ph.D.

3. STUDY PERSONNEL

The following personnel contributed to the conduct and reporting of the studies reported herein:

Name:Title:Role:Hansjörg Lehnherr, Ph.D.Chief scientistStudy directorAndrea Kroj, Ph.D.Research scientistHands-on-research

4. PERFORMING LABORATORY

PTC Phage Technology Center GmbH Siemensstraße 42 D- 59199 Bönen

Tel.: 49 (0) 2383 919 174 Fax: 49 (0) 2383 919 179

5. STUDY OBJECTIVE

Determine the bacterial load reduction of a *S.* Typhimurium strain on raw turkey breast processed to ground meat, resulting from the application of *Applied Phage Meat S2* after 4 h to evaluate the efficacy of the bacteriophage product at 4°C.

6. TEST MATRIX

The used raw turkey breast was obtained from a supermarket in Hamm, NRW, Germany. Samples were not washed or pre-treated prior to the studies.

7. COCKTAIL LOT AND APPLICATION

Applied Phage Meat S2 lot # 6072022Applied Phage Meat S2 titer: 5×10^9 PFU/mL per phage component.

The application titer was 2.5 x 10⁹ PFU/mL per phage component.

8. BACTERIAL STRAINS USED TO EVALUATE COCKTAIL EFFICIENCY

Each turkey sample was challenged with 1×10^4 bacterial cells of the *S*. Typhimurium strain indicated below. The total reduction in *Salmonella* bacterial load was measured.

• A chloramphenicol resistant *Salmonella* Typhimurium isolate was used for the experiments.

9. MEDIA AND REAGENTS

- LB broth Lennox (Roth, Karlsruhe, Germany; catalog # X964.4) with 34 µg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- LB agar Lennox (Roth, Karlsruhe, Germany; catalog # X965.2)
 with 34 μg/mL Chloramphenicol (Roth, Karlsruhe, Germany; catalog # 3886.2)
- PBS (8 g/L NaCl, 0.2 g/L KCl, 1.15 g/L Na₂HPO₄, 0.2 g/L KH₂PO₄; pH 7.5)

10. GENERAL OUTLINE OF THE STUDY

- Two original turkey pieces (1000 g/sample) were used
- Applied Phage Meat S2 with an application titer of 2.5 x 10⁹ PFU/mL.
- 10 g of each turkey breast were cut from the 1000 g piece and were not contaminated with bacteria to serve as the uncontaminated, untreated controls.
- The two samples were homogenously contaminated with 1×10^4 cells/g of an overnight culture of the test strain.
- The samples were incubated for 30 min at 4°C (±1°C).
- One contaminated turkey sample was treated with 4 mL of *Applied Phage Meat S2* with a titer of 2.5×10^9 PFU/mL, resulting in an application concentration of 1×10^7 PFU/g.

4 mL of PBS buffer was applied to the remaining sample as the contaminated, untreated control.

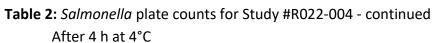
- Incubation period was 4 h at 4°C (±1°C).
- The turkey breasts were minced to ground meat and 25 g portions of the ground meat were analyzed
- To each meat portion 225 mL of PBS buffer were added and then the portions were treated for 5 min in a stomacher.
- The supernatant was plated on LB agar plates containing chloramphenicol.
- LB agar plates were incubated at 37°C overnight and the numbers of viable *Salmonella* cells were determined by counting colonies.
- The tests were performed with ten (n = 10) replicates.
- Three independent experiments were performed.

11. RESULTS

1. Raw Data

Table 1: Salmonella plate counts for Study #R022-004 After 4 h at 4°C

Experi- ment	Treatment	Weight (g)	Temperature (°C)	Bacteria	Number of samples	Total CFU/g
	PBS	25.00	4	Yes	10	5304
						6104
						8029
						7904
						6779
						5654
						6929
						7104
						6179
1						5729
	1 x 10 ⁷ PFU/g	25.00	4	Yes	10	999
						949
						1299
						1299
						699
						724
						1149
						724
						1199
						949



Experi- ment	Treatment	Weight (g)	Temperature (°C)	Bacteria	Number of samples	Total CFU/g
	PBS	25.00	4	Yes	10	5797
						6747
						9772
						7622
						6247
						6397
						7472
						7922
						6347
2						6797
	1 x 10 ⁷ PFU/g	25.00	4	Yes	10	1861
						711
						1761
						1036
						1161
						1561
						1361
						1136
						1186
						1161

Experi- ment	Treatment	Weight (g)	Temperature (°C)	Bacteria	Number of samples	Total CFU/g
	PBS	25.00	4	Yes	10	4385
						5110
						5435
						5285
						5535
						6185
						6385
						4685
						5485
3						4835
3	1 x 10 ⁷ PFU/g	25.00	4	Yes	10	1017
						1442
						1167
						842
						642
						767
						467
						692
						517
						842

2. Tabular presentation of results

Table 3: Reduction of *Salmonella* counts in ground meat samples after treatment with *Applied Phage Meat S2* phage solution $(1 \times 10^7 \text{ PFU/g})$ at 4°C prior to grinding.

*** highest significant with p < 0.001

Experiment	Treatment	Replicates	Mean CFU/g	% Reduction	Significance
1	PBS	10	6572	84.80	Yes***
	1 x 10 ⁷	10	999		
	PFU/g				
2	PBS	10	7112	81.81	Yes***
	1 x 10 ⁷	10	1294		
	PFU/g				
3	PBS	10	5333	84.26	Yes***
	1 x 10 ⁷	10	840		
	PFU/g				

3. Graphical presentation of results

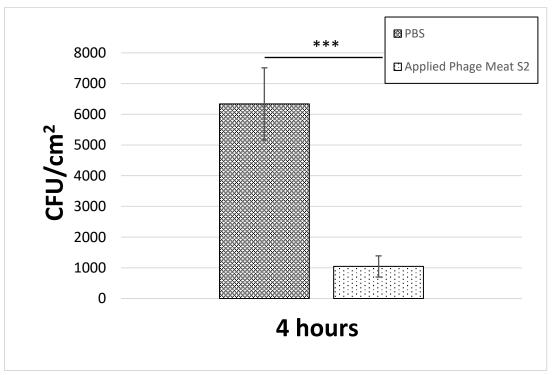


Figure 1: Reduction of viable *Salmonella* in ground meat samples after treatment with *Applied Phage Meat S2* phage solution $(1 \times 10^7 \text{ CFU/g})$ at 4°C prior to grinding.

^{***} highest significant with p < 0.001

4. Statistical analysis

Statistical analysis was performed using Office 2013 Excel for Windows (Microsoft Corporation, Redmond, WA).

The efficacy of the *Applied Phage Meat S2* treatment in reducing the number of viable *Salmonella* Typhimurium on experimentally contaminated raw turkey processed to ground meat was evaluated by comparing the data obtained for PBS control samples and for *Applied Phage Meat S2* treated samples.

Table 4: Analysis of *Applied Phage Meat S2* induced *Salmonella* reduction in ground meat samples by independent samples t-test.

T-test	Adjusted p value	Significance level	Significance	Summary
PBS vs. Applied Phage Meat S2	1,04E-22	$\alpha = 0.001$	Yes	***

Applying 1.0×10^7 PFU/g *Applied Phage Meat S2* to raw turkey breast prior to grinding (ground meat samples of 25.00 g) reduced the number of viable *Salmonella* by 83.53 % after 4 h of incubation at 4°C. The observed reduction was highest statistically significant (p < 0.001).

12. SUMMARY CONCLUSION OF THE STUDY

13. SIGNATURES

Applied Phage Meat S2 can significantly reduce viable Salmonella Typhimurium levels on experimentally contaminated turkey by 83.53 % in 4 h contact time at 4°C, when used at $1.0 \times 10^7 \, PFU/g$.

Andrea Kroj, Ph.D. Research scientist	09.12.2011 Date
Hansjörg Lehnherr, Ph.D.	09. 12. 2022 Date

The scientists of FinkTec provide the following answers to the questions raised by the FDA:

GRN 1038 Additional FDA Questions 01/13/2022

1. In the November 22, 2022 amendment, in response to question 4, the notifier states "*E. coli* and *Salmonella* are two closely related members of the *Enterobacteriaceae* family. The differences between them, that result in the taxonomic distinction, are not always relevant for a bacteriophage infection. For example, both bacteria express a porin protein called OmpC. A bacteriophage that recognizes OmpC as a surface receptor will thus be able to infect and grow on both bacterial species."

For the administrative record, please describe the selectivity (i.e., the host range) of the phage preparations that are the subject of GRN 001038, including relevant citations to the literature as applicable.

That bacteriophages with activity against *Salmonella* also can show activity against *E. coli* (and vice versa) has been described in the literature, see for example bacteriophage P1 (Murooka and Harada, 1979) or bacteriophage SFP10 (Park *et al.*, 2012). In our hands this feature is relatively common. Six out of eleven bacteriophages described in this notice show dual host specificity as shown in the table below:

Bacteriophage	Salmonella enterica	E. coli K12
ELB17 (DSM 26158)	+	+
MP82 (DSM 26173)	+	+
KAZ99a (DSM 33039)	+	+
RMP11k (DSM 33040)	+	+
RMS3b (DSM 33043)	+	-
TAT2F (DSM 33044)	+	-
DIN2 (DSM 33045)	+	-
MP75 (DSM 104023)	+	+
FV7M4 (DSM 26125)	+	+
RMP9 (DSM 26157)	+	-
OBO18 (DSM33041)	+	-

2. In question 15 of our November 7, 2022 questions to the notifier, we requested that the notifier provide results from a minimum of three (preferably five) non-consecutive batches to demonstrate that the phage preparations can be manufactured to meet the specifications listed in Table 1 on page 16 of the notice, including the limit for lead.

In the November 22, 2022 amendment, the notifier provided the results of three non-consecutive batch analyses for lead. We note that according to Table 1, the specifications for the phage preparation include additional parameters for which the results of batch analyses were not provided in the amendment. Please provide results from a minimum of three non-consecutive batch analyses for the following specification parameters listed in Table 1: concentration, appearance, pH, and microbiological parameters. We also request that the notifier confirm that the method used for lead analysis was validated for the intended use.

The missing parameters for concentration, appearance and pH of four non-consecutive batches are provided below:

Batch number	titer (PFU/mL)	color	рН
8012019	3,00E+09	colorless	7,2
6082019	5,80E+09	colorless	7,4
29032021	4,10E+09	colorless	7,3
18012022	8,70E+09	colorless	7,4

The microbiological parameters are determined by an external, accredited laboratory. The specifications for the same four non-consecutive batches are provided as attachments to this response.

We confirm that the lead analyses were performed by an external, accredited laboratory and the method used (DIN EN ISO 11885:2009-09) has been validated for the detection of lead in potable water.

3. In the November 22, 2022 amendment, in response to question 22, the notifier states "As *Salmonella* and *E. coli* are very closely related bacterial genera, all bacteriophages were also tested for their ability to grow on *E. coli*" but did not describe the results of this analysis. For the administrative record, please summarize the results of this analysis and discuss the host range of the phage preparations that are the subject of GRN 001038.

A table summarizing the host range analyses has been provided in the answer to question 1. In our eyes the dual host specificity of the bacteriophages described in this notice has no practical relevance for the intended use to control *Salmonella enterica* in food. In terms of food safety an unintentional reduction of an *E. coli* contamination from food would even be positive, rather than negative.

4. In response to question 11, the notifier states that Table 1 can be found on p. 12 of the notice. We note that p. 12 of the notice only contains a flow diagram of the manufacturing process of the ingredient. We believe Table 1 is located on p. 11. Please confirm this discrepancy.

We confirm that in the original notice Table 1 is located on page 11/36.

5. In question 14, we requested that the notifier provide a specification limit for lead. In the notifier's response the revised table was labeled "Table 2: Product specifications of "Applied Phage Vegetable S2." We note that throughout the original notice the ingredient is referred to as "Applied Phage Meat S2." Please clarify the discrepancy in the name of the ingredient.

That is a mistake, the product specification should correctly refer to the "Applied Phage Meat S2" ingredient.

List of attachments:

- 1. Microbiological specification of batch 8012019
- 2. Microbiological specification of batch 6082019
- 3. Microbiological specification of batch 29032021
- 4. Microbiological specification of batch 18012022

References:

Murooka, Y. and Harada, T. (1979) 'Expansion of the host range of coliphage P1 and gene transfer from enteric bacteria to other gram-negative bacteria', *Applied and Environmental Microbiology*, 38(4), pp. 754–757. doi: 10.1128/aem.38.4.754-757.1979.

Park, M. *et al.* (2012) 'Characterization and comparative genomic analysis of a novel bacteriophage, SFP10, simultaneously inhibiting both Salmonella enterica and Escherichia coli O157:H7', *Applied and Environmental Microbiology*, 78(1), pp. 58–69. doi: 10.1128/AEM.06231-11.





Report number: A-2_58

Date of analysis: 02-02-2022

ANALYSIS REPORT

Sample information

Sample internal ID	Sample description	Batch no.
38849	Applied Phage Meat SO2	8012019

Analytical results

Parameter	Method	Result	Unit
Aerobic colony count, BA, 30°C	ISO 4833-1	<10	cfu/g
Mould	NMKL 98 mod.	<10	cfu/g
Yeast	NMKL 98 mod.	<10	cfu/g
Enterobacteriaceae	ISO 21528	<1	cfu/g
Anaerobic sulphite-reducing spores	ISO 15213	<1	cfu/g
Staphylococcus aureus	ISO 6888-1	<1	cfu/g
Salmonella	NMKL 71	n.d.	in 25 g

Legend:

The laboratory is accredited by DANAK. Information on the methods and their uncertainty can be supplied upon request.

The results are only valid for the tested samples. The report shall not be reproduced except in full, without the laboratory's written approval.

Date:

08-02-2022

Signature:

Name: Dr. Dragana Stanojević

Position: Microbiologist, Project Manager

<: less than, >: more than, n.t.r.: nothing to report, n.d.: not detected, # not accredited





Report number: A-2_61
Date of analysis: 02-02-2022

ANALYSIS REPORT

Sample information

Sample internal ID	Sample description	Batch no.
38852	Applied Phage Meat SO2	6082019

Analytical results

Parameter	Method	Result	Unit
Aerobic colony count, BA, 30°C	ISO 4833-1	<10	cfu/g
Mould	NMKL 98 mod.	<10	cfu/g
Yeast	NMKL 98 mod.	<10	cfu/g
Enterobacteriaceae	ISO 21528	<1	cfu/g
Anaerobic sulphite-reducing spores	ISO 15213	<1	cfu/g
Staphylococcus aureus	ISO 6888-1	<1	cfu/g
Salmonella	NMKL 71	n.d.	in 25 g

Legend:

The laboratory is accredited by DANAK. Information on the methods and their uncertainty can be supplied upon request.

The results are only valid for the tested samples. The report shall not be reproduced except in full, without the laboratory's written approval.

Date: 08-02-2022

Signature:

Name: Dr. Dragana Stanojević

Position: Microbiologist, Project Manager

<: less than, >: more than, n.t.r.: nothing to report, n.d.: not detected, # not accredited





Report number: A-2_57
Date of analysis: 02-02-2022

ANALYSIS REPORT

Sample information

Sample internal ID	Sample description	Batch no.
38848	Applied Phage Meat SO2	29032021

Analytical results

Parameter	Method	Result	Unit
Aerobic colony count, BA, 30°C	ISO 4833-1	<10	cfu/g
Mould	NMKL 98 mod.	<10	cfu/g
Yeast	NMKL 98 mod.	<10	cfu/g
Enterobacteriaceae	ISO 21528	<1	cfu/g
Anaerobic sulphite-reducing spores	ISO 15213	<1	cfu/g
Staphylococcus aureus	ISO 6888-1	<1	cfu/g
Salmonella	NMKL 71	n.d.	in 25 g

Legend:

The laboratory is accredited by DANAK. Information on the methods and their uncertainty can be supplied upon request.

The results are only valid for the tested samples. The report shall not be reproduced except in full, without the laboratory's written approval.

Date:

08-02-2022

Signature:

-

Name:

Dr. Dragana Stanojević

Position:

Microbiologist, Project Manager

<: less than, >: more than, n.t.r.: nothing to report, n.d.: not detected, # not accredited





Report number: A-2_63

Date of analysis: 02-02-2022

ANALYSIS REPORT

Sample information

Sample internal ID	Sample description	Batch no.	
38854	Applied Phage Meat SO2	18012022	

Analytical results

Parameter	Method	Result	Unit
Aerobic colony count, BA, 30°C	ISO 4833-1	<10	cfu/g
Mould	NMKL 98 mod.	<10	cfu/g
Yeast	NMKL 98 mod.	<10	cfu/g
Enterobacteriaceae	ISO 21528	<1	cfu/g
Anaerobic sulphite-reducing spores	ISO 15213	<1	cfu/g
Staphylococcus aureus	ISO 6888-1	<1	cfu/g
Salmonella	NMKL 71	n.d.	in 25 g

Legend:

The laboratory is accredited by DANAK. Information on the methods and their uncertainty can be supplied upon request.

The results are only valid for the tested samples. The report shall not be reproduced except in full, without the laboratory's written approval.

Date:

08-02-2022

Signature:

.

Name: Dr. Dragana Stanojević

Position: Microbiologist, Project Manager

<: less than, >: more than, n.t.r.: nothing to report, n.d.: not detected, # not accredited

Four pages have been removed in accordance with copyright laws. The removed reference citation is:

Y. Murooka, and T. Harada, "Expansion of the Host Range of Coliphage P1 and Gene Transfer from Enteric Bacteria to Other Gram-Negative Bacteria", APPLIED AND ENVIRONMENTAL MICROBIOLOGY, vol. 38, no. 4, pp. 754-757, 1979.

Twelve pages have been removed in accordance with copyright laws. The removed reference citation is:

M. Park, J. Lee, H. Shin, et al., "Characterization and Comparative Genomic Analysis of a Novel Bacteriophage, SFP10, Simultaneously Inhibiting both Salmonella enterica and Escherichia coli O157:H7", APPLIED AND ENVIRONMENTAL MICROBIOLOGY, vol. 78, no. 1, pp. 58-69, 2012.

The scientists of FinkTec provide the following answer to the question raised by the FDA:

March 02, 2023

FDA Questions/Comments Regarding GRN 001038:

1. For the administrative record, please clarify whether all the 11 phages identified in GRN 001038 are double-stranded DNA phages.

The genomes of all eleven bacteriophages identified in GRN 001038 were sequenced (double-stranded DNA sequencing) and annotated. Using the latest taxonomy update by the ICTV (Turner et al, 2022), all the bacteriophages could be assigned to the clade "Duplodnaviria" (viruses with genomes of double-stranded DNA) and the class "Caudoviricetes" (bacterial and archaeal viruses with head-tail morphology). The bacteriophages could be further assigned to various genera within this class:

Genus Seoulvirus (ELB17) Genus Seunavirus (MP82) Genus Felixounavirus (KAZ99a, RMP11k, RMS3b, TAT2F) Genus Rosemountvirus (DIN2) Genus Kuttervirus (MP75) Genus Tlsvirus (FV7M4) Genus Chivirus (RMP9) Genus Jerseyvirus (OBO18)

Thus, we can confirm that all the bacteriophages described in GRN 001038 have a genome composed of double-stranded DNA.

Overbey, Katie

From: Kristi Smedley <smedley@cfr-services.com>

Sent: Tuesday, March 14, 2023 4:19 PM

To: Overbey, Katie

Cc: h.lehnherr@ptc-phage.com

Subject: [EXTERNAL] RE: GRN 1038 - Note on Uses

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Dr. Overbey:

Yes, that is consistent with FINK Tec's understanding. Fink Tec agrees with USDA the phage preparation would be applied to trim prior to grinding.

Kristi O. Smedley, Ph.D.

Center for Regulatory Services, Inc. 5200 Wolf Run Shoals Rd. Woodbridge, VA 22192

Ph. 703-590-7337 Cell 703-786-7674 Fax 703-580-8637



50 Years of Service

From: Overbey, Katie [mailto:Katie.Overbey@fda.hhs.gov]

Sent: Tuesday, March 14, 2023 8:50 AM

To: Kristi Smedley

Subject: GRN 1038 - Note on Uses

Hello Dr. Smedley,

During review of GRN 1038, the USDA had an additional note for the use of the phage preparation. The USDA wanted to note that the phage can be used on trim prior to grinding, but not on final ground product. Can you please confirm if this was the intended use of this phage preparation? If not, please let me know.

Thank you, Katie

Katie Overbey, Ph.D., M.S (she/her/hers)

Regulatory Review Scientist

Division of Food Ingredients Office of Food Additive Safety

Center for Food Safety and Applied Nutrition U.S. Food and Drug Administration Tel: 240-402-7536 katie.overbey@fda.hhs.gov



Overbey, Katie

From: Kristi Smedley <smedley@cfr-services.com>
Sent: Wednesday, April 19, 2023 11:12 AM

To: Overbey, Katie

Cc: h.lehnherr@ptc-phage.com

Subject: [EXTERNAL] RE: GRN 1038 - Additional Question

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FinkTec has conferred with the laboratory that performed the lead assessment, based on this conversation offer the following:

GRN 1038 Additional FDA Question 04/03/2023

In our previous answer we stated that the (DIN EN ISO 11885:2009-09) method has been validated for the detection of lead in potable water. The "Applied Phage Meat S2." ingredient is a water-based solution with the same quality as potable water. Neither the organic components (bacteriophages) nor the buffer components (PBS) in any way interfere with the detection of lead by the ICP-OES method. Thus it is the labs and our understanding that the method is appropriate to monitor the lead concentrations in "Applied Phage Meat S2."

Kristi O. Smedley, Ph.D.

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Ph. 703-590-7337 Cell 703-786-7674 Fax 703-580-8637



50 Years of Service

From: Overbey, Katie [mailto:Katie.Overbey@fda.hhs.gov]

Sent: Monday, April 03, 2023 12:46 PM

To: Kristi Smedley

Subject: GRN 1038 - Additional Question

Hello Dr. Smedley,

We have an additional question for the notifier that came up during our review of GRN 1038:

1. We note in your January 25, 2023 amendment that you state that the lead analysis method "has been validated for the detection of lead in potable water." Please confirm that this method has been validated for it's intended use to measure lead in the notified ingredient.

You may respond directly to this question via email. Please do not include any confidential information in your response. We request a response within 10 business days, please let me know if that timeframe will not work.

Thank you, Katie

Katie Overbey, Ph.D., M.S (she/her/hers)

Regulatory Review Scientist

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Tel: 240-402-7536
katie.overbey@fda.hhs.gov

