#889

Longevity Labs
IT'S NATURAL TO BE HEALTHY.

September 23rd, 2019

Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
Att.: Ms. Szabina Stice
5001 Campus Drive
College Park, MD, 20740-3835

Subject: GRAS Notification for spermidine rich wheat germ extract (SpermidineLife®)

Dear Ms. Stice!

In accordance with 21 CFR 170 subpart E, (81 FR 54960; August 17, 2016), TLL The Longevity Labs GmbH, Austria, through The Executive Consulting INC., USA as its organizer hereby provides notice of a claim that the food ingredient "spermidine rich wheat germ extract" as a nutrient described in the enclosed notification document is exempt from the premarket approval requirement of the Federal Food, Drug, and Cosmetic Act because it has been determined to be Generally Recognized As Safe (GRAS), based on scientific procedures.

We would kindly ask you to only have the redacted version of the notification document published. Some slight redactions have been made due to European privacy laws, as it's unlawful to disclose personal information (including names and other personal data). Other redactions apply to some numbers of production batches which were analyzed; knowing these numbers can reveal the applied processes to competitors. However, neither the redaction of the names nor the redaction of the batch numbers affect the overall statement and conclusion of the analyses reports and/or the notification document in any kind.

For additional questions or required additional information, please feel free to contact us or our contact in US, Ms. Barbara Boedenauer by phone at +1 (404)388-9870 or by E-mail at barbara.boedenauer@exponentialmatters.com.

Sincerely,

[redacted]
Dr. Gerald Sitte
General Manager

[redacted]
Herbert Pock
General Manager

GENERALLY RECOGNIZED AS SAFE (GRAS) ASSESSMENT OF A SPERMIDINE RICH WHEAT GERM EXTRACT

Submitted by:
TLL The Longevity Labs GmbH
8010 Graz
AUSTRIA

Submitted to:
U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
HFS-200
5100 Paint Branch Parkway
College Park, MD 20740-3835
USA

Contact for Inquiries in USA
Baerbel Boedenauer
The Executive Consulting, Inc. 410 Peachtree Pkwy 400. Suite 4245
Cumming, GA 30041

23rd of September, 2019

GENERALLY RECOGNIZED AS SAFE (GRAS) ASSESSMENT OF SPERMIDINE RICH WHEAT GERM EXTRACT

TABLE OF CONTENTS

1. Part 1 – SIGNED STATEMENTS AND CERTIFICATION

1.1. Basis of Conclusion

This GRAS conclusion for use of Spermidine Rich Wheat Germ Extract as a food ingredient has been reached in accordance with requirements described in 21 CFR 170.220, subpart E.

1.2. Name and Address of Notifier

TLL The Longevity Labs GmbH
Kratkystrasse 2,
8020 GRAZ
AUSTRIA

1.3. Name of Notified Substance

The name of the substance that is subject of this GRAS conclusion is "spermidine rich wheat germ extract" (current brand name: SpermidineLife®).

1.4. Intended Conditions of Use

TLL The Longevity Labs GmbH (TLL) intends to use spermidine rich wheat germ extract (SpermidineLife®) at levels up to 2.7 g/serving (reference amounts customarily consumed, 21 CFR 101.12) in foods such as food bars and yogurt drinks. It is recognized that there are Standard of Identity requirements for some of these specified foods and these foods will not be referred by their commonly recognized names. Additionally, foods that are intended for infants and toddlers, such as infant formulas or foods formulated for babies or toddlers, as well as meat and poultry products that come under USDA jurisdictions are excluded from the list of intended food uses of the subject spermidine rich wheat germ extract (SpermidineLife®).

1.5. Statutory Basis for GRAS Determination

This GRAS conclusion is based on scientific procedures in accordance with 21 CFR 170.30(a) and 170.30(b).

1.6. Exclusion from Premarket Approval

TLL has concluded that the use of spermidine rich wheat germ extract (SpermidineLife®) is Generally Recognized As Safe, consistent with Section 201(s) of the *Federal Food, Drug, and Cosmetic Act*. This GRAS conclusion has been reached in accordance with requirements in 21 CFR 170.220. Therefore, the use of spermidine rich wheat germ extract (SpermidineLife®) is exempt from the requirement of premarket approval requirements of the FD&C Act.

1.7. Availability of Data & Information

The data and information that are the basis for this GRAS conclusion will be made available to FDA upon request by contacting Dr. Sitte or Mrs. Boedenauer at the below addresses. The data and information will be made available to FDA in a form in accordance with that requested under 21 CFR 170.225(c)(7)(ii)(A) or 21 CFR 170.225(c)(7)(ii)(B).

Dr. Gerald Sitte
General Manager

TLL The Longevity Labs GmbH
Kratkystrasse 2, 8020 GRAZ, AUSTRIA
Phone: +43 664 245 2863
E-Mail: gerald.sitte@thelongevitylabs.com

or

Baerbel Boedenauer
The Executive Consulting, INC.

410 Peachtree Pkwy, Building 400. Suite 4245
Cumming, GA 30041
Phone: (404)388-9870
E-mail: barbara.boedenauer@exponentialmatters.com

1.8. Data Exemption from Disclosure

Part I through Part VII of this GRAS assessment dossier does not contain any privileged or confidential information, such as trade secrets and/or commercial or financial information, and can be made publicly available.

1.9. Certification

TLL certifies that, to the best of its knowledge, this GRAS conclusion is based on a complete, representative, and balanced dossier that includes all relevant information, available and obtainable by TLL, including any favorable or unfavorable information, and pertinent to the evaluation of the safety and GRAS status of the use of spermidine rich wheat germ extract (SpermidineLife®). TLL accepts responsibility for the GRAS determination that has been made for spermidine rich wheat germ extract (SpermidineLife®) as described in this dossier.

1.10. Name, Position/Title of Responsible Person who Signs the Dossier and Signature

Gerald Sitte, Ph.D.
General Manager
TLL The Longevity Labs GmbH
Kratkystrasse 2
A-8020 Graz, AUSTRIA

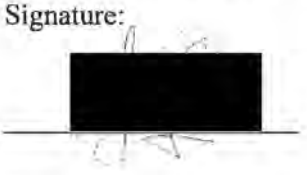
Phone: +43 664 245 28 63
E-Mail: gerald.sitte@thelongevitylabs.com

Signature:

Herbert Pock, MSc.
General Manager
TLL The Longevity Labs GmbH
Kratkystrasse 2
A-8020 Graz, AUSTRIA

Phone: +43 699 14 90 50 50
E-Mail: herbert.pock@thelongevitylabs.com

Signature:



1.11. FSIS/USDA – Use in Meat and/or Poultry

TLL does not intend to add spermidine rich wheat germ extract (SpermidineLife®) to any meat and/or poultry products that come under USDA jurisdiction. Therefore, 21 CFR 170.270 does not apply.

2. Part 2 – IDENTITY, SPECIFICATION, MANUFACTURING AND TECHNICAL EFFECTS

2.1. Identity

2.1.1. Description

The subject of this GRAS assessment is a standardized wheat germ extract also known as spermidine rich wheat germ extract (SpermidineLife®) prepared from the grains of wheat plant *Triticum aestivum*. Wheat germ has been consumed for decades in food to maintain good health with no published evidence of safety concerns associated with its use.

Spermidine rich wheat germ extract (SpermidineLife®), produced by TLL The Longevity labs, is largely water-soluble extract of natural wheat germ, thus containing similar nutrients compared with the raw material wheat germ, but in a differing relative composition. In particular spermidine and the closely related but less abundant polyamine spermine are specifically enriched.

Spermidine [N-(3-aminopropyl)-1,4-diaminobutane] is a saturated linear triamine often classed as an intermediate in the synthesis of spermine. It has molecular formula $C_7H_{19}N_3$ and molar mass 145.25 g/mol and is a small, water-soluble, amphiphilic molecule with the ability to penetrate biological membranes. It occurs throughout many organisms, regardless of taxonomic classification.

The spermidine rich wheat germ extract as produced by TLL is currently marketed under the trade name SpermidineLife®, a different branding for future applications is currently under consideration. General descriptive characteristics and properties of spermidine rich wheat germ extract manufactured by TLL are summarized in Table 1.

Table 1. General Descriptive Characteristics of spermidine rich wheat germ extract (SpermidineLife®)

Parameter	Description*
Botanical source	*Triticum aestivum*
Botanical family	Poaceae
Plant part used	wheat germ
Appearance	white to yellowish powder
Color	white-yellowish
Odor	Typical of grain
Taste	Sweet/sour to lemony
Functional use	Food and beverage ingredient
Shelf life	18 months[5]

**Based on information from TLL (2019), Appendix I*

[5]Complex and exhausted stress test has been performed by the RCPE Research Center for Pharmaceutical Engineering.

2.1.2. Taxonomy of Botanical Source

The hierarchical classification of the source plant is presented in Table 2. In the classical period botanists such as Columella, and in sixteenth and seventeenth century herbals, divided wheats into two groups, Triticum corresponding to free-threshing wheats, and Zea

corresponding to hulled ('spelt') wheats. *Triticum aestivum,* also known as bearded spring wheat, was first characterized by the Swedish botanist Carl Linnaeus. The free-threshing status is important in traditional classification, especially in comparison with the hulled wheats, because the different forms are usually grown separately, and have very different post-harvesting processing. *Triticum aestivum* is the commonly used industrial strain for common cereal products ("Triticum astivum L.", 2006)

Table 2. Taxonomical Classification of *Triticum aestivum*

Parameter	Description*
Kingdom	Plantae
Subkingdom	Tracheobionta
Infrakingdom	Spermatophyta
Superdivision	Magnoliophyta
Class	Liliopsida
Superclass	Commelinidae
Order	Cyperales
Family	Poaceae
Genus	Triticum L.
Species	*Triticum aestivum L.*

**Based on Information of the Natural Resources Conservation Service.*

Common or bread wheat (*Triticum aestivum*) is a species of plant belonging to the grass family (*Poaceae*). It is of great economic importance, being used to produce different baked goods, malt, animal fodder and starch. With its large number of different varieties, wheat is the most commonly cultivated grain in most areas of the world today. A grain of wheat contains 2% - 3% wheat germ, which is separated, along with the wheat bran, from the rest of the grain during conventional flour production (Brandolini and Hidalgo, 2012). These morphological components are not separated off in the production of whole meal flour and whole meal products. In order to enhance the keeping properties of products, the wheat germ is often added back to the wheat flour shortly before use. Wheat germ is often marketed to consumers for addition to muesli, yogurt or other food, with a recommended daily serving of up to 14 tablespoons (approximately 100 g). In order to increase its shelf-life, wheat germ is often stabilized before being sold to end consumers.

2.1.3. Origin of wheat germ

The wheat germ, which represents the source material for the production of spermidine rich wheat germ extract (SpermidineLife®), is procured from Good Mills Austria GmbH, HOCHDORF Swiss Nutrition Ltd. or similar manufacturers. These are produced exclusively from food-grade wheat grown in EU countries, Switzerland or North America. The preparation of the raw materials for the production is in accordance with IFS (International Food Standard) and encompasses both the principles of HACCP and the quantification of common pesticides, harmful substances and microorganisms within the framework of quality control (see Appendix II for detailed specifications). This way, the high quality of the starting materials is guaranteed. The wheat germ is obtained in a stabilized form to prevent oxidation of unsaturated fatty acids. The raw material is used for production of the spermidine rich wheat germ extract within the indicated shelf life of the producer.

The raw material wheat germ is already being added to flour for decades to increase the quality of baked goods. The production of the extract thus offers an alternative for the processing of this by-product of the wheat flour industry (Moreira-Rosario et al., 2016).

2.2. Specifications

Spermidine rich wheat germ extract (SpermidineLife®) produced by TLL is essentially a water-soluble extract of natural wheat germ, thus containing the same nutrients compared with the raw material wheat germ, but in a differing relative composition, with spermidine and spermine enriched as depicted in Table 3. Food grade specifications (including relevant limits of toxins and microbiological parameters) of spermidine rich wheat germ extract (SpermidineLife®) have been established by TLL and are summarized in Table 3.

Table 3. Specifications summary of spermidine rich wheat germ extract (Spermidine Life®).

Nutritional values	
Substance	**Value**
Spermidine	≤ 6 mg/g
Spermine	≤ 3 mg/g
Putrescine	< 1.2 mg/g
Cadaverine	< 0.1 mg/g
Mycotoxins	
Aflatoxins	< 0.4 µg/kg
Deoxynivalenol	< 500 µg/kg
Microbiology	
Total aerobic bacteria	< 10 000 CFU/g
Yeast and moulds	< 100 CFU/g
Escherichia coli	< 10 CFU/g
Salmonella spp.	negative/25g
Listeria monocytogenes	negative/25g
Metals	
Pb	< 1 mg/kg
Cd	< 1 mg/kg
Hg	< 0.1 mg/kg
As	< 0.2 mg/kg

The certificate of analysis from three non-consecutive lots demonstrate that the TLL wheat germ extract is consistently manufactured to meet the current specifications as well as legislative limits of additional harmful substances (Appendices V, VI and VII).

The polyamine content of the extract (SpermidineLife®) currently produced at TLL amounts to ~1.3 mg/g spermidine, ~0.3 mg/g spermine and ~0.2 mg/g putrescine (Appendix VII). TLL is in the process of improving manufacturing of SpermidineLife® to obtain a product that contains higher levels of spermidine but within the limits presented in Table 3.

In addition to these specifications the composition of the extract with its nutrient contents are listed in Tables Table *4*-Table *8*. Harmful substances and their content within the range of legal and food safe limitations are listed in Table 9. The external and accredited institutions Eurofins Analytik GmbH and HYGIENICUM® Institut für Mikrobiologie & Hygiene-Consulting

GmbH conducted the analyses of the extract. The analytical results from three non-consecutive lots are provided in Appendix V and VI at the end of this document. The certificate of analysis from all lots demonstrate that SpermidineLife® is consistently manufactured to meet the food grade specifications. Nevertheless, due to the intended use of natural resources within the production process a significant fluctuation between measurements is given.

Table 4. Nutritional analysis of wheat germ extract— the values listed in the table represent the range of repeated, independent measurements. *The utilized methods and accreditations are listed in Appendix V.*

Nutritional information per 100 g	
Energy	1571-1634 kJ (372-387 kcal)
Fat	6.7-7.6 g
of which saturated fatty acids	1.4-1.6 g
Carbohydrates	49.1-54.2 g
of which sugars	23.7-26.0 g
Total dietary fibers	1.15-3.21 g
Proteins	25.8-26.2 g
Water	2.4-8.6 g
Ash	7.4-7.8 g
Salt (Sodium)	<0.025-0.04 g
Potassium	2.8 g
Phosphorus (total)	1.2 g

Table 5. Vitamins – The listed contents of vitamins represent the range of repeated independent measurements. *The utilized methods and accreditations are listed in Appendix V.*

Vitamins per 100 g	
B1	3.05-3.2 mg
B2	0.587-0.677 mg
B3	3.62-4.80 mg
B6	0.781-0.834 mg
B8	19.0-24.0 µg
B9	358-438 µg
B12	0.0354-0.0477 µg
E	< 5 µg
A	< 0.1 mg

Table 6. Sugar profile – The concentrations of different sugars were calculated based on repeated independent measurements. *The utilized methods and accreditations are listed in Appendix V.*

Sugar	g/100 g Extract
Fructose	1.2-1.6
Glucose	1.0-2.1
Sucrose	20.0-23.8
Maltose	<0.5
Lactose	<0.5
Total sugars (calculated)	23.7-26.0

Table 7. Amino acid profile – The total amounts of different amino acids were determined in repeated independent measurements. *The utilized methods and accreditations are listed in Appendix V.*

Amino acid	g/100 g Extract
Cystine + Cysteine	0.417-0.475
Methionine	0.399-0.434
Tryptophan	0.249-0.257
Alanine	1.43-1.57
Aspartic acid	2.29-2.44
Total arginine	1.86-2.07
Glutamic acid	2.91-3.14
Glycine	1.33-1.44
Histidine	0.536-0.591
Isoleucine	0.566-0.624
Leucine	1.10-1.20
Lysine	1.35-1.38
Phenylalanine	0.580-0.691
Proline	0.787-0.979
Serine	0.875-0.970
Tyrosine	0.544-0.631
Valine	0.996-1.08
Threonine	0.974-1.08
Hydroxyproline	<0.05
Ornithine	<0.05

Table 8. Fatty acid profile – The percentages of different fatty acids within the total fat contents of the extract were determine in repeated independent measurements. *The utilized methods and accreditations are listed in Appendix V.*

Fatty acid	%
C 4:0	<0.1
C 6:0	<0.1
C 8:0	<0.1
C 10:0	<0.1
C 10:1 + isomers	<0.1
C 12:0	<0.1
C 14:0	0.1
C 14:1 + isomers	<0.1
C 15:0	<0.1
C 15:1 + isomers	<0.1
C 16:0	18.6-18.7
C 16:1 + isomers	0.2-
C 17:0	<0.1
C 17:1 + isomers	<0.1
C 18:0	0.8-0.9
C 18:1-9	12.7-15.3
C 18:1-11	1.3-1.4
C 18:1-13	<0.1
C 18:1 (trans)	<0.1-0.3
C 18:2	54.0-55.8
C 18:2 (trans/trans)	<0.1
C 18:2 (cis/trans)	0.1
C 18:2 (trans/cis)	<0.1
C 18:3 (alpha-linolenic acid)	6.2-6.4
C 18:3 (gamma-linolenic acid)	<0.1
C 18:3 (trans/cis/trans)	<0.1
C 18:3 (cis/cis/trans)	<0.1
C 18:3 (cis/trans/cis)	<0.1
C 18:3 (trans/cis/cis)	<0.1
C 18:4	<0.1
C 20:0	0.2
C 20:1 + isomers	1.3-1.4
C 20:2 + isomers	0.1-0.2
C 20:3	<0.1
C 20:4	<0.1
C 20:5	<0.1
C 22:0	0.2
C 22:1 + isomers	0.3
C 22:2 + isomers	<0.1
C 22:5	<0.1
C 22:6	<0.1
C 23:0	<0.1
C 24:0	0.2
C 24:1 + isomers	0.1-0.2
saturated fatty acids	20.3-20.5
monounsaturated fatty acids	16.0-18.8
polyunsaturated fatty acids	60.4-62.3
total trans-fatty acids	0.4-0.6
other	0.1-0.6

Table 9. Contaminants, heavy metals and toxins – The concentrations of all contaminants or impurities are derived from repeated independent measurements. *The utilized methods and accreditations are listed in Appendix V.*

Harmful substances	Concentration	
Metals		
Pb	<0.05-0.41*	mg/kg
Cd	0.09-0.14*	mg/kg
Hg	<0.005	mg/kg
As	<0.1	mg/kg
Dioxins and Furans		
2,3,7,8-TetraCDD	<0.125	pg/g
1,2,3,7,8-PentaCDD	<0.0164	pg/g
1,2,3,4,7,8-HexaCDD	<0.0250	pg/g
1,2,3,6,7,8-HexaCDD	<0.0341	pg/g
1,2,3,7,8,9-HexaCDD	<0.0322	pg/g
1,2,3,4,6,7,8-HeptaCDD	<0.0525	pg/g
OctaCDD	<0.381	pg/g
2,3,7,8-TetraCDF	<0.0341	pg/g
1,2,3,7,8-PentaCDF	<0.0236	pg/g
2,3,4,7,8-PentaCDF	<0.0368	pg/g
1,2,3,4,7,8-HexaCDF	<0.0387	pg/g
1,2,3,6,7,8-HexaCDF	<0.0355	pg/g
1,2,3,7,8,9-HexaCDF	<0.0263	pg/g
2,3,4,6,7,8-HexaCDF	<0.0322	pg/g
1,2,3,4,6,7,8-HeptaCDF	<0.0368	pg/g
1,2,3,4,7,8,9-HeptaCDF	<0.0256	pg/g
OctaCDF	<0.0788	pg/g
WHO (2005)-PCDD/F TEQ incl. BG	0.0333-0.0677	pg/g
WHO (2005)-PCDD/F TEQ excl. BG	not detectable	
Dioxin-like PCBs (12 WHO-PCBs)		
PCB 77	<6.57	pg/g
PCB 81	<0.177	pg/g
PCB 105	<2.56	pg/g
PCB 114	<0.348	pg/g
PCB 118	<9.19	pg/g
PCB 123	<0.263	pg/g
PCB 126	<0.164	pg/g
PCB 156	<1.44	pg/g
PCB 157	<0.269	pg/g
PCB 167	<0.722	pg/g
PCB 169	<0.788	pg/g
PCB 189	<0.263	pg/g
WHO (2005)-PCB TEQ incl. BG	0.0400-0.0412	pg/g

WHO (2005)-PCB TEQ excl. BG	not detectable	
WHO-PCDD/F+PCB TEQ		
WHO (2005)-PCDD/F+PCB TEQ incl. BG	0.107-0.109	pg/g
WHO (2005)-PCDD/F+PCB TEQ excl. BG	not detectable	
PCB - 6 ICES (Food/Feed)		
PCB 28	<0.0657	ng/g
PCB 52	<0.0657	ng/g
PCB 101	<0.0657	ng/g
PCB 138	<0.0657	ng/g
PCB 153	<0.0657	ng/g
PCB 180	<0.0657	ng/g
Sum of 6 NDL-PCBs incl. BG	0.388-0.394	ng/g
Sum of 6 NDL-PCBs excl. BG	not detectable	
PAH 4		
Benz[a]anthracene	<0.5	µg/kg
Benzo[a]pyrene	<0.5	µg/kg
Benzo[a]fluoranthene	<0.5	µg/kg
Chrysene	<0.5	µg/kg
Sum of all determined PAHs	not applicable	
Nitrogenous organic pesticides	not detectable	
Pesticides NCI-GHT	not detectable	
Organochlorine pesticides, pyrethroids	not detectable	
Organophosphorus pesticides	<0.02 mg/kg	
Pesticide screening via LC-GHT		
Screened pesticides	not detectable	
NCI-GHT	not detectable	
Aflatoxins, low LOQ		
Aflatoxin B1	<0.1	µg/kg
Aflatoxin B2	<0.1	µg/kg
Aflatoxin G1	<0.1	µg/kg
Aflatoxin G2	<0.1	µg/kg
Sum of determined aflatoxins	<0.4	µg/kg
Citrinin	<30	µg/kg
Ochratoxin A	<0.2-0.2*	µg/kg
Deoxynivalenol	140-213**	µg/kg

**Maximum levels below the threshold defined by Commission Regulation (EC) No 1881/2006 from 19. December 2006, Commission Regulation (EC) No 1126/2007 from 28. September 2007 and Commission Regulation (EU) No 488/2014 from 12. May 2014.*

***According to 2.4.4 and 2.4.6 of the act No 1881/2006 below the threshold for immediate consumption of grain products (750 µg/kg) and bakery goods (500 µg/kg).*

2.3. Spermidine as a substance

Spermidine (N-(3-aminopropyl)butan-1,4-diamine) is a linear saturated triamine, which is often classified as an intermediate of spermine synthesis. It is present in all tissues of the human body and found ubiquitously in many other organisms, including animals, plants and thus typical human foods, however with varying concentrations (Ali et al., 2011a, Nishimura et al., 2006). High concentrations are present in germinating and growing plants (e.g. wheat germ, soybeans, sweet peas).

Synthetic spermidine has been used for decades in molecular biology for the mild precipitation of DNA, and it is known to reversibly bind to DNA without changing its structure, even in biological materials. Spermidine is present in all investigated tissues of mammals (including humans) and can be mobilized by the body when a need arises. Around one-third of the body's spermidine is synthesized from putrescine, and another two-thirds of the body's internal reservoir are derived from food or the metabolic activity of intestinal microbiota. The last two routes are therefore especially suited for interventions that increase the spermidine concentrations in blood and tissues.

2.4. Manufacturing Process

The wheat germ used as raw material for the production of the spermidine rich wheat germ extract (SpermidineLife®) is obtained from Good Mills Austria GmbH, HOCHDORF Swiss Nutrition Ltd or similar manufacturers and is produced exclusively from food-grade wheat grown in EU countries, Switzerland or North America (Appendix II – Geyer HOCHDORF Specification).

After separation of the wheat germ from the rest of the wheat kernel, the raw material is stabilized by drying the wheat germ using moisture-reduced air. This gives rise to drying, which leads, in parallel, to less enzyme activity and slower oxidative decomposition of the unsaturated fatty acids, thus greatly increasing the shelf life of the raw material and the extract subsequently obtained from it.

The raw materials used for production are prepared observing the IFS (International Food Standard) and — in addition to the quality of those materials being guaranteed by adherence to HACCP plans — common pesticides, harmful substances and microorganisms are also continually quantified through quality controls. The starting material is thus guaranteed to be of high quality.

In the second step, the volume of dry matter to the amount of polyamines is reduced in order to increase spermidine concentration. Here, a multi-step solid-liquid extraction process at TLL (**Figure *1***) produces the spermidine-rich extract. In order to prevent the enzymatic decomposition of this substance and the associated production of putrescine (an undesired biogenic amine), temperature is controlled during this process and kept low at all times. Only food safe solvents (water and ethanol) with natural additives authorized for use in the food industry are used for the extraction. Additives serve production purposes and prevent oxidation of nutrients and microbial growth and the used amounts are within the limits accepted by the FDA. Liquid and solid phases are separated by centrifugation with constant cooling.

In the final step, the substances dissolved in the liquid phase are separated from the solvent by vacuum evaporation and/or lyophilization procedures. During the whole production process, high temperatures are avoided and no substances are used, which would promote unusual reactions and thus the formation of harmful substances. Only food certified materials are used.

Following this step, thorough quality control is carried out to ensure that the extract is safe in the sense that it does not contain contaminants and that it contains the desired concentration of spermidine in accordance with the specification set out in Section 2.1.

The production process and standards were developed and established in cooperation with the University of Graz and leading companies in the field of food process optimization. Due to our university cooperation and these companies' many years of experience in the development, optimization and standardization of industrial processes for different areas of industry (e.g. chemistry, pharmacy, energy, food), the process used to produce the plant extract in question is guaranteed to be optimum, taking into account environmental, hygiene, energy and technical considerations. All the production processes follow industry HACCP and ISO 22000 standards.

Quality control on the starting material and the extract is carried out with entities possessing the relevant accreditation. Entry controls on the raw materials consist of a quantitative polyamine analysis in which biogenic amines (putrescine and cadaverine) as well as spermidine and spermine are measured. Microbiological checks are also performed at this stage. 500 g of raw material is kept for a period of 3 years for subsequent analyses. These extra analyses involve the quantification of heavy metals, mycotoxins, pesticides and products arising from the decomposition of the active substances.

Further quality control is carried out after production of the extract is completed, before it is further processed into various foods, such as food bars and yogurt drinks. At this stage, the most important quality characteristics are measured, including all relevant harmful substances and bacterial counts. In order to be able to guarantee that the product is of high quality, the polyamines spermidine and spermine along with the other specifications are measured. The results are evaluated by comparing the values measured with the specification in Table 3 and the legally prescribed reference ranges. Polyamine analysis is carried out by our in-house quality department and regularly validated by an independent institution at JOANNEUM RESEARCH Forschungsgesellschaft mbH in Graz, Austria, using an SPE-LC-MS/MS (liquid chromatography tandem mass spectrometry) method (Magnes et al., 2014).

After quality control, the extract is packaged in accordance with HACCP standards and sold/used for further food preparation.

Picture of Technical Process

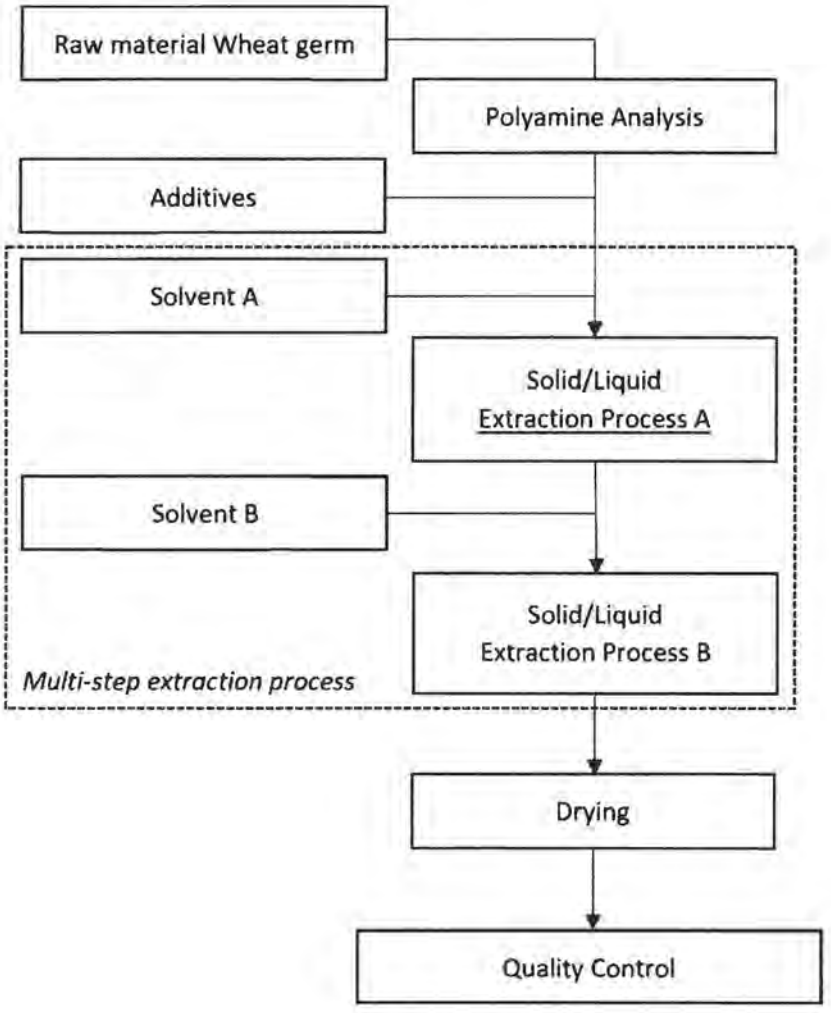


Figure 1. Manufacturing process of spermidine rich wheat germ extract (SpermidineLife®). The production process includes multi-step solid/liquid extraction procedures. Additives (natural substances) and all solvents are based on food safe components and exclusively authorized for use in the food industry.

2.4. Technical Effects

The intended uses of spermidine rich wheat germ extract (SpermidineLife®) is as a nutrient source in selected foods. The nutritional values of wheat germ are commonly known. Wheat germ is a good source of nutrients and can therefore help to maintain a healthy lifestyle. Thus, the intended use of spermidine rich wheat germ extract (SpermidineLife®) is as an addition to specific foods for individuals who wish to increase and/or supplement their daily intake of specific nutrients.

3. Part 3 – DIETARY EXPOSURE

3.1. Background, Intended Use Levels and Food Categories

Food products containing spermidine rich wheat germ extract (SpermidineLife®) are intended as an addition to a normal and balanced diet with an equivalent spermidine intake of up to 12 mg per day. Since the extract is derived from wheat products, it contains gluten. The product should therefore be avoided in case of gluten intolerance, coeliac disease or wheat allergies. With spermidine rich wheat germ extract (SpermidineLife®), common foods can be enriched with valuable nutrients of wheat germ, such as spermidine, polyunsaturated fatty acids and vitamins. Such food products will never contain higher amounts of any of these nutrients than already present in recommended and generally accepted as safe amounts of its source wheat germ (equivalent to max. 24 g wheat germ).

The dietary importance of spermidine has only emerged in recent years (Ali et al., 2011b; Kiechl et al., 2018; Madeo et al., 2018). Therefore, a recommended amount of the daily intake of spermidine has not yet been established. The applicant's suggested daily intake levels of spermidine is based on available studies on the average consumption of polyamines from food in humans, as well as on indicative toxicological values from pre-clinical studies on animals. The average daily intake of spermidine was estimated to ~8 mg in the US and to about 13 mg on average based on data obtained from several European countries (Zoumas-Morse et al., 2007). The typical Mediterranean diet contains significantly higher levels of up to 26 mg per day (Bardócz, 1995, Ali et al., 2011a). The recommended amount of spermidine estimated according to SNO (Swedish Nutrition Recommendations Objectified) is about 30 mg per day for males and 25 mg per day for females (Ali et al., 2011b). This calculation uses known spermidine contents of various foods together with their recommended amounts of daily intake as part of a standard healthy diet.

In conclusion, the amount of spermidine that is considered safe when consumed through foods containing wheat germ extract (up to 12 mg spermidine per day) is less than the difference of a typical US or European diet to healthy Mediterranean levels. In other words, in the US the use of foods containing spermidine rich wheat germ extract (SpermidineLife®) complements up to 70% of its gap to the values of a typical healthy nutrition estimated based on SNO data or from Mediterranean diet, which is generally considered a safe and healthy diet. The proposed use of TLL spermidine rich wheat germ extract at levels up to 2.7 g/serving in baked goods (food bars) and fluid milk (yogurt) are summarized in Table 10. It should be noted that the use levels mentioned in Table 10 are for currently manufactured spermidine rich wheat germ extract.

3.1.1. Estimated Daily Intake from the Intended Uses

The possible daily intake of spermidine rich wheat germ extract (SpermidineLife®) is estimated as per FDA guidelines using "maximum" intended use levels of the extract or spermidine and mean consumption estimates of designated food categories using intake by USDA, Continuing Survey of Food Intakes by Individuals (CSFII) 1994-96 database (Smiciklas-Wright et al., 2002). Based on USDA CSFII surveys for quantities of foods consumed daily, the mean and 90th percentile (high intake; mean x 2) consumption of spermidine rich wheat germ extract from the proposed uses in baked goods and fluid milk

products (Table 10). The CSFII data provides the intake levels of several different types of baked goods. In Table 10, values for cakes, cookies, pastries, pies are included.

Table 10. Estimated Daily Intake of spermidine-rich wheat germ extract (SpermidineLIFE) from Proposed Uses

Food Category	USDA Category	Serving size	Use levels (g/serving)	USDA Mean Grams of Food Consumed	Mean Additive Consumed (g/day)	Mean x 2 Additive Consumed (g/day)
Baked goods	Cakes, cookies, pastries, pie (Granola bars, breakfast bars)	40 g	2.7 g	38	2.57	5.14
Fluid milk	Milk drinks yogurt drinks; could be fruit/vegetable or energy drink	240 ml	2.3 g	227	2.18	4.36
Total intake of spermidine-rich wheat germ extract from all proposed uses (g/person/day)					**4.75**	**9.50**

Serving size: RACC-Reference amounts customarily consumed (21 CFR 101.12)
Intake Source: DATA TABLES: Results from the USDA's 1994-96 Continuing Survey of Food Intakes by Individuals and 1994-96 Diet and Health Knowledge Survey Table Set 10 Food Surveys Research Group, Beltsville Human Nutrition Research Center, Agricultural Research Service, U.S. Department of Agriculture, 10300 Baltimore Ave., Bldg. 005, Rm 102, BARC-West, Beltsville, Maryland 20705-2350.

The intended use of spermidine rich wheat germ extract (SpermidineLife®) at levels up to 2.7 g per serving will result in mean and 90th percentile intake of 2.57 and 5.14 g/person/day, respectively. For safety assessment purposes high levels of 9.5 g/person/day is considered. Taking up to 9.5 g of the extract per day provides an amount of up to 12 mg of spermidine per day.

Based on the polyamine content of the extract currently produced at TLL, which amounts to ~1.3 mg/g spermidine, ~0.3 mg/g spermine and ~0.2 mg/g putrescine (Appendix VII), the corresponding maximum intake levels of spermidine from proposed uses of wheat germ extract are presented in Table 11. TLL is in the process of improving manufacturing of SpermidineLife to obtain a product that contains higher levels of spermidine within the limits presented in Table 3. For the product with higher levels of spermidine, the addition levels of SpermidineLife to food products (Table 10) will be adjusted such that the consumer exposure to spermidine (and the other polyamines) will not be affected.

Table 11. Estimated Daily Intake of Spermidine from Proposed Uses of Wheat Germ Extract

Food Category	USDA Category	Serving size	Use levels (mg/serving)	USDA Mean Grams of Food Consumed	Mean Additive Consumed (mg/day)	Mean x 2 Additive Consumed (mg/day)
Baked goods	Cakes, cookies, pastries, pie (Granola bars, breakfast bars)	40 g	3.5 mg	38	3.32	6.65
Fluid milk	Milk drinks yogurt drinks; could be fruit/vegetable or energy drink	240 ml	3.0 mg	227	2.84	5.68
Total intake of spermidine from all proposed uses (mg/person/day)					**6.16**	**12.33**

Serving size: RACC-Reference amounts customarily consumed (21 CFR 101.12)
Intake Source: DATA TABLES: Results from the USDA's 1994-96 Continuing Survey of Food Intakes by Individuals and 1994-96 Diet and Health Knowledge Survey Table Set 10 Food Surveys Research Group, Beltsville Human Nutrition

Research Center, Agricultural Research Service, U.S. Department of Agriculture, 10300 Baltimore Ave., Bldg. 005, Rm 102, BARC-West, Beltsville, Maryland 20705-2350.

Given the composition of the product, the maximum daily intake of spermidine and other nutrients from spermidine-rich wheat germ extract is equivalent to ~24 g or 3 ½ tablespoons of stabilized wheat germ. For comparison, some manufactures and seller of wheat germ (e.g. *DR. GRANDL VOLLGRAN Weizenkeime* or *EDMONDS NATURAL WHEAT GERM*) recommend up to 100 g of wheat germ per day, which corresponds to about 50 mg of spermidine (Table 12).

Table 12. Wheat germ products from different manufactures, showing their recommended daily intake and the calculated spermidine values based on these recommendations.

Manufacturer	Product	Recommended intake (written on product back site)	Calculated spermidine amount
VOLLGRAN	"Weizenkeime"	50 g	25 mg
EDMONDS Natural	WHEAT GERM	100 g	50 mg
GENUSS PLUS	WEIZENKEIME	30 g	15 mg
Seitenbacher	Weizenkeime	50 g	25 mg
Resana	Weizenkeime	37.5 g	18.75 mg
KRETSCHMER	Wheat germ	15 g	7.5 mg

The use of this extract (SpermidineLife®) is based on the equivalence of the composition of the raw material, wheat germ, and that of the extract. At the same time, it should be noted that the polyamines in the extract are specifically concentrated. This makes it possible to administer an equivalent amount of the active ingredient of up to 12 mg spermidine per day through the ingestion of low amounts of the extract up to 9.5 g/day depending on the specific spermidine concentration of the product), comparable with ~24 g of wheat germ (approx. 3 ½ tablespoons).

4. Part 4 – SELF LIMITING LEVELS OF USE

Food products containing spermidine rich wheat germ extract (SpermidineLife®) will cost more as a source of spermidine and other nutrients (vitamins, unsaturated fatty acids) than its original wheat germ. As such, users will control the amounts used due to economic reasons.

5. Part 5 – EXPERIENCE BASED ON COMMON USE IN FOODS BEFORE 1958

The statutory basis for the conclusion of GRAS status of spermidine rich wheat germ extract (SpermidineLife®) in this document is not based on common use in food before 1958. The GRAS conclusion of spermidine rich wheat germ extract (SpermidineLife®) is based on scientific procedures. Notwithstanding this, it is reasonable to conclude that, since the source material is food, humans are exposed to wheat germ suggesting that it was present in food

before 1958. As described below, wheat germ was commonly used since 1936. One of the first brands who sold wheat germ in the year of 1936 was Kretschmer with its branded product the Kretschmer Wheat Germ. An Advertisement of the product is seen in Figure 2.

Figure 2. Advertisement for The Kretschmer Wheat Germ

6. Part 6 – NARRATIVE

6.1. Traditional and Current Uses of Wheat

The first known cultivation of wheat occurred about 10,000 years ago, as part of the 'Neolithic Revolution'. This cultural change lead to a transition from hunting and gathering of food to settled agriculture. The earliest forms of wheat were diploid called einkorn and further tetraploid called emmer wheat. These first wheat genomes originated from the south-eastern part of Turkey (Dubcovsky and Dvorak, 2007). About 9,000 years ago the first hexaploidy bread wheat (*Triticum aestivum*) made its first appearance (Feldman, 2000).

The earliest cultivation was clearly a non-scientific form of plant breeding. Farmers mostly selected wheat from wild populations, presumably because of their superior yield and other characteristics. This process however was also associated with the selection of genetic traits that separated them from their wild relatives. Typical domestication traits are the loss of shattering of the spike at maturity, which results in seed loss at harvesting and the change from hulled forms, in which the glumes adhere tightly to the grain, to free-threshing naked forms (Nalam et al., 2006).

Cultivated forms of diploid, tetraploid, and hexaploid wheat all have a tough rachis apart from the spelt form of bread wheat. Since einkorn and emmer clearly developed from the domestication of natural populations they have significant differences than the today known bread wheat (*Triticum aestivum)*, that has only existed in cultivation. *Triticum aestivum* was developed by hybridization of cultivated emmer with the unrelated wild grass *Triticum tauschii*. This hybridization probably occurred several times independently, being selected by farmers for its superior properties (Feldman, 2000).

Today about 95% of the wheat grown worldwide is hexaploid bread wheat (*Triticum aestivum*). The 5% remaining is tetraploid durum wheat. The latter is more adapted to the dry Mediterranean climate. It is often used for pasta. Small amounts of other wheat species (einkorn, emmer, spelt) are grown in small portions in some regions including Spain, Turkey, the Balkans, and the Indian subcontinent. The evolution of modern wheats is shown in Figure 3. **Evolution of modern wheat and examples of spikes and grains.** Adopted from (Shewry, 2009) ..

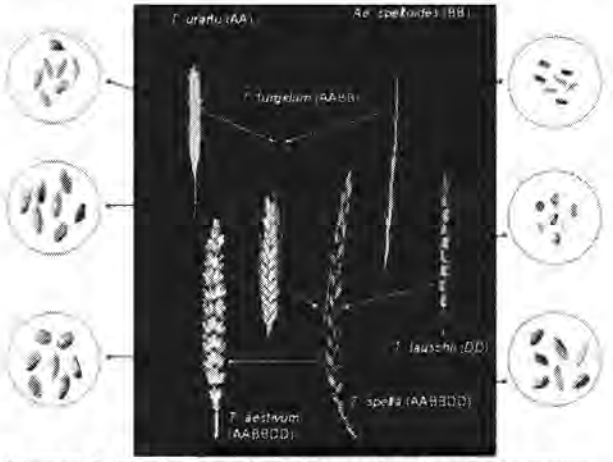


Figure 3. Evolution of modern wheat and examples of spikes and grains. *Adopted from (Shewry, 2009)* .

6.1.1. Current Uses of Wheat Germ and Wheat Germ Products

Spermidine rich wheat germ extract (currently available under the brand name SpermidineLife®) is already used in Europe and has been granted a novel food approval (Appendices III and IV) by the European Food Safety Agency (EFSA) (*https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R2470&from=EN*). It is intended as a dietary food supplement for adults (30+). The recommended use level in Europe is equivalent of up to 6 mg spermidine per day. Given the composition of the product, the daily intake amount is equivalent to approximately 12 g or ~2 tablespoons of stabilized wheat germ. For comparison, some makers of wheat germ (e.g. VollGran) recommend up to 5 tablespoons of wheat germ per day.

Wheat germ and wheat germ products (e.g. wheat germ oil, defatted wheat germ, fermented wheat germ) have been consumed in many countries, including the United States as food product or dietary supplement. Several other wheat germ products are approved and in use in Europe and USA, such as "Avemar" (Telekes et al. 2009). Wheat germ is known to be one of the potentially most excellent sources of vitamins, minerals, dietary fiber, calories, proteins, and some functional microcomposition. It is produced as a byproduct of the flour milling industry and praised as "the natural nutrient treasure-house and life source of mankind" due to its high nutritive value and palatability. With the development of food industry technology, the overall wheat germ production took a massive leap forward, increasing its keeping quality as well as the reprocessing quality. As a result, there is a rich annual deposit of wheat germ in the world, ensuring high availability of the raw material. However, the processing and application of wheat germ as food has only been recorded since the last century. Currently most of the produced wheat germ is used in animal feed formulations. The usability of wheat germ and its level of industrial utilization has been still at the initial stage (Ge et al., 2000).

Wheat germ is an excellent raw source for the preparation of foods such as bread cookies, muffins, comminuted meat products and more. Additionally, with its highly concentrated nutrients wheat germ is a potentially nutritious food supplement. Better nutrient separation from the kernel and improved fractioning techniques could provide high-purity molecules with positive health benefits (Brandolini and Hidalgo, 2012).

Wheat as a food source derives its importance from its ability to adapt to new climate conditions and market requirements. From wheat to flour, the conscientious efforts of wheat farmers working with scientists, researchers, and technicians to provide the American public and consumers of the world one of the most economical, plentiful, and nutritious groups of food available. Producing spermidine rich wheat germ extract (SpermidineLife®) provides an effective way to use wheat germ for additional applications and improves the current state of the art process of wheat processing.

6.1.1.1. Common Knowledge of Safe Use of Wheat

There is common knowledge of human consumption of wheat without any safety concerns. The modern bread wheat described above is known to be a major resource for nearly every cultures diet. For 10,000 years humans cultivate and eat different forms of wheat, wheat is referenced in the Bible and indeed held in reverence as noted in the Lord's Prayer.

Wheat was transplanted to North America by Russian Mennonites between 1874 and 1884. The Mennonites, who settled in Kansas in the late 1800's, brought with them seeds of Turkey Red Wheat, a hard winter wheat that proved to be a productive staple for future American families. Today, wheat is produced in almost every state of the United States and is the principal cereal grain grown in the country. The United States is ranked fifth in production volume of wheat worldwide. About 47 million tons produced in the year of 2017. The United States ranks first in crop export volume; almost 50% of its total wheat production is exported. Wheat production and trade in North America has been an important industry ever since the Europeans came across the vast prairies of the West and Northwest. Currently available figures show an average annual global production of about 680 million tonnes (mt) over the 5-year period from 2008 to 2012, with almost 700 mt being produced in 2011 (FAOStat *http://faostat.fao.org/site/291/default.aspx*). This makes it the third most important crop in terms of global production, the comparative values for the production of the two other major cereals over the same period being 704 mt for rice and 874 mt for maize. In summary, for over 10,000 years wheat plays an increasing role in human diets worldwide. The available information suggests that there is a long history and common knowledge of exposure to wheat as a food (staple) in South America as well as in the USA. This suggests that wheat and wheat germs can be safely consumed by human beings.

6.1.1.2. Nutritional Value of wheat

Wheat is generally known to be a major source for several food products. As source material for flour it gets processed into, bread, noodles, baking goods and many more meals. Further wheat can also be processed into cereals, muesli bars and more. Wheat is a long-time staple favorite of eaters around the world. Wheat is considered as a highly nutritious product that provides a broad variety of carbohydrates, fats, protein, vitamins, minerals, and fiber. In addition to be a starch and energy provider, wheat also contains substantial amounts of several components which are essential or beneficial for health, notably protein, vitamins (notably B vitamins), dietary fiber, and phytochemicals. Especially wheat is an important source of dietary fiber, there are well-established relationships between the consumption of cereal dietary fiber and reduced risk of cardio-vascular disease, type 2 diabetes and forms of cancer (Shewry and Hey, 2015).

When it comes to further processing for food production, wheat wholemeal and white flour are two typical types of sources material. Typical contents of essential amino acids reported for wholemeal wheat and white flour are compared with the minimum physiological requirements for adults in Table 13. This data supports the widely accepted view that essential amino acids being present in adequate amounts and unlikely to cause any adverse effects.

Table 13. Minimum physiological requirements (g/100 g protein) for essential amino acids for adults (g/100 g protein) [WHO/FAO/UNU Expert Consultation (2002, Geneva, Switzerland)] and ranges of % total protein (%N × 5.7) (as is basis) and essential amino acid compositions (g/100g protein) for wholemeal and white wheat flour. *Adopted from Shewry & Hey, 2015*

WHO adult intake			Sample	No. Samples	Range		Mean
					Min	Max	
Total Protein			Wholemeal	22	7.70	17.20	14.35
			White flour	29	7.50	15.08	13.09
Tryptophan	0.6		Wholemeal	-	-	-	-
			White flour	7	0.68	1.01	0.85
Threonine	2.3		Wholemeal	22	1.74	3.10	2.54
			White flour	29	1.60	2.80	2.24
Isoleucine	3.0		Wholemeal	22	2.05	4.00	3.14
			White flour	29	2.13	4.30	3.09
Leucine	5.9		Wholemeal	22	3.79	7.10	5.94
			White flour	29	3.93	7.00	5.65
Lysine	4.5		Wholemeal	22	2.50	3.82	2.88
			White flour	29	1.70	2.90	2.22
Methionine	1.6	2.2	Wholemeal	16	1.00	1.40	1.20
			White flour	29	0.83	1.50	1.13
Cysteine	0.6		Wholemeal	16	2.10	2.80	2.43
			White flour	29	1.40	3.30	2.17
Phenylalanine	3.8		Wholemeal	22	1.79	4.90	3.90
			White flour	29	1.87	5.00	3.75
Tyrosine			Wholemeal	22	1.10	1.90	1.54
			White flour	29	1.02	1.80	1.39
Valine	3.9		Wholemeal	22	2.56	4.80	3.88
			White flour	29	2.34	4.40	3.54
Histidine	1.5		Wholemeal	22	2.20	3.66	2.66
			White flour	29	1.90	3.71	2.69

The overall consumption of wheat is increasing globally. Even in countries with climates that are not suitable for wheat production. Further, wheat-based foods provide a high variety of essential and beneficial components to the human diet, including protein, B vitamins, phytochemicals and dietary fibers.

6.1.1.3. Nutritional Value of wheat germ

Wheat germ is a nutrient rich food, acting as a good source of some of the B vitamins, phosphorus, zinc, iron, selenium and potassium. Wheat provides essential vitamins, minerals and fiber which help regulate the digestive system. Wheat germs are about 2.5-3.8% of total seed weight (Brandolini and Hidalgo, 2012). The germ contains about 10-15% lipids, 26-35% proteins, 17% sugars, 1.5-4.5% fiber and 4% minerals, as well as significant quantities of bioactive compounds such as tocopherols [300–740 mg/kg dry matter (DM)], phytosterols (24–50 mg/kg), policosanols (10 mg/kg), carotenoids (4–38 mg/kg), thiamin (15–23 mg/kg) and riboflavin (6–10 mg/kg) (Brandolini and Hidalgo, 2012).

The proximate analysis of wheat germ is provided in Table 14, while nutrient content comparison, essential amino acids comparison and mineral content comparison with other common foods are presented in Tables Table ***15***,Table ***16*** and

Table *17*, respectively. Importantly, the nutrient profiles of spermidine-rich wheat germ extract shows high similarity to that from its source material wheat germ. Wheat germ data was derived from the USDA National Nutrient Database for Standard Reference on crude wheat germ (Release 28, September 2015, Revised May 2016).

Table 14. Proximate analysis of wheat germ compared to spermidine rich wheat germ extract (SpermidineLife®). Per 100 g dry weight.

Component	Wheat germ	Spermidine rich wheat germ extract (SpermidineLife®)
Energy	360 kcal	372-387 kcal
Fat	9.72 g	6.7-7.6 g
Carbohydrates	51.80 g	49.1-54.2 g
Ash	4.21 g	7.4-7.8 g
Fiber	13.2 g	1.15-3.21 g
Protein	23.15 g	25.8-26.2 g
Cholesterol	0 g	0 g

Table 15. Nutrient contents of wheat, wheat germ, SpermidineLife® and selected foods. Per 100 g dry weight.

Parameters	Wheat	Wheat Germ	Spermidine rich wheat germ extract (SpermidineLife®)	Maize	Rice
Energy (Kcal/100 g)	392	360	372-387	408	372
Fat (g/100 g)	2.3	9.72	6.7-7.6	4.7	2.2
Total Carbohydrates (g/100 g)	78.4	51.80	49.1-54.2	81.1	80.4
Iron (mg/100 g)	3.8	6.26	~5.1	0.7	3.8
Zinc (mg/100 g)	4.7	12.29	~29	0.6	4.7
Protein (g/100 g)	14.3	23.15	25.8-26.2 g	10.2	7.6

Table 16. Essential amino acid pattern of wheat, wheat germ and soy, compared to spermidine rich wheat germ extract (SpermidineLife®) and FAO reference pattern for adults (1973) for evaluating proteins in mg per g of protein

	Amino acid content (mg/g protein)				
Amino acid	Wheat	Wheat Germ	Spermidine rich wheat germ extract (SpermidineLife®)	Soy	FAO*
Isoleucine	38	8	6	47	40
Leucine	66	16	12	70	70
Lysine	25	15	14	63	55
Phenylalanine	45	9	6	46	
Tyrosine	30	7	6	36	
Cystine	22	5	4	14	
Methionine	17	5	4	14	
Threonine	29	10	10	39	40
Tryptophan	13	3	2	12	10
Valine	47	12	10	49	50

*Assuming a safe level of protein intake of 0.55 g per kg per day (averaged value for men and women).

Table 17. Comparison of mineral content in barley, yellow corn, wheat and wheat germ.

Crop	Ca (%)	P (%)	Mg (%)	K (%)	Na (ppm)	Fe (ppm)	Cu (ppm)	Mn (ppm)	Zn (ppm)
Barley	0.08	0.42	0.12	0.56	200	50	8	16	15
Yellow corn	0.07	0.36	0.14	0.39	900	21	—	—	—
Wheat	0.05	0.36	0.16	0.52	900	50	7	14	—
Wheat germ*	0.04	0.84	0.24	0.89	120	63	8	133	123

**Full Report (All Nutrients): 20078, Wheat germ, USDA National Nutrient Database for Standard Reference (Release 28, September 2015, Revised May 2016)*

6.2. Safety Related Studies

Wheat germ, processed wheat germ and wheat germ products such as wheat germ oil, defatted wheat germ and fermented wheat germ extract (FWGE) are used as food additives and nutritional supplements for decades, because it is believed to contribute to a balanced and healthy nutrition with a high nutrient value and even potential health effects (Table Table *18*Table 19) (Brandolini and Hidalgo, 2012, Otto et al., 2016). To our knowledge, no safety concerns regarding wheat germ products are known when taken in different recommended amounts and no safety related studies, except for Schwarz et al., 2018 (discussed below in section 6.2.1), have been published. Therefore, we predominantly discuss potential safety concerns of spermidine and other polyamines present in spermidine rich wheat germ extract (SpermidineLife®) or thereof provided food products. The estimated maximum intake of spermidine-rich wheat germ extract (SpermidineLife®) contains less spermidine and spermine than present in the recommended daily amounts of wheat germ (generally considered as a healthy and safe food item). Therefore, solely based on the similarity of spermidine rich wheat germ extract to its source material wheat germ, it can be considered as safe at the proposed intake levels.

6.2.1. Human Studies of wheat germ extracts and products

In the course of the SmartAge study (see also Table 19) at Charité Universitätsmedizin in Berlin, Germany, the safety of spermidine rich wheat extract (SpermidineLife®) produced by TLL The Longevity Labs GmbH has been tested in a double-blinded and randomized study design (Schwarz et al., 2018). The aim of this study was to test both, the safety of long-term regular usage of spermidine-rich plant extracts for elderly, and the potential of dietary spermidine intake to prevent or slow down the development of cognitive decline, Alzheimer's disease and other neurodegenerative diseases. In this study, 30 individuals 65+ year of age that have no clinically identifiable traits of compromised cognitive function but have reported self-observed memory loss were tested and compared to a placebo, using various psychological, medical, molecular and biochemical tests over the course of several months. The results demonstrated, that oral spermidine intake using spermidine-rich wheat extract is safe and well-tolerated in older adults based on vital signs, weight, clinical chemistry and haematological parameters, as well as on self-reported health status at the end of intervention. (Schwarz et al.,

2018). Clinical chemistry and hematological parameters did not differ significantly at the end of intervention between the two groups. As regards adverse effects, two participants (7.1%) reported a serious adverse event (SAE) during the intervention phase, classified by system organ classes of "immune system disorders" (spermidine group: n = 1) and "infections and infestations" (placebo group: n = 1). Both SAEs were categorized as "mild intensity without permanent damage". Their relationship to intervention was rated as "unlikely related" (allergic reaction after animal contact, after 2.5 months of treatment) and "not related"" (pneumonia), respectively. No specific actions were taken with regard to these events.

In another study, the supplementation of up to 100 g Natto (spermidine-rich fermented soy beans) to the daily diet of human volunteers (mimicking a high polyamine diet) for 2 months showed no negative side effects (Soda et al., 2009b). 100 g Natto contain about 15 mg spermidine, which exceeds the recommended daily intake of spermidine rich wheat germ extract (SpermidineLife®).

A number of other human studies addressed safety of wheat germ itself and of various other wheat germ products (e.g. defatted wheat germ, Viogerm®PB1) and observed no adverse effects or safety related concerns. A summary of these studies investigating the effects of wheat germ or wheat germ products is provided in Table 18.

Table 18. Studies investigating the effects of wheat germ products in humans.

References	Conditions	Study participants	Treatment	Estimated spermidine intake per day	Results	Conclusion
(Schwarz et al., 2018)	Healthy volunteers with self-reported cognitive decline	30 individuals aged 65+ with self-reported memory loss	Spermidine-rich wheat germ extract (750 mg/d for 3 months)	1.2 mg	No changes in any measured parameter (vital signs, weight, clinical chemistry and hematological parameters of safety, as well as in self-reported health status at the end of intervention)	The intake of spermidine rich wheat germ extract is safe and well tolerated.
(Moreira-Rosario et al., 2016; 2019)	Healthy volunteers	55 healthy volunteers	Wheat bread with wheat germ (6 g/d) compared with wheat bread without wheat germ for 4 weeks	3 mg	No significant effect of daily intake of wheat germ on cholesterol and triglycerides levels, on postprandial glucose response and on insulin sensitivity. None of the participants reported adverse effects.	Wheat germ up to 6 g/day has no adverse effects on CVD risk factors.
(Cara et al., 1991)	Hyperchole sterolemia, Hypertrigly ceridemia	10 subjects with high cholesterol levels and some also with high triglyceride levels	Wheat germ (30 g/d for 4 weeks)	15 mg	No change in glycemia but decrease in total plasma cholesterol (especially in VLDL cholesterol), plasma triglycerides and Apoprotein B and A1. No changes in LDL and HDL cholesterol.	Wheat germ has a beneficial effect on lipid metabolism in humans

(Cara et al., 1992)	Hypercholesterolemia, Hypertriglyceridemia	Two separate groups consisting of 10 and 9 subjects with high cholesterol levels and some also with high triglyceride levels	Raw wheat germ compared with partially defatted wheat germ (20 g/d for 4 weeks followed by 30 g/d for 14 weeks)	10 mg (1st phase)/ 15 mg (2nd phase)	Raw wheat germ supplementation decreased plasma cholesterol and VLDL cholesterol after 4 weeks and additional 14 weeks. Also decrease in plasma triglycerides and ApoB:ApoA1 ratio. Defatted wheat germ supplementation transiently decreased plasma triglycerides and cholesterol after 4 weeks.	Short- and long-term wheat germ intake reduces hypercholesteremia and could play a beneficial role in hyperlipidemia patients
(Matteuzzi et al., 2004)	Healthy volunteers	32 healthy volunteers	Wheat germ preparation "Viogerm®PB1" or placebo (20 days)	-	Faecal samples showed a decrease in pH and coliform population, increase in lactobacilli and bifidobacteria in subjects with low basal levels. No changes observed for the other bacterial groups and when treated with placebo.	Wheat germ preparation "Viogerm ®PB1" exhibits prebiotic effects.
(Grant et al., 2001)	Giardiasis	63 subjects with giardiasis	Asymptomatic subjects: wheat germ (2 g, 3 times a day) or placebo (cornstarch, 2 g, 3 times a day) for 10 days, followed by metronidazole (250 mg 3 times a day) for 7 days. Symptomatic subjects: Wheat germ or placebo plus metronidazole (250 mg 3 times a day) for 7 days.	3 mg	Asymptomatic subjects taking wheat germs: cyst passage and coproantigen levels were reduced by about 50% compared with the placebo group Symptomatic subjects: cyst passage and coproantigen levels fell in response to metronidazole therapy and no clinically important differences between wheat germ supplementation group and control group, but symptoms resolved more rapidly in the subjects taking wheat germs in addition to metronidazole.	Wheat germ either alone or in combination with antiprotozoal agents can influence the course of human giardiasis
(Haripriya and Premakumari, 2010)	Diabetes	30 subjects with diabetes	Wheat germ supplementation (60 g per day for 6	30 mg	Fasting and post prandial glucose and glycosylated hemoglobin levels were significantly lower in the	Wheat germ lowers blood

			months) compared with control group without wheat germ supplementation		wheat germ supplemented group ($p<0.01$) compared to the control group. Additionally, a drastic reduction in physiological symptoms was observed.	glucose levels in diabetic humans.

6.2.2. Animal Studies of wheat germ extracts and products

In course of the SmartAge study (Schwarz et al., 2018), spermidine rich wheat germ extract (SpermidineLife®) has also been tested on rodents in a repeated dose 28-day oral toxicity protocol recommended by OECD (Organisation for Economic Co-operation and Development, [SOURCE: OECD: Guidelines for the testing of Chemicals - "Test 407: Repeated Dose 28-day Oral Toxicity Study in Rodents"]) using 10 male and 10 female BALBc/Rj mice. General behavior, food and water intake, body and organ weights and histopathological tissues parameters were investigated. This study found no adverse effects of any of the doses tested. *"In a preclinical study, supplementation of spermidine using this extract did not result in morbidities or changes in behavior in BALBc/Rj mice during the 28-days repeated-dose tolerance study. Post mortem examination of the mice organs showed no increase in tumorigenic and fibrotic events."* (Schwarz et al., 2018). The oral intake of ~60 mg spermidine per kg body weight equals 4.86 mg spermidine per kg body weight in humans (= 340 mg per 70 kg person), based on scientifically accepted methods of dose translation that uses body surface area differences between mice and humans (Reagan-Shaw et al., 2008). Employing FDA recommended safety factors of 100-fold (21 CFR 170.22), the studied dose corresponds to 0.6 mg/kg-bw/day (42 mg for a 70 kg person) in men. Further animal studies are listed in Table 19.

Table 19. Summary of Animal Studies with Wheat germs and it's preparations.

Reference	Animal species; age at start; Sample size (n)	Trial length	Control diet; Intervention diet	Wheat germ (products) in diet	Estimated spermidine intake per day	Main outcome measure	Key findings
(Schwarz et al., 2018)	BALBc/Rj mice; 12 weeks; 40	28 days	control chow; chow supplemented with a polyamine-rich wheat extract	0.5, 5 and 50 g wheat germ extract/ kg-bw/day	0.6/6/60 mg/kg-bw	behavior, food and water intake, body and organ weights, histopathological tissue analyzes	Oral intake of spermidine-rich wheat extract did not result in morbidities or changes in behavior in BALBc/Rj. Post mortem examination of the organs showed no increase in tumorigenic and fibrotic events.
(Yun et al., 2018)	BALBc mice; ?; 60	14 days	regular chow without wheat germ agglutinin;	60, 120 and 240 mg wheat germ	n.a.*	immune function	Results of wheat germ agglutinin group indicated a protective function against

			regular chow with different doses of wheat germ agglutinin	agglutinin/ kg-bw/day			cyclophosphamide (CTX) induced immunosuppression. Wheat germ agglutinin could also strengthen macrophage phagocytosis capacity and NK cell activity. Further results indicated that wheat germ agglutinin could enhance CD4+ and CD8+ splenic T lymphocytes, inflammatory cytokines (IL-β, IL-6, IL-12, TNF-α mRNA), receptor protein (TLR2, TLR4) and protein kinase (IRAK4, TRAF6, TAK1, p38-MAPK, pho-p38-MAPK, NF-κB p65, and nucleu-NF-κB p65) production.
(Zhang et al., 2015)	female BALB/c nude mice; 4-6 weeks; 40	30 days	regular chow; fermented wheat germ extract with Lactobacillus plantarum dy-1 (LFWGE)	2 or 1 g fermented wheat germ extract kg/bw/d		Tumor weight	In both groups with LFWGE supplementation, tumor volume and weights decreased Additionally, the cell apoptosis rate of the LFWGE group (2 g/kg/d, 60.1%±4.4%; 1 g/kg/d, 58.6%±6.9%) was significantly higher than that of the control group (11.5%±1.6%) and 5-FU group (32.1%±3.5%). Moreover, the real-time fluorescent quantitative PCR and Western blot method further confirmed these enhancing apoptosis and growth inhibition effects.

(Leenhardt et al., 2008)	Male wistar rats; 5 weeks; 24	3 weeks	control chow (without vitamin E); stabilized wheat germ or wheat germ oil.	20% (w/w) stabilized wheat germ or 1% (w/w) wheat germ oil .	15 mg/kg-bw	Improvement of antioxidant status	The 20% wheat germ group showed significantly increased plasma and liver vitamin E levels compared to the low vitamin E basal diet, and decreased the susceptibility of heart and liver lipids to oxidation, as well as the plasma. No changes in triglycerides (TG) or cholesterol levels in plasma or liver compared to controls. Similar results were obtained in the wheat germ oil group.
(Ojo et al., 2017)	Male C57BL/6 mice; 6 weeks; 48	12 weeks	control chow (10% fat kcal); control chow + 10% wheat germ, or high fat-sucrose diet (60% fat kcal), or high fat sucrose diet + 10% wheat germ.	10% wheat germ (w/w)	7.5 mg/kg-bw	Improved cardiac mitochondrial metabolic functions	High fat-sucrose + wheat germ supplemented mice had significantly less visceral fat (−16 %, P =0·006) compared with the high fat-sucrose group. Wheat germ significantly reduced serum insulin (P=0·009), insulinotropic hormone, gastric inhibitory peptide (P =0·0003), and surrogate measure of IR (P =0·006). High fat-sucrose diet significantly elevated (45 %, P=0·02) cardiac complex 2 mitochondrial VO2, suggesting increased metabolic stress. Wheat germ ameliorated this effect Consequently, genes which mediate antioxidant defense and mitochondrial biogenesis (superoxide dismutase 2 (Sod2) and PPARγ coactivator 1-α (Pgc1a), respectively) were significantly reduced (P <0·05) in

							the heart of the HFS group, whereas wheat germ supplementation tended to up-regulate both genes. wheat germ significantly increased hepatic gene expression of Sod2 (P=0·048) but not Pgc1a.
(Abdel-Rahim and Mahmoud, 2011)	Male albino rats; ?; 60	3 months	Normal diet consisting of casein 15%, cotton seed oil 10%, cellulose 5%, salt mixture 4%, vitamins mixture 1% and starch 65% (Lane-Peter and Pearson, 1971); 20% wheat germ in diet, with or without profenofos	20% wheat germ (w/w)	15 mg/kg-bw	Protective effects against the toxic influence of profenofos	Wheat germ supplementation as treatment of profenofos-induced animals resulted in significant improvements in lipid fraction content and enzyme activity (G6PD and 6PGD), and improved disturbed metabolic fractions of the lipid profiles.
(Kandeil et al., 2018)	Male Sprague Dawley rats; ?; 40	45 days	Control chow; gentamicin group (120 mg/kg/day i.p. for 15 days), vitamin E group (200 mg/kg orally for 45 days) and wheat germ group (20% of the diet for 45 days).	20% wheat germ (w/w)	15 mg/kg-bw	Protective effects against the toxic effects of gentamicin on kidney; high anti-apoptotic and antioxidant activity	Wheat germ significantly decreased BAX/BCL-2 ratio, decreased MDA levels and increased total antioxidant capacity (TAC) level and catalase (CAT) activity. Wheat germ also ameliorated deteriorated serum creatinine, urea, sodium and potassium levels.

*n.a., not available, as spermidine content has not been determined in respective supplements

6.2.3. Safety of high levels of spermidine from animal studies

In various animal studies, spermidine has been supplemented in high doses to food or water without showing any adverse effects, as reviewed in Madeo, 2018 and the most relevant examples are listed in Table 20 and explained below.

After 7 months of supplementing mice with 3 mM (equals ~435 mg/L) spermidine *ad libitum* in drinking water, no negative effects were reported (Yue et al., 2017). The positive effects found were that spermidine alleviates CCl_4-induced liver fibrosis and prevents hepatocellular carcinoma. Additionally, no changes in body weights were observed in wild type mice and a life span extension of about 25% was determined by lifelong spermidine administration (Yue et al., 2017). Another study using the same concentrations of spermidine administration (3 mM spermidine *ad libitum* in drinking water) also couldn't find any adverse effects after 6 months or lifelong supplementation (Eisenberg et al., 2016). Assuming a daily water intake of 0.2 ml water per g body weight of adult mice (Eisenberg et al., 2016), the amount of spermidine intake of the above-mentioned studies equals that of 87 mg spermidine/kg body weight per day. A ten times higher spermidine concentration (30 mM in drinking water; 870 mg spermidine/kg bw/day) was used by Guo et al., to show that spermidine alleviates autoimmune encephalitis in mice (Guo et al., 2011). Besides the reported positive effects, no adverse effects were found after 25 days of spermidine administration.

Table 20. Animal studies involving spermidine supplementation

Reference	Animal species	Trial length	Spermidine in diet	Estimated spermidine intake/day*	Observed effects	Observed adverse effects
(LaRocca et al., 2013)	Male C57BL6 mice	4 weeks	Water supplemented with 3 mM spermidine	87 mg/kg-bw	Spermidine reversed age-induced arterial stiffness with a reduction in oxidative damage of endothelial cells in old mice; vascular health promoting	none
(Michiels et al., 2016)	Apolipoprotein E-deficient (ApoE(-/-)) mice	20 weeks	Western-type diet with 5 mM spermidine in the drinking water	145 mg/kg-bw	Spermidine alleviated formation of atherosclerotic plaques in apolipoprotein E–deficient (ApoE−/−) mice; vascular health promoting	none
(Eisenberg et al., 2016)	Aged wild-type C57BL/6J mice	about 6 months	Water supplemented with 3 mM spermidine	87 mg/kg-bw	Dietary spermidine protected from cardiac aging	none
(Guo et al., 2011)	Myelin oligodendrocyte glycoprotein-induced EAE mice	25 days	Water supplemented with 30 mM spermidine	870 mg/kg-bw	Spermidine attenuated disease progression and improves visual functions and decreased loss of retinal ganglion cells	none

(Yue et al., 2017)	Wild-type (MAP1S+/+) and MAP1S knockout mice (MAP1S−/−)	7 months	Water supplemented with 3 mM spermidine	87 mg/kg-bw	Dietary spermidine reduced the severity of liver fibrosis and the incidence of hepatocellular carcinomas induced by chemical insults	none

*Based on water intake information provided in (Eisenberg et al., 2016).

6.2.4. NOAEL from toxicological studies in animals

The concentrations of spermidine, spermine, putrescine and cadaverine in Spermidine rich wheat germ extract (SpermidineLife®) are comparable to those in many common foods (Table 21), whose spermidine concentrations were collected from different references to establish a polyamine food database (Ali et al., 2011a). This also includes the quantities, which would arise in connection with the consumption of stabilized wheat germ. Importantly, the estimated intake level of spermidine and other polyamines from spermidine-rich wheat germ extract are well below the NOAEL (No Observed Adverse Effect Level) for these substances. The NOAEL in rats for spermidine is 1000 ppm (83 mg/kg body weight/day) and 200 ppm (19 mg/kg body weight/day) for spermine (Til et al., 1997). The study by Til et al. analyzed acute and subacute toxicity of five biogenic amines: tyramine, spermidine, spermine, putrescine and cadaverine were investigated in 8-13 week old Wistar rats. The results were obtained from oral (via food) and intravenous spermidine and spermine administration at different doses, monitoring parameters such as organ weights, histopathological observation of several tissues, renal function, blood pressure, food and water intake, and several behavior-related phenotypes (Til et al., 1997). Considering a 100-fold safety factor, the NOAEL observed in rats corresponds to 0.83 mg/kg-bw/day of spermidine for humans (58.1 mg/day for a 70 kg person).

Thus, the resulting daily intake of maximum 12 mg spermidine per day from spermidine rich wheat germ extract is much lower than the estimated safe level for a person of 70 kg weight. Employing a scientifically accepted conversion factor based on body surface differences (Reagan-Shaw et al., 2008), 83 mg/kg-bw/day spermidine in mice corresponds to ~6.7 mg/kg-bw/day in humans. This equals ~470 mg/day for a 70 kg person and thus is approximately 50-fold higher than the maximum intake of spermidine (12 mg) from spermidine rich wheat germ extract.

Table 21. Mean spermidine content of various food products.

Food product	Mean spermidine content (mg/kg)	Mean spermidine content (mg/serving size*)
Wheat germ	500	12.5 (25 g)
SpermidineLife-containing food	87.5 (baked goods); 12.5 (fluid milk)	3.5 (40 g); 3.0 (240 ml)
Cheddar (aged 1 year)	199.5	19.5 (100 g)
Mushrooms	88.6	4.4 (50 g)
Peas (cooked)	65.2	9.1 (140 g)
Broccoli	41.3	4.2 (100 g)
Pear	52.8	6.6 (125 g)

** Serving size according to Ali et al., 2011a (except for wheat germ, which is obtained from average manufacture's indications)*

Similar calculations can be provided for spermine: The NOAEL observed during the *in vivo* toxicology study in rats (Til et al., 1997) corresponds to 0.19 mg/kg-bw/day of spermine for humans (13.3 mg/day for a 70 kg person). The maximum recommended intake of spermine from spermidine-rich wheat germ extract (6 mg per day) is below these safety limits. Again, based on the scientific conversion factor by Reagan-Shaw et al. (2008), 19 mg/kg-bw/day spermine in mice would conform to ~1.52 mg/kg-bw/day in humans. This equals ~106 mg/day for a 70 kg person and is more than 10x higher than the maximum intake through products derived from spermidine-rich wheat germ extract.

For the amines cadaverin and putrescine, NOAEL in Wistar rats was 180 mg/kg-bw/day for both putrescin and cadaverin and therefore considerably higher than that of the polyamines spermidine and spermine (Til et al., 1997). Since the concentrations of both amines (putrescine and cadaverin) in spermidine-rich wheat germ extract or products derived thereof are much lower than that of the polyamines spermidine and spermine, adverse effects by these amines are highly unlikely. Again, comparable or higher amounts of these amines are found in several foods of human nutrition (Ali et al., 2011a, Nishimura et al., 2006).

Interestingly, the potential toxicity of polyamines has also been investigated in an *in vitro* study employing human intestinal cell cultures (del Rio et al., 2019). The authors of this study conclude that the polyamine concentrations found in typical food items are much lower than the lowest concentration of spermine or spermidine found to be cytotoxic for the intestinal cell cultures (LOAEL=10 mM, equivalent to 1452.50 mg/kg for spermidine; LOAEL=3.23 mM, equivalent to 653.56 mg/kg for spermine). Given the equivalence of polyamine concentrations in foods produced from spermidine-rich wheat germ extract to other spermidine-rich food items (Table 21), also foods produced from spermidine-rich wheat germ extract can be considered safe.

The concentration of histamine in the extract is below the sensitivity limit of the commercially available histamine assays (Ultrasensitive Histamin ELISA assay, Abcam). These results are further supported by the fact that wheat products are described as low-histamine and are included on the list of allowed foods for people who suffer from histamine intolerance.

The extract is obtained from wheat products and therefore contains gluten. People who suffer from gluten intolerance, coeliac disease or wheat intolerance should therefore avoid the product. Consumers who suffer from these conditions are adequately informed by the name of the product and the ingredient 'spermidine rich wheat germ extract' stated on the label of produced foods.

6.2.5. Safety issues on polyamine catabolism

6.2.5.1. Toxicity of DAO products

Diamine oxidase (DAO, histaminase) is responsible for breaking down histamine. This biogenic amine is responsible for the transduction of inflammatory signals in the body and plays a decisive role in allergies and in acute and chronic inflammation. Inhibition of this enzyme, or competitive inhibition of it by other diamines, leads to the accumulation of histamine, which can give rise to the symptoms of histamine intolerance. According to the International Society of DAO Deficiency, putrescine and cadaverine can be competitively broken down by diamine oxidase. *In vitro* enzyme activity experiments with human DAO have shown that the same is not true of spermidine or spermine (see Conferencia Déficit DAO, 2015 - *http://www.deficitdao.org/en/dao-deficiency/histamine/food-which-interferes-in-histamine-metabolism/food-rich-in-other-amines/*; information retrieved on May 20th, 2019). Therefore, toxic byproducts of metabolizing spermidine by DAO is highly unlikely, because it shows poor activity toward spermidine. Spermidine-rich wheat germ extract (SpermidineLife®) is therefore strictly controlled to contain low levels of putrescine and cadaverine (see specifications at Table 3).

DAO metabolizes mainly putrescine to form the reactive aldehyde 4-aminobutanal, but it is limited to exert any potential toxic effects due to its immediate cyclization to Δ1-pyrroline (Pegg, 2013).

6.2.5.2. Toxicity of Acrolein

Acrolein is a ubiquitously occurring dietary and environmental pollutant, which can also be produced endogenously by lipid peroxidation, anti-cancer drugs, or by catabolism of amino acids and polyamines (Moghe et al., 2015). As a highly reactive aldehyde, acrolein is seen as the key toxic compound produced from spermine and spermidine by different amine oxidases, but it remains unknown to which extent the conversion of spermidine and spermine to acrolein occurs, and to which extend the endogenously formation of acrolein is relevant compared to dietary intake and respiratory inhalation (Abraham et al., 2011, Moghe et al., 2015, Pegg, 2013, Sakata et al., 2003). Endogenously, acrolein is mainly produced from spermine by the enzyme spermine oxidase (SMO), and less effectively from spermidine by the enzyme acetylpolyamine oxidase (AcPAO), the other main cellular polyamine oxidase (Igarashi et al., 2018, Pegg, 2013, Saiki et al., 2011, Uemura et al., 2016). Additionally, spermine, when administered parenterally, seems to be about 20 times more nephrotoxic than spermidine in healthy animals (Tabor and Rosenthal, 1956). Therefore, recent studies focused on spermine as main contributor to acrolein formation, rather than spermidine.

Acrolein has shown to play a role in renal failure (Sakata et al., 2003), brain infarction (Saiki et al., 2011) and other pathologies involving cell damage. In healthy cells, spermidine and spermine mainly exist as a complex with RNA, predominantly on ribosomes (Igarashi et al., 2018) and not as free form, therefore acrolein cannot be effectively produced. In injured cells during brain infarction, accumulated hydroxyl radicals and Ca^{2+} ions are responsible for the release of spermine and further for the production of acrolein (Igarashi et al., 2018, Saiki et al., 2011). In patients suffering from renal failure, the production of acrolein is a common feature but irrespective of the original disease (Sakata et al., 2003). In summary, results from various studies suggest that endogenous production of acrolein is especially relevant in patients suffering from renal failure, uremia and brain infarction, but irrelevant in healthy cells. It remains unknown if or how much dietary polyamines contribute to endogenous acrolein production, especially in such patients. *"However, acrolein is not effectively produced under normal conditions, likely because polyamines mainly exist as a RNA–polyamine complex, not as a free form. We hypothesized that acrolein is effectively produced when cells are damaged, so that acrolein may become a good biochemical marker for pathologies involving cell damage."* (Igarashi and Kashiwagi, 2010).

Irrespective of the lack of scientific data on the precise amounts of acrolein produced in the human body from dietary polyamines, considering the NOAEL of spermidine and spermine from animal studies (see below) and the fact that the resulting maximum intake from the proposed uses of SpermidineLife® contains less spermidine and spermine than present in the recommended daily amounts of wheat germ (generally considered as a healthy and safe food item), it is highly unlikely that polyamine catabolism from the spermidine-rich wheat germ extract reaches problematic acrolein levels in humans.

6.2.6. Benzoxazinones

Benzoxazinones, especially dihydroxy-7-methoxy-1,2-benzoxazin-3-one [sic] (DIMBOA) and 2,4-dihydroxy-1,4-benzoxazin-3-one (DIBOA), are produced only during the germination of species of the *Gramineae* or *Poaceae* family, including in the case of common wheat (*Triticum aestivum*) . Only wheat germ which is not germinating (and not wheat germ sprouts) is used as raw material for the production of 'spermidine-rich wheat germ extract'. There is thus no possibility of DIMBOA and DIBOA being produced or accumulating.

6.2.7. Polyamines and cancer

Polyamines are essential in cell growth and proliferation, which raises the question of their potential involvement in cancer initiation and progression. Up to date, there is no direct evidence that polyamines can initiate cancer. For example, Soda et al. and Eisenberg et al., (Eisenberg et al., 2016, Soda et al., 2009a) reported no increase in oncogenic transformation in healthy wild-type mice fed a high polyamine diet.

Although not able to initiate cancer, polyamines are potentially involved in accelerating growth in preexisting tumors. Cancerous cells of various tissues show elevated levels of polyamines, suggesting their involvement in cancer (Wallace and Caslake, 2001). Accordingly, several animal studies showed a significant inhibition of tumor growth by feeding a polyamine

reduced diet with additional inhibitors of polyamine production, for example for DFMO as an inhibitor of ODC (ornithine decarboxylase) (Chamaillard et al., 1997, Seiler et al., 1990). While showing promising results in mouse models, clinical trials with the use of DFMO, whether alone or in combination with other inhibitors, failed to prove efficacy in humans (Miller-Fleming et al., 2015), which complicates the involvement of polyamines in cancer in humans. In contrast to these results, supplementation of spermidine can reduce tumorigenesis through induction of autophagy in healthy cells (Madeo et al., 2018) and reduced the tumor growth of transplantable tumors in mice (Pietrocola et al., 2016a, Pietrocola et al., 2016b). These tumor-protective effects are attributed to its function as autophagy inducer (Morselli et al., 2011), whereas in tumor tissue, spermidine favors autophagy-dependent release of ATP, which in turn favors immunosurveillance. Altogether, results indicate that polyamines do not trigger cancer (Kalac, 2014) and spermidine even exerts positive effects towards reduced tumorigenesis and growth.

Finally, epidemiological studies corroborate the protective effects of spermidine against cancer-associated death. Nutrition rich in spermidine (> 12 mg/day) resulted in significantly reduced cancer-related death and lower overall mortality rates in humans compared to low spermidine nutrition. Similar results were observed for spermine. This reduction in mortality risk was comparable to that associated with a 5.7 years younger age (Kiechl et al., 2018).

Moreover, one large-scale prospective study yielded preliminary evidence for an inverse association between high dietary polyamine intake and risk of colorectal cancer in overweight women (Vargas et al., 2015).

Overall, there is no convincing evidence for tumor-promoting effects of a moderate intake of spermidine in experimental and epidemiological studies (but rather the opposite).

6.2.8. Safety of wheat germ lectins

Lectins are present in most plants and play a role in protection against pathogens, like yeast, insects and bacteria. Many scientifically unsubstantiated assumptions cast a bad light on lectins. Specifically, the lectin wheat germ agglutinin (WGA) has been studied and is proposed of having adverse health effects by binding to the epithelium in the gut, damaging the cells and reducing nutrient-uptake. Additionally, WGA is able to block glucose- and insulin-receptors which contributes to celiac disease and the growth of harmful bacteria (van Buul and Brouns, 2014). Despite that, there are no *in vivo* studies in humans assessing the potential negative health effects of WGA. On contrary, the consumption of whole grain products containing WGA has been reported to result in a significant reduction in the incidence of type 2 diabetes, heart diseases, some types of cancer and weight gain (van Buul and Brouns, 2014). A recent study in mice even showed a potential improvement of immune function after feeding with WGA (Yun et al., 2018). **In conclusion, there is no scientific evidence at present that raises concerns for consumption of WGA in humans.**

6.3. Expert Panel Review, Summary and Discussion

TLL The Longevity Labs GmbH (TLL) intends to use spermidine rich wheat germ extract (SpermidineLife®) at levels up to 2.7 g/serving (reference amounts customarily consumed, 21 CFR 101.12) in selected food categories such as baked goods and yogurt. The product is a light beige to yellowish powder with a grainy odour and nutty and sweet to lemony taste. The wheat germ used as a raw material for the production of the spermidine rich wheat germ extract (SpermidineLife®) is obtained from Good Mills Austria GmbH, HOCHDORF Swiss Nutrition Ltd or similar manufactures and is prepared observing the IFS (International Food Standard) and HACCP plans for continuous quality controls. It is manufactured at a facility according to HACCP and ISO 22000 standards. The intended use of spermidine rich wheat germ extract (SpermidineLife®) will result in mean and 90th percentile (maximum) intake of 4.75 and 9.50 g/person/day. The corresponding mean and 90th percentile intake of spermidine from the proposed uses will be 6.16 and 12.33 mg/person/day. For safety assessment purpose high levels of 12.33 mg spermidine/person/day is considered. Given the variation in spermidine levels, the use levels of the extract in foods will be adjusted such that the spermidine intake will not exceed 12.33 mg/day.

Wheat has been consumed since about 10,000 years, whereas the processing and application of wheat germ as food has only been recorded since the last century. Wheat germ has been consumed for decades in food to maintain good health with no published evidence of safety concerns associated with its use. Wheat germ and wheat germ products (e.g. wheat germ oil, defatted wheat germ, fermented wheat germ) have been consumed in many countries, including the United States as food product or dietary supplement. Wheat germ is foodstuff and listed in the USDA's inventory of grains used as food sources.

The available safety related studies indicate that spermidine rich wheat germ extract (SpermidineLife®) is safe and well tolerated in older adults and mice (Schwarz et al., 2018). In mice, a dosage of 50 g/kg-bw/day extract, corresponding to 60 mg spermidine/kg-bw/day, was applied and considered as safe (Schwarz et al., 2018) and is in line with previous reports on the NOAEL of spermidine and other polyamines (Til et al., 1997). Using scientific conversion factors based on body surface area calculations (Reagan-Shaw et al., 2008) this amount corresponds to 4.05 g/kg-bw/day of the extract or 4.86 mg/kg-bw/day of spermidine in humans (~280 g extract or 340 mg spermidine for a 70 kg person per day). Even applying 100-fold safety factor yields amounts (35 g extract or 42 mg spermidine for a 70 kg person per day), the resulting intake from the proposed uses of the extract is clearly below the maximum recommended amount of spermidine rich wheat germ extract ($\leq$ 9.5 g) and that of spermidine ($\leq$ 12 mg).

The safety of spermidine rich wheat germ extract (SpermidineLife®) can also be extrapolated from the safe use of wheat germ and wheat germ products, also because spermidine rich wheat germ extract (SpermidineLife®) contains no more but less than amounts of wheat germ generally considered as safe. The maximum recommended daily amount of spermidine rich wheat germ extract (SpermidineLife®) is equivalent to 24 g or 3 ½ tablespoons of stabilized wheat germ, whereas some manufacturers and seller of wheat germ (e.g. VollGran) recommend up to 100 g of wheat germ per day, which corresponds to about 50 mg of spermidine. Additionally, recommended healthy diets, such as the Mediterranean diet, consist of about 26

mg spermidine/day (Ali et al., 2011a), Thus the proposed daily intake amount of spermidine rich wheat germ extract (SpermidineLife®) equivalent to 12 mg spermidine is well below the levels known from a typical healthy nutrition.

There is sufficient qualitative and quantitative scientific information to determine the safety-in-use of spermidine rich wheat germ extract (SpermidineLife®) for its proposed uses. The GRAS status of spermidine rich wheat germ extract (SpermidineLife®) for its intended use in food is supported by:

- Wheat is known as an "ancient grain," that has been consumed by humans for thousands of years with no known significant adverse effects.
- Wheat is a valuable food source which has a reputation of a "complete food".
- Wheat germ is used extensively as a food product with no safety concerns.
- Wheat germ contains high amounts of Vitamin E, minerals, fiber and high-quality protein.
- High spermidine content as in wheat germ or spermidine rich wheat germ extract (SpermidineLife®) is part of a typical healthy and safe diet as the Mediterranean diet.
- Spermidine rich wheat germ extract (SpermidineLife®) is manufactured at facility operating according to HACCP and ISO 22000 standards.
- The safety of spermidine rich wheat germ extract (SpermidineLife®) for the intended use in food at levels resulting in daily intake of up to 9.5 g/person/day equivalent to maximum 12 mg spermidine/person/day is supported by recommendations of wheat germ manufacturers and sellers of intake of wheat germ equivalent to 50 mg spermidine per person per day and the high spermidine levels of established healthy diets without observing any adverse effects.
- The recommended daily intake of maximum 12 mg spermidine per day by ingesting spermidine rich wheat germ extract (SpermidineLife®) is lower by a factor of ~15 than the NOAEL estimated for a person of 70 kg weight.

In summary, the cumulative scientific information on spermidine rich wheat germ extract (SpermidineLife®) – specifically considering the human experiences and associated testing, anticipated human consumption levels, and germane supporting information – provides the basis for the conclusion that daily exposure of spermidine rich wheat germ extract (SpermidineLife®) at levels equivalent to maximum 12 mg spermidine is safe. The proposed uses are compatible with current regulations, i.e., spermidine rich wheat germ extract (SpermidineLife®) is used as a food nutrient in a limited number of foods when not otherwise precluded by a Standard of Identity, and is produced at facility operating according to HACCP and ISO 22000 standards.

6.4. Expert Panel Conclusion

Based on a critical evaluation of the publicly available data, summarized above, the Expert Panel members whose signatures appear below, have individually and collectively concluded that spermidine rich wheat germ extract (SpermidineLife®), meeting the specifications cited above, and when used as a nutrient [21 CFR 170.3(o)(20)] at levels up to 2.7 g/serving (reference amounts customarily consumed, 21 CFR 101.12) in selected food categories such as baked goods and yogurt, when not otherwise precluded by a Standard of Identity, and resulting in the 90th percentile estimated intake of 9.50 g/person/day (spermidine intake of 12.33 mg/person/day) is safe and GRAS.

It is also our opinion that other qualified and competent scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion. Therefore, we have also concluded that when used as described, spermidine rich wheat germ extract (SpermidineLife®) is GRAS based on scientific procedures.

Signatures

[redacted]

Lorenzo Galluzzi, Ph.D. — July 9, 2019 Date

[redacted]

Guido Kroemer, M.D., Ph.D. — July 10, 2019 Date

[redacted]

Valter Longo, Ph.D. — July 10, 2019 Date

[redacted]

Madhusudan G. Soni, Ph.D., F.A.C.N., F.A.T.S. — July 11, 2019 Date

7. Part 7 – SUPPORTING DATA AND INFORMATION

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GRAS Notification for spermidine rich wheat germ extract (SpermidineLife®)

TLL The Longevity Labs, GmbH, Austria

Appendix I:

SpermidineLife ® Specifications (TLL)

Cover page + 2 pages

Longevity Labs

IT'S NATURAL TO BE HEALTHY.

Specification of „spermidine-rich wheat germ extract" of *TLL The Longevity Labs GmbH*

(current brand name **SPERMIDINE**LIFE®)

Product description

- Spermidine-rich wheat germ extract
- Current brand name: **SPERMIDINE**LIFE®
- Botanical source: Triticum aestivum
- Botanical family: Poaceae
- Plant part used: wheat germ

Composition of product

- Spermidine-rich wheat germ extract
- Purely herbal. Lactose-free. No added sugar or artificial colorings. Contains gluten.
- Free of synthetic spermidine

Recommended use levels:

- For use as a food or beverage ingredient.
- Maximum recommended daily intake: 2 g (equivalent to max. 12 mg spermidine)

Active ingredients and limits:

Substance	Value
Spermidine	≤ 6 mg/g
Spermine	≤ 3 mg/g
Putrescine	< 1.2 mg/g
Cadaverine	< 0.1 mg/g
Mycotoxins	
Aflatoxins	< 0.4 µg/kg
Deoxynivalenol	< 500 µg/kg
Microbiology	
Total aerobic bacteria	< 10 000 CFU/g
Yeast and moulds	< 100 CFU/g
Escherichia coli	< 10 CFU/g
Salmonella spp.	negative/25g
Listeria monocytogenes	negative/25g
Metals	
Pb	< 1 mg/kg
Cd	< 1 mg/kg
Hg	< 0.1 mg/kg
As	< 0.2 mg/kg

Sensory parameter

- Color: white – yellowish (depending on raw material)
- Odor: inconspicuous / typical of grain
- Flavor: Sweetish/sourish to lemony

Physical parameter

- Particle size: < 1mm, microporous structure of lyophilisation
- Bulk density: not shaked approx. 380 g/ltr
- Water solubility: well solvable in cold and warm water (by stiring)

Storage conditions

- Minimum durability: 18 months
- Storage conditions: to be stored in a dry place, protected from heat and light

Allergens

- Grain containing gluten
- Wheat

GRAS Notification for spermidine rich wheat germ extract (SpermidineLife®)

TLL The Longevity Labs, GmbH, Austria

Appendix II:

Wheat Germ Specifications (HOCHDORF)

Cover page + 6 pages

HOCHDORF
BEST PARTNER

Product Specification

VIOGERM® Gold Grains

Wheat Germ

Art.-No. 13155

The client agrees to treat this information confidentially

Ingredients

Wheat germ (Switzerland, EU, North America).

Nutritional Values (analysed average values)

Description	Unit	per 100 g	Tolerances per 100 g	
			min.	max.
Energy	kJ	1561	1326	1795
	kcal	371	315	427
Fat	g	7.0	5.5	8.5
- saturated FA	g	1.2	0.6	1.8
- monounsaturated FA	g	1.4	0.7	2.1
- polyunsaturated FA	g	3.7	2.9	4.5
Carbohydrates	g	38	32	44
- Sugars	g	12	9.4	14
- Starch	g	18	14	22
Fibres	g	14	11	18
Protein (N x 6.25)	g	32	26	38
Salt	g	0.01		0.05

Product Specification
VIOGERM® Gold Grains
13155

Description	Unit	per 100 g*	Tolerances per 100 g		NRV
			min.	max.	
Vitamins and other functional ingredients					
- Vitamin E	mg	12	8.7	16	100%
- Vitamin B1	µg	1900	1300	2500	173%
- Vitamin B2	µg	500	350	650	36%
- Vitamin B6	µg	1200	830	1500	86%
- Niacin	µg	3000	2100	3900	19%
- Folate	µg	174	122	226	87%
Minerals					
- Magnesium	mg	262	183	380	70%
- Potassium	mg	1150	804	1670	58%
- Phosphorous	mg	1220	855	1770	174%
- Iron	mg	7.2	5.0	10	51%
- Zinc	mg	12	8.2	17	120%

*subject to natural fluctuations

Sensoric parameters

Appearance	Beige-coloured to light brown
Odour	Cereal
Taste	Nutty, cereals
Texture	Granulate, free flowing

Microbiology*

Description	Unit	Limits	Methods
total plate count	CFU/g	10000	ISO 4833
Salmonella spp.	absence in [g]	5x25g	ISO 6579 modif.
Enterobacteriaceae	CFU/g	100	ISO 21528-2
Staphylococci (coag. pos.)	CFU/g	100	EN/ISO 6888-2
Bacillus cereus	CFU/g	1000	ISO 7932

* Monitoring

Physical / chemical Parameters

Description	Unit	Typical Values	Tolerances	Methods
Water content	%	4.5	2.7-6.3	SLMB 2003, gravimetric

Granulation	mm	0.8-2.0	min. 80%	DIN 66165
Bulk density	g/l	540	520-580	IDF 134A

GMO

Delivered product is not won from any main- or preliminary state of genetically altered raw products or bacterial cultures. No genetically altered hereditary matter is contained. No enzymes or other biotechnological substances derived from GMO's employed for the production. No declaration of the raw product with GMO in accordance with Swiss GMO-directives and EC-Regulation EC 1829/2003 and 1830/2003 is required.

Ionising Rays

The product or its ingredients did not undergo a treatment with ionising rays.

Allergens

Description	Limits in mg/kg based on CH-Reg. LKV, Art. 8	Direct processing		Possible cross-contaminations can be excluded
		Yes	No	Yes
Grain products (derivatives)(1)	200	[x]	[ ]	[ ]
Milk (derivatives)	1000	[ ]	[x]	[x]
Egg (derivatives)	1000	[ ]	[x]	[x]
Fish (derivatives)	1000	[ ]	[x]	[x]
Crustacea (derivatives)	1000	[ ]	[x]	[x]
Soy beans (derivatives)	1000	[ ]	[x]	[x]
Nuts (2)	1000	[ ]	[x]	[x]
Sesame seeds (derivatives)	1000	[ ]	[x]	[x]
Celery (derivatives)	1000	[ ]	[x]	[x]
Mustard (derivatives)	1000	[ ]	[x]	[x]
Mollusca (derivatives)	1000	[ ]	[x]	[x]
Lupines (derivatives)	1000	[ ]	[x]	[x]
Sulphides	10	[ ]	[x]	[x]

(1) Wheat, rye, barley, oats, spelt, kamut or their hybridised strains - Gluten max. 200 mg per kg food.

(2) Peanuts, walnuts, cashew nuts, hazelnuts, macadamia nuts, almond nuts, para nuts, pecan nuts, pistachio nuts.

The risk of an cross contamination is controlled	yes ☒	no ☐

Quality management system

Description	Yes	No
Quality management system according to norm ISO 9001:2008 available	☒	☐
Technical GFSI-Standard according BRC (British Retail Consortium) fulfilled	☒	☐
Hygienic directives according Swiss hygienic regulations resp. EC 852/2004 and 853/2004 fulfilled	☒	☐
Traceability according to Swiss and EC-regulation (178/2002, art. 18) fulfilled	☒	☐
HACCP and preventive programs to avoid hygienic problems and any contamination exist.	☒	☐
For the manufacturing of the product in-/online checks as well as end production checks are carried out	☒	☐
Certificate with analyses values and quality parameters, based on the indications of this specification is possible (per order of CHF 5000.- or more of good value).	☒	☐

Shelf life/ Storage

Shelf life from production	365 days
Storage conditions	≤23 °C / < 65% rel. humidity, in the unopened original packing

Package size

Art.- no. 13155104	Bag of 5 kg
Art.- no. 13155109	Bag of 10 kg
Art.- no. 13155119	Bag of 20 kg
Art.- no. 13155124	Bag of 25 kg
Art.- no. 13155381	Sprinkler of 135 g
Art.- no. 13155404	Cardboard box of 250 g
Art.- no. 13155840	Big bag of 500 kg

Details about country of origin, producer and registration

Country of production	Switzerland
Customs tariff no. CH	1104.3089
Customs tariff no. EU	
Compliance	Regulation (EC) 1881/2006 and ist updates for setting maximum levels for certain contaminants in foodstuffs Regulation (EC) No 396/2005 and ist updates on maximum residue levels of pesticides
Confirmation	The companies of the HOCHDORF-Group are licensed for food processing and trading of food. HOCHDORF Swiss Nutrition AG is qualified for GFSI-Standard and the factories are regularly inspected by the official food control and BRC-auditors. The delivered merchandise fully complies with the requirements of EC and Swiss Food Regulations, especially regarding traceability, hygiene, allergens as well as regarding other residues and foreign matters. In the production, neither raw material of genetically modified origin nor raw materials that were treated with gamma-rays are used. The responsibility of the legal compliance of the product rests with the customer.
Address	HOCHDORF Swiss Nutrition Ltd Siedereistrasse 9 CH-6280 Hochdorf LU Tel +41 41 914 65 65 Fax +41 41 914 67 00 cereals@hochdorf.com www.hochdorf.com

GRAS Notification for spermidine rich wheat germ extract (SpermidineLife®)

TLL The Longevity Labs, GmbH, Austria

Appendix III:

EFSA Approval of Spermidine-Rich Wheat Germ Extract

Cover page + 3 pages

COMMISSION IMPLEMENTING REGULATION (EU) 2017/2470

of 20 December 2017

establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001 [1], and in particular Article 8 thereof,

Whereas:

(1) Regulation (EU) 2015/2283 lays down rules for the placing on the market and use of novel foods within the Union.

(2) Pursuant to Article 8 of Regulation (EU) 2015/2283, the Commission has to establish the Union list of novel foods authorised or notified under Regulation (EC) No 258/97 of the European Parliament and of the Council [2].

(3) The Union list of novel foods is to apply without prejudice to other provisions laid down in sector specific legislation.

(4) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

Union list of authorised novel foods

The Union list of novel foods authorised to be placed on the market within the Union as referred to in Article 6(1) of Regulation (EU) 2015/2283 is hereby established and set out in the Annex to this Regulation.

Article 2

This Regulation shall enter into force on the twentieth day following that of its publication in the Official Journal of the European Union.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 20 December 2017.

For the Commission

The President

Jean-Claude JUNCKER

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[1] OJ L 327, 11.12.2015, p. 1.

[2] Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients (OJ L 43, 14.2.1997, p. 1).

ANNEX

UNION LIST OF NOVEL FOODS

Content of the list

1. The Union list shall consist of Tables 1 and 2.

2. Table 1 includes the authorised novel foods and contains the following information:

Column 1: Authorised novel food

Column 2: Conditions under which the novel food may be used. This column is further subdivided into two: Specified food category and Maximum levels

Column 3: Additional specific labelling requirements

Column 4: Other requirements

3. Table 2 includes the specifications on novel foods and contains the following information:

Column 1: Authorised novel food

Column 2: Specifications

Authorised novel food	Conditions under which the novel food may be used		Additional specific labelling requirements	Other requirements
	Specified food category	*Maximum levels of DHA*		
	Bakery products (breads, rolls and, sweet biscuits)	200 mg/100 g		
	Cereal bars	500 mg/100 g		
	Cooking fats	360 mg/100 g		
	Non-alcoholic beverages (including dairy analogue and milk-based drinks)	80 mg/100 ml		
	Infant formula and follow-on formula as defined in Regulation (EU) No 609/2013	In accordance with Regulation (EU) No 609/2013		
	Processed cereal-based foods and baby foods for infants and young children as defined in Regulation (EU) No 609/2013	200 mg/100 g		
Fermented soybean extract	*Specified food category*	*Maximum levels*	1. The designation of the novel food on the labelling of the foodstuffs containing it shall be 'Fermented soybean extract'. 2. The labelling of food supplements containing fermented soybean extract shall bear a statement that persons taking medication should only consume the product under medical supervision.	
	Food Supplements as defined in Directive 2002/46/EC (capsules, tablets or powder form) intended for the adult population, excluding pregnant and lactating women	100 mg/day		
Spermidine-rich wheat germ extract (*Triticum aestivum*)	*Specified food category*	*Maximum levels*	The designation of the novel food on the labelling of the food supplements containing it shall be 'spermidine-rich wheat germ extract'	
	Food Supplements as defined in Directive 2002/46/EC intended for the adult population	Equivalent of max. 6 mg/day spermidine		

GRAS Notification for spermidine rich wheat germ extract (SpermidineLife®)

TLL The Longevity Labs, GmbH, Austria

Appendix IV:

Analytical Results of SpermidineLife ®
(EUROFINS ANALYTIK)

Cover page + 19 pages

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ÖSTERREICH

Person in charge Mrs N. Heckert - 1704
Client support Mrs N. Heckert - 1704

Report date 17.07.2018

Analytical report AR-17-JK-075623-02

This report replaces report number: AR-17-JK-075623-01

Sample Code 703-2017-00670869

Reference	Wheat germ extract [redacted]
Nr. of sample containers	2
Gross weight / volume	897,79 g
Reception temperature	room temperature
Ordered by	[redacted]
Submitted by	
Sender	Bote
Packaging	plastic bag
Reception date time	09.06.2017
Start/end of analyses	09.06.2017 / 04.07.2017

TEST RESULTS

Physical-chemical Analysis

JK09M	**Water content**		
Method :	Internal method, , Gravimetry		
Water content		2.7	g/100 g
JK09N	**Ash**		
Method :	Internal method, , Gravimetry		
Ash		7.8	g/100 g
JK09Q	**Raw protein**		
Method :	Internal method, , Kjeldahl (titrimetry)		
Nitrogen		4.1	g/100 g
Protein (Nx6,25)		25.8	g/100 g
JK09R	**Fat total**		
Method :	Internal method, , Gravimetry		
Fat, total		6.8	g/100 g
JK09T	**Fatty acid profile**		
Method :	Internal method, , GC-FID		
C 4:0 (Butyric Acid)		<0.1	* %
C 6:0 (Caproic acid)		<0.1	* %
C 8:0 (Caprylic acid)		<0.1	* %
C 10:0 (Capric acid)		<0.1	* %
C 10:1 (Decenic acid) + isomeres		<0.1	* %
C 12:0 (Lauric acid)		<0.1	* %
C 14:0 (Myristic acid)		0.1	%

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Analytical report AR-17-JK-075623-02
Sample Code 703-2017-00670869

This report replaces report number: AR-17-JK-075623-01

C 14:1 (Myristoleic acid) + isomeres	<0.1	*	%
C 15:0 (Pentadecanic acid)	<0.1	*	%
C 15:1 (Pentadecenoic acid) + Isomers	<0.1	*	%
C 16:0 (Palmitic acid)	18.6		%
C 16:1 (Palmitoleic acid) + isomeres	0.2		%
C 17:0 (Margaric acid)	<0.1	*	%
C 17:1 (Heptadecenoic acid) + isomers	<0.1	*	%
C 18:0 (Stearic acid)	0.9		%
C 18:1-9 (Oleic acid)	15.3		%
C 18:1-11 (cis-Vaccenic acid)	1.4		%
C 18:1-13 (13-oleic acid)	<0.1	*	%
C 18:1 (trans) Elaidic acid	<0.1	*	%
C 18:2 (Linoleic acid)	54.0		%
C 18:2 (trans/trans)	<0.1	*	%
C 18:2 (cis/trans)	0.1		%
C 18:2 (trans/cis)	<0.1	*	%
C 18:3 (alpha-linolenic acid)	6.2		%
C 18:3 (gamma-linolenic acid)	<0.1	*	%
C 18:3 (trans/cis/trans)	<0.1	*	%
C 18:3 (cis/cis/trans)	<0.1	*	%
C 18:3 (cis/trans/cis)	<0.1	*	%
C 18:3 (trans/cis/cis)	<0.1	*	%
C 18:4 (Octadecatetraenic acid)	<0.1	*	%
C 20:0 (Arachidic acid)	0.2		%
C 20:1 (Eicosenoic acid) + isomers	1.4		%
C 20:2 (Eicosodienoic acid) + isomeres	0.2		%
C 20:3 (Eicosatrienoic acid)	<0.1	*	%
C 20:4 (Arachidonic acid)	<0.1	*	%
C 20:5 (Eicosapentaenic acid)	<0.1	*	%
C 22:0 (Behenic acid)	0.2		%
C 22:1 (Docosenic acid) + isomers	0.3		%
C 22:2 (Docosadienoic acid) + isomeres	<0.1	*	%
C 22:5 (Docosapentaenic acid)	<0.1	*	%
C 22:6 (Docosahexaenic acid)	<0.1	*	%
C 23:0 (Tricosanoic acid)	<0.1	*	%
C 24:0 (Lignoceric acid)	0.2		%
C 24:1 (Tetracosenoic acid) + isomeres	0.2		%
saturated fatty acids total	20.3		%
mono-unsaturated fatty acids total	18.8		%
poly-unsaturated fatty acids total	60.4		%
Trans-fatty acids total	0.4		%
others	0.1		%

J3083 Total dietary fibre (#)

Method : § 64 LFGB L 00.00-18, mod., PV 00303, Gravimetry

Total dietary fibre	2.67		g/100 g

JK09S Sugar profile

Method : Internal method, , LC-RI

Fructose	1.2		g/100 g
Glucose	1.0		g/100 g
Sucrose	23.8		g/100 g
Maltose	<0.5	*	g/100 g
Lactose	<0.5	*	g/100 g
Total sugars (calculated)	26.0		g/100 g

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Analytical report AR-17-JK-075623-02
Sample Code 703-2017-00670869

This report replaces report number: AR-17-JK-075623-01

JK09U	**Sodium**		
Method :	§ 64 LFGB L 07.00-56, mod., , F-AES		
(Modification: Applicable to all food and feed matrices)			
Sodium (Na)		160	mg/kg
JJL2E	**Carbohydrates calculated (difference)**		
Method :	, Calculation		
Carbohydrate calculated (difference)		54.2	g/100 g
JKB7S	**Nutrient value in 100 g**		
Method :	according to regulation 1169/2011, , Calculation		
Energy		1633	kJ
Energy		387	kcal
Fat		6.8	g
of which saturates		1.4	g
Carbohydrate		54.2	g
of which sugars		26.0	g
Protein		25.8	g
Salt		0.04	g
DJ011	**Cystine, methionine (oxidative)**		
Method :	EU 152/2009 (F), ISO 13903:2005, , IC-UV		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Cystein +Cystine		0.475	g/100 g
Methionine		0.408	g/100 g
DI004	**Amino acids (acid hydrolysis)**		
Method :	EU 152/2009 (F), ISO 13903:2005, AMSUR, IC-UV		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Alanine		1.56	g/100 g
Aspartic acid		2.40	g/100 g
Arginine		2.04	g/100 g
Glutamic acid		3.14	g/100 g
Glycine		1.44	g/100 g
Histidine		0.591	g/100 g
Isoleucine		0.624	g/100 g
Leucine		1.18	g/100 g
Lysine		1.38	g/100 g
Phenylalanine		0.580	g/100 g
Proline		0.941	g/100 g
Serine		0.949	g/100 g
Tyrosine		0.594	g/100 g
Valine		1.05	g/100 g
Threonine		1.06	g/100 g
Hydroxyproline		<0.05 (LOQ)	g/100 g
Ornithine		<0.05 (LOQ)	g/100 g
DJ009	**Tryptophane**		
Method :	EU 152/2009, , IC-UV		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Tryptophan (Total)		0.249	g/100 g
A7273	**Vitamin B1 - Thiamine base**		
Method :	EN 14122:2003, mod., , LC-FLD		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Thiamine (vitamin B1)		3.05	mg/100 g
A7289	**Vitamin B12, microbiological**		
Method :	AOAC 952.20, , Nephelometry		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Vitamin B12 (cyanocobalamin)		0.0354	µg/100 g

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Analytical report AR-17-JK-075623-02
Sample Code 703-2017-00670869

This report replaces report number: AR-17-JK-075623-01

A7274 Vitamin B2 - riboflavin
Method : EN 14152:2003, mod., 852, LC-FLD
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.

Riboflavin (vitamin B2)	0.657		mg/100 g

DJB05 Vitamin B3 (Total Niacin) EN-HPLC
Method : EN 15652:2009, , LC-FLD
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.

Niacin (vitamin B3)	3.97		mg/100 g

A7251 Vitamin B6
Method : EN 14164, , LC-FLD
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.

Pyridoxine (vitamin B6)	0.834		mg/100 g

A7284 Vitamin B8 - biotin, microbiological
Method : analog. to FDA method, LST AB 266.1,1995, 866, Nephelometry
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.

Biotin (vitamin B8)	22.1		µg/100 g

A7286 Vitamin B9 - Total folate, microbiological
Method : NMKL 111:1985, 870, Nephelometry
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.

Folate (vitamin B9)	438		µg/100 g

A7291 Vitamin C (Ascorbic acid + dehydroascorbic acid)
Method : Food Chemistry, 94 626-631, , LC-DAD
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.

Ascorbic acid (vitamin C)	1710		mg/100 g

J8306 Lead (Pb)
Method : DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Lead (Pb)	0.41		mg/kg

J8308 Cadmium (Cd)
Method : DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Cadmium (Cd)	0.09		mg/kg

JCHG2 Mercury (Hg)
Method : DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Mercury (Hg)	<0.005	*	mg/kg

J8312 Arsenic (As)
Method : DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Arsenic (As)	<0.1	*	mg/kg

GFL05 Dioxins and Furans (17 PCDD/F)
Method : Internal, GLS DF 110, GC-MS/MS
Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.

2,3,7,8-TetraCDD	< 0.0123	pg/g
1,2,3,7,8-PentaCDD	< 0.0162	pg/g
1,2,3,4,7,8-HexaCDD	< 0.0246	pg/g
1,2,3,6,7,8-HexaCDD	< 0.0336	pg/g
1,2,3,7,8,9-HexaCDD	< 0.0317	pg/g
1,2,3,4,6,7,8-HeptaCDD	< 0.0517	pg/g

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Analytical report AR-17-JK-075623-02
Sample Code 703-2017-00670869

This report replaces report number: AR-17-JK-075623-01

OctaCDD	< 0.375		pg/g
2,3,7,8-TetraCDF	< 0.0336		pg/g
1,2,3,7,8-PentaCDF	< 0.0233		pg/g
2,3,4,7,8-PentaCDF	< 0.0362		pg/g
1,2,3,4,7,8-HexaCDF	< 0.0382		pg/g
1,2,3,6,7,8-HexaCDF	< 0.0349		pg/g
1,2,3,7,8,9-HexaCDF	< 0.0259		pg/g
2,3,4,6,7,8-HexaCDF	< 0.0317		pg/g
1,2,3,4,6,7,8-HeptaCDF	< 0.0362		pg/g
1,2,3,4,7,8,9-HeptaCDF	< 0.0252		pg/g
OctaCDF	< 0.0776		pg/g
WHO(2005)-PCDD/F TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCDD/F TEQ (upper-bound)	0.0667		pg/g

GFL11 polychlorinated biphenyls (12 WHO PCB + 6 ICES PCB)

Method : Internal, GLS DF 110, GC-MS/MS

Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.

PCB 77	< 6.47		pg/g
PCB 81	< 0.175		pg/g
PCB 105	< 2.52		pg/g
PCB 114	< 0.343		pg/g
PCB 118	< 9.06		pg/g
PCB 123	< 0.259		pg/g
PCB 126	< 0.162		pg/g
PCB 156	< 1.42		pg/g
PCB 157	< 0.265		pg/g
PCB 167	< 0.712		pg/g
PCB 169	< 0.776		pg/g
PCB 189	< 0.259		pg/g
WHO(2005)-PCB TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCB TEQ (upper-bound)	0.0406		pg/g
PCB 28	< 0.0647		ng/g
PCB 52	< 0.0647		ng/g
PCB 101	< 0.0647		ng/g
PCB 138	< 0.0647		ng/g
PCB 153	< 0.0647		ng/g
PCB 180	< 0.0647		ng/g
Total 6 ndl-PCB (lower-bound)	ND		ng/g
Total 6 ndl-PCB (upper-bound)	0.388		ng/g

GFTE1 TEQ-Totals WHO-PCDD/F and PCB

Method : Internal, GLS DF 110, 120, 130, 140, Calculation

Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.

WHO(2005)-PCDD/F+PCB TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCDD/F+PCB TEQ (upper-bound)	0.107		pg/g

JC00U PAH 4

Method : Internal, CON-PV 01176 (2018-04), GC-MS

Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Benz(a)anthracene	<0.5	*	µg/kg
Benzo(a)pyrene	<0.5	*	µg/kg
Benzo(b)fluoranthene	<0.5	*	µg/kg
Chrysene	<0.5	*	µg/kg
Sum PAH 4	Inapplicable		µg/kg

JJ0ES Citrinin (rice, cereals)

Method : Internal, CON-PV 01126 (2017-08), LC-MS/MS

Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Citrinin	<30	*	µg/kg

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Analytical report AR-17-JK-075623-02
Sample Code 703-2017-00670869

This report replaces report number: AR-17-JK-075623-01

SP205 Organonitrogen Pesticides and others (GC-MS)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected		

SP206 Pesticides NCI-GHT
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-NCI-MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected		

SP201 Organochlorine Pesticides and Pyrethroids (GC-ECD)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-ECD
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected		

SP203 Organophosphorus Pesticides (GC-FPD)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-FPD
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Chlorpyrifos (-ethyl)	Traces < 0.02		mg/kg
Other screened pesticides	Not Detected		

SP914 Pesticide Screening LC-GHT
Method : DIN EN 15662:2009-02, P-14.141, LC-MS/MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected		

JJ0F0 Aflatoxins B1, B2, G1, G2 (spices, special matrix) low LOQ
Method : internal method based on EN 14123, CON-PV 00873 (2017-06), IAC-LC-FLD
(Modification: sample weight, extraction solvent, IAC-volumina and buffer, extension of the scope to other food and feed)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Aflatoxin B1	<0.1	*	µg/kg
Aflatoxin B2	<0.1	*	µg/kg
Aflatoxin G1	<0.1	*	µg/kg
Aflatoxin G2	<0.1	*	µg/kg
Sum of all positive Aflatoxins	<0.4	*	µg/kg

JJ0FH Ochratoxin A (spices, special matrix) low LOQ
Method : DIN EN 14132, mod., CON-PV 00850 (2017-05), IAC-LC-FLD
(Modification: sample weight, extraction solvent, IAC-volumina and buffer, postcolumn derivatization, extension of the scope to other food and feed)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Ochratoxin A (OTA)	<0.2	*	µg/kg

Molecularbiological Analysis

JJ604 Detection of gluten (#)
Method : r-biopharm Test-Combination R7001, mod., PV 01193, ELISA [Sandwich ELISA]
(Modification: apply also on equipment and commodities from the food production as well as cleaning water)

Gluten	>50		mg/kg

* = Below indicated quantification level

(#) = Eurofins Analytik GmbH is accredited for this test.

Remark: For this matrix complete validation data for each test (firbre) are not available.

Signature [redacted]

Analytical Service Manager (Nancy Heckert)

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Person in charge Mrs N. Heckert - 1704
Client support Mrs N. Heckert - 1704

Report date 17.07.2018

Analytical report AR-17-JK-075624-02

This report replaces report number: AR-17-JK-075624-01

Sample Code 703-2017-00670870

Reference	Wheat germ extract [redacted]
Nr. of sample containers	2
Gross weight / volume	813,1 g
Reception temperature	room temperature
Ordered by	[redacted]
Submitted by	
Sender	Bote
Packaging	plastic bag
Reception date time	09.06.2017
Start/end of analyses	09.06.2017 / 04.07.2017

TEST RESULTS

Physical-chemical Analysis

JK09M	**Water content**		
Method :	Internal method, , Gravimetry		
Water content		2.4	g/100 g
JK09N	**Ash**		
Method :	Internal method, , Gravimetry		
Ash		7.7	g/100 g
JK09Q	**Raw protein**		
Method :	Internal method, , Kjeldahl (titrimetry)		
Nitrogen		4.1	g/100 g
Protein (Nx6,25)		25.9	g/100 g
JK09R	**Fat total**		
Method :	Internal method, , Gravimetry		
Fat, total		6.7	g/100 g
JK09T	**Fatty acid profile**		
Method :	Internal method, , GC-FID		
C 4:0 (Butyric Acid)		<0.1	* %
C 6:0 (Caproic acid)		<0.1	* %
C 8:0 (Caprylic acid)		<0.1	* %
C 10:0 (Capric acid)		<0.1	* %
C 10:1 (Decenic acid) + isomeres		<0.1	* %
C 12:0 (Lauric acid)		<0.1	* %
C 14:0 (Myristic acid)		0.1	%

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C 14:1 (Myristoleic acid) + isomeres	<0.1	*	%
C 15:0 (Pentadecanic acid)	<0.1	*	%
C 15:1 (Pentadecenoic acid) + Isomers	<0.1	*	%
C 16:0 (Palmitic acid)	18.7		%
C 16:1 (Palmitoleic acid) + isomeres	0.2		%
C 17:0 (Margaric acid)	<0.1	*	%
C 17:1 (Heptadecenoic acid) + isomers	<0.1	*	%
C 18:0 (Stearic acid)	0.8		%
C 18:1-9 (Oleic acid)	14.0		%
C 18:1-11 (cis-Vaccenic acid)	1.3		%
C 18:1-13 (13-oleic acid)	<0.1	*	%
C 18:1 (trans) Elaidic acid	<0.1	*	%
C 18:2 (Linoleic acid)	55.1		%
C 18:2 (trans/trans)	<0.1	*	%
C 18:2 (cis/trans)	0.1		%
C 18:2 (trans/cis)	<0.1	*	%
C 18:3 (alpha-linolenic acid)	6.4		%
C 18:3 (gamma-linolenic acid)	<0.1	*	%
C 18:3 (trans/cis/trans)	<0.1	*	%
C 18:3 (cis/cis/trans)	<0.1	*	%
C 18:3 (cis/trans/cis)	<0.1	*	%
C 18:3 (trans/cis/cis)	<0.1	*	%
C 18:4 (Octadecatetraenic acid)	<0.1	*	%
C 20:0 (Arachidic acid)	0.2		%
C 20:1 (Eicosenoic acid) + isomers	1.4		%
C 20:2 (Eicosodienoic acid) + isomeres	0.1		%
C 20:3 (Eicosatrienoic acid)	<0.1	*	%
C 20:4 (Arachidonic acid)	<0.1	*	%
C 20:5 (Eicosapentaenic acid)	<0.1	*	%
C 22:0 (Behenic acid)	0.2		%
C 22:1 (Docosenic acid) + isomers	0.3		%
C 22:2 (Docosadienoic acid) + isomeres	<0.1	*	%
C 22:5 (Docosapentaenic acid)	<0.1	*	%
C 22:6 (Docosahexaenic acid)	<0.1	*	%
C 23:0 (Tricosanoic acid)	<0.1	*	%
C 24:0 (Lignoceric acid)	0.2		%
C 24:1 (Tetracosenoic acid) + isomeres	0.2		%
saturated fatty acids total	20.4		%
mono-unsaturated fatty acids total	17.5		%
poly-unsaturated fatty acids total	61.6		%
Trans-fatty acids total	0.4		%
others	0.1		%

J3083 Total dietary fibre (#)

Method : § 64 LFGB L 00.00-18, mod., PV 00303, Gravimetry

Total dietary fibre	3.21	g/100 g

JK09S Sugar profile

Method : Internal method, , LC-RI

Fructose	1.3		g/100 g
Glucose	1.1		g/100 g
Sucrose	23.6		g/100 g
Maltose	<0.5	*	g/100 g
Lactose	<0.5	*	g/100 g
Total sugars (calculated)	26.0		g/100 g

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JK09U	**Sodium**			
Method :	§ 64 LFGB L 07.00-56, mod., , F-AES			
(Modification: Applicable to all food and feed matrices)				
Sodium (Na)		<100	*	mg/kg
JJL2E	**Carbohydrates calculated (difference)**			
Method :	, Calculation			
Carbohydrate calculated (difference)		54.1		g/100 g
JKB7S	**Nutrient value in 100 g**			
Method :	according to regulation 1169/2011, , Calculation			
Energy		1634		kJ
Energy		387		kcal
Fat		6.7		g
of which saturates		1.4		g
Carbohydrate		54.1		g
of which sugars		26.0		g
Protein		25.9		g
Salt		< 0.025		g
DJ011	**Cystine, methionine (oxidative)**			
Method :	EU 152/2009 (F), ISO 13903:2005, , IC-UV			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Cystein +Cystine		0.459		g/100 g
Methionine		0.434		g/100 g
DI004	**Amino acids (acid hydrolysis)**			
Method :	EU 152/2009 (F), ISO 13903:2005, AMSUR, IC-UV			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Alanine		1.57		g/100 g
Aspartic acid		2.44		g/100 g
Arginine		2.07		g/100 g
Glutamic acid		3.11		g/100 g
Glycine		1.44		g/100 g
Histidine		0.584		g/100 g
Isoleucine		0.621		g/100 g
Leucine		1.20		g/100 g
Lysine		1.38		g/100 g
Phenylalanine		0.691		g/100 g
Proline		0.979		g/100 g
Serine		0.970		g/100 g
Tyrosine		0.631		g/100 g
Valine		1.08		g/100 g
Threonine		1.08		g/100 g
Hydroxyproline		<0.05 (LOQ)		g/100 g
Ornithine		<0.05 (LOQ)		g/100 g
DJ009	**Tryptophane**			
Method :	EU 152/2009, , IC-UV			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Tryptophan (Total)		0.257		g/100 g
A7273	**Vitamin B1 - Thiamine base**			
Method :	EN 14122:2003, mod., , LC-FLD			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Thiamine (vitamin B1)		3.10		mg/100 g
A7289	**Vitamin B12, microbiological**			
Method :	AOAC 952.20, , Nephelometry			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Vitamin B12 (cyanocobalamin)		0.0361		µg/100 g

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A7274	**Vitamin B2 - riboflavin**		
Method :	EN 14152:2003, mod., 852, LC-FLD		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Riboflavin (vitamin B2)		0.677	mg/100 g
DJB05	**Vitamin B3 (Total Niacin) EN-HPLC**		
Method :	EN 15652:2009, , LC-FLD		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Niacin (vitamin B3)		3.62	mg/100 g
A7251	**Vitamin B6**		
Method :	EN 14164, , LC-FLD		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Pyridoxine (vitamin B6)		0.781	mg/100 g
A7284	**Vitamin B8 - biotin, microbiological**		
Method :	analog. to FDA method, LST AB 266.1,1995, 866, Nephelometry		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Biotin (vitamin B8)		24.0	µg/100 g
A7286	**Vitamin B9 - Total folate, microbiological**		
Method :	NMKL 111:1985, 870, Nephelometry		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Folate (vitamin B9)		422	µg/100 g
A7291	**Vitamin C (Ascorbic acid + dehydroascorbic acid)**		
Method :	Food Chemistry, 94 626-631, , LC-DAD		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Ascorbic acid (vitamin C)		1720	mg/100 g
J8306	**Lead (Pb)**		
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS		
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)			
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.			
Lead (Pb)		0.33	mg/kg
J8308	**Cadmium (Cd)**		
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS		
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)			
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.			
Cadmium (Cd)		0.09	mg/kg
JCHG2	**Mercury (Hg)**		
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS		
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)			
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.			
Mercury (Hg)		<0.005 *	mg/kg
J8312	**Arsenic (As)**		
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS		
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)			
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.			
Arsenic (As)		<0.1 *	mg/kg
GFL05	**Dioxins and Furans (17 PCDD/F)**		
Method :	Internal, GLS DF 110, GC-MS/MS		
Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.			
2,3,7,8-TetraCDD		< 0.0125	pg/g
1,2,3,7,8-PentaCDD		< 0.0164	pg/g
1,2,3,4,7,8-HexaCDD		< 0.0250	pg/g
1,2,3,6,7,8-HexaCDD		< 0.0341	pg/g
1,2,3,7,8,9-HexaCDD		< 0.0322	pg/g
1,2,3,4,6,7,8-HeptaCDD		< 0.0525	pg/g

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OctaCDD	< 0.381		pg/g
2,3,7,8-TetraCDF	< 0.0341		pg/g
1,2,3,7,8-PentaCDF	< 0.0236		pg/g
2,3,4,7,8-PentaCDF	< 0.0368		pg/g
1,2,3,4,7,8-HexaCDF	< 0.0387		pg/g
1,2,3,6,7,8-HexaCDF	< 0.0355		pg/g
1,2,3,7,8,9-HexaCDF	< 0.0263		pg/g
2,3,4,6,7,8-HexaCDF	< 0.0322		pg/g
1,2,3,4,6,7,8-HeptaCDF	< 0.0368		pg/g
1,2,3,4,7,8,9-HeptaCDF	< 0.0256		pg/g
OctaCDF	< 0.0788		pg/g
WHO(2005)-PCDD/F TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCDD/F TEQ (upper-bound)	0.0677		pg/g

GFL11 polychlorinated biphenyls (12 WHO PCB + 6 ICES PCB)

Method : Internal, GLS DF 110, GC-MS/MS

Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.

PCB 77	< 6.57		pg/g
PCB 81	< 0.177		pg/g
PCB 105	< 2.56		pg/g
PCB 114	< 0.348		pg/g
PCB 118	< 9.19		pg/g
PCB 123	< 0.263		pg/g
PCB 126	< 0.164		pg/g
PCB 156	< 1.44		pg/g
PCB 157	< 0.269		pg/g
PCB 167	< 0.722		pg/g
PCB 169	< 0.788		pg/g
PCB 189	< 0.263		pg/g
WHO(2005)-PCB TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCB TEQ (upper-bound)	0.0412		pg/g
PCB 28	< 0.0657		ng/g
PCB 52	< 0.0657		ng/g
PCB 101	< 0.0657		ng/g
PCB 138	< 0.0657		ng/g
PCB 153	< 0.0657		ng/g
PCB 180	< 0.0657		ng/g
Total 6 ndl-PCB (lower-bound)	ND		ng/g
Total 6 ndl-PCB (upper-bound)	0.394		ng/g

GFTE1 TEQ-Totals WHO-PCDD/F and PCB

Method : Internal, GLS DF 110, 120, 130, 140, Calculation

Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.

WHO(2005)-PCDD/F+PCB TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCDD/F+PCB TEQ (upper-bound)	0.109		pg/g

JC00U PAH 4

Method : Internal, CON-PV 01176 (2018-04), GC-MS

Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Benz(a)anthracene	<0.5	*	µg/kg
Benzo(a)pyrene	<0.5	*	µg/kg
Benzo(b)fluoranthene	<0.5	*	µg/kg
Chrysene	<0.5	*	µg/kg
Sum PAH 4	Inapplicable		µg/kg

JJ0ES Citrinin (rice, cereals)

Method : Internal, CON-PV 01126 (2017-08), LC-MS/MS

Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Citrinin	<30	*	µg/kg

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SP205 Organonitrogen Pesticides and others (GC-MS)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected	

SP206 Pesticides NCI-GHT
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-NCI-MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected	

SP201 Organochlorine Pesticides and Pyrethroids (GC-ECD)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-ECD
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected	

SP203 Organophosphorus Pesticides (GC-FPD)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-FPD
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Chlorpyrifos (-ethyl)	Traces < 0.02	mg/kg
Other screened pesticides	Not Detected	

SP914 Pesticide Screening LC-GHT
Method : DIN EN 15662:2009-02, P-14.141, LC-MS/MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected	

JJ0F0 Aflatoxins B1, B2, G1, G2 (spices, special matrix) low LOQ
Method : internal method based on EN 14123, CON-PV 00873 (2017-06), IAC-LC-FLD
(Modification: sample weight, extraction solvent, IAC-volumina and buffer, extension of the scope to other food and feed)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Aflatoxin B1	<0.1	*	µg/kg
Aflatoxin B2	<0.1	*	µg/kg
Aflatoxin G1	<0.1	*	µg/kg
Aflatoxin G2	<0.1	*	µg/kg
Sum of all positive Aflatoxins	<0.4	*	µg/kg

JJ0FH Ochratoxin A (spices, special matrix) low LOQ
Method : DIN EN 14132, mod., CON-PV 00850 (2017-05), IAC-LC-FLD
(Modification: sample weight, extraction solvent, IAC-volumina and buffer, postcolumn derivatization, extension of the scope to other food and feed)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Ochratoxin A (OTA)	0.2	µg/kg

Molecularbiological Analysis

JJ604 Detection of gluten (#)
Method : r-biopharm Test-Combination R7001, mod., PV 01193, ELISA [Sandwich ELISA]
(Modification: apply also on equipment and commodities from the food production as well as cleaning water)

Gluten	>50	mg/kg

* = Below indicated quantification level

(#) = Eurofins Analytik GmbH is accredited for this test.

Remark: For this matrix complete validation data for each test (firbre) are not available.

Signature [redacted]

Analytical Service Manager (Nancy Heckert)

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Person in charge Mrs N. Heckert - 1704
Client support Mrs N. Heckert - 1704

Report date 31.07.2018

Analytical report AR-18-JK-093780-01

Sample Code 703-2018-00856648

Reference	Wheat germ extract
Lot-no.	SBC180417
Nr. of sample containers	2
Gross weight / volume	635,2 g
Reception temperature	room temperature
Ordered by	[redacted]
Submitted by	
Sender	Bote
Packaging	plastic container with screw closure
Reception date time	18.07.2018
Start/end of analyses	18.07.2018 / 31.07.2018

TEST RESULTS

Physical-chemical Analysis

JK09M	**Water content**		
Method :	Internal method, , Gravimetry		
Water content		8.6	g/100 g
JK09N	**Ash**		
Method :	Internal method, , Gravimetry		
Ash		7.4	g/100 g
JK09Q	**Raw protein**		
Method :	Internal method, , Kjeldahl (titrimetry)		
Nitrogen		4.2	g/100 g
Protein (Nx6,25)		26.2	g/100 g
JK09R	**Fat total**		
Method :	Internal method, , Gravimetry		
Fat, total		7.6	g/100 g
JK09T	**Fatty acid profile**		
Method :	Internal method, , GC-FID		
C 4:0 (Butyric Acid)		<0.1	* %
C 6:0 (Caproic acid)		<0.1	* %
C 8:0 (Caprylic acid)		<0.1	* %
C 10:0 (Capric acid)		<0.1	* %
C 10:1 (Decenic acid) + isomeres		<0.1	* %
C 12:0 (Lauric acid)		<0.1	* %

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C 14:0 (Myristic acid)	0.1		%
C 14:1 (Myristoleic acid) + isomeres	<0.1	*	%
C 15:0 (Pentadecanic acid)	<0.1	*	%
C 15:1 (Pentadecenoic acid) + Isomers	<0.1	*	%
C 16:0 (Palmitic acid)	18.7		%
C 16:1 (Palmitoleic acid) + isomeres	0.2		%
C 17:0 (Margaric acid)	<0.1	*	%
C 17:1 (Heptadecenoic acid) + isomers	<0.1	*	%
C 18:0 (Stearic acid)	0.9		%
C 18:1-9 (Oleic acid)	12.7		%
C 18:1-11 (cis-Vaccenic acid)	1.4		%
C 18:1-13 (13-oleic acid)	<0.1	*	%
C 18:1 (trans) Elaidic acid	0.3		%
C 18:2 (Linoleic acid)	55.8		%
C 18:2 (trans/trans)	<0.1	*	%
C 18:2 (cis/trans)	0.1		%
C 18:2 (trans/cis)	<0.1	*	%
C 18:3 (alpha-linolenic acid)	6.3		%
C 18:3 (gamma-linolenic acid)	<0.1	*	%
C 18:3 (trans/cis/trans)	<0.1	*	%
C 18:3 (cis/cis/trans)	<0.1	*	%
C 18:3 (cis/trans/cis)	<0.1	*	%
C 18:3 (trans/cis/cis)	<0.1	*	%
C 18:4 (Octadecatetraenic acid)	<0.1	*	%
C 20:0 (Arachidic acid)	0.2		%
C 20:1 (Eicosenoic acid) + isomers	1.3		%
C 20:2 (Eicosodienoic acid) + isomeres	0.2		%
C 20:3 (Eicosatrienoic acid)	<0.1	*	%
C 20:4 (Arachidonic acid)	<0.1	*	%
C 20:5 (Eicosapentaenic acid)	<0.1	*	%
C 22:0 (Behenic acid)	0.2		%
C 22:1 (Docosenic acid) + isomers	0.3		%
C 22:2 (Docosadienoic acid) + isomeres	<0.1	*	%
C 22:5 (Docosapentaenic acid)	<0.1	*	%
C 22:6 (Docosahexaenic acid)	<0.1	*	%
C 23:0 (Tricosanoic acid)	<0.1	*	%
C 24:0 (Lignoceric acid)	0.2		%
C 24:1 (Tetracosenoic acid) + isomeres	0.1		%
saturated fatty acids total	20.5		%
mono-unsaturated fatty acids total	16.0		%
poly-unsaturated fatty acids total	62.3		%
Trans-fatty acids total	0.6		%
others	0.6		%

J3083 Total dietary fibre (#)

Method : § 64 LFGB L 00.00-18, mod., PV 00303, Gravimetry

Total dietary fibre	1.15		g/100 g

JK09S Sugar profile

Method : Internal method, , LC-RI

Fructose	1.6		g/100 g
Glucose	2.1		g/100 g
Sucrose	20.0		g/100 g
Maltose	<0.5	*	g/100 g
Lactose	<0.5	*	g/100 g
Total sugars (calculated)	23.7		g/100 g

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JK09U	**Sodium**		
Method :	§ 64 LFGB L 07.00-56, mod., , F-AES		
(Modification: Applicable to all food and feed matrices)			
Sodium (Na)		150	mg/kg
JJL2E	**Carbohydrates calculated (difference)**		
Method :	, Calculation		
Carbohydrate calculated (difference)		49.1	g/100 g
JKB7S	**Nutrient value in 100 g**		
Method :	according to regulation 1169/2011, , Calculation		
Energy		1571	kJ
Energy		372	kcal
Fat		7.6	g
of which saturates		1.6	g
Carbohydrate		49.1	g
of which sugars		23.7	g
Protein		26.2	g
Salt		0.04	g
DJ011	**Cystine, methionine (oxidative)**		
Method :	EU 152/2009 (F), ISO 13903:2005, , IC-UV		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Cystein +Cystine		0.417	g/100 g
Methionine		0.399	g/100 g
DI004	**Amino acids (acid hydrolysis)**		
Method :	EU 152/2009 (F), ISO 13903:2005, AMSUR, IC-UV		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Alanine		1.43	g/100 g
Aspartic acid		2.29	g/100 g
Arginine		1.86	g/100 g
Glutamic acid		2.91	g/100 g
Glycine		1.33	g/100 g
Histidine		0.536	g/100 g
Isoleucine		0.566	g/100 g
Leucine		1.10	g/100 g
Lysine		1.35	g/100 g
Phenylalanine		0.637	g/100 g
Proline		0.787	g/100 g
Serine		0.875	g/100 g
Tyrosine		0.544	g/100 g
Valine		0.996	g/100 g
Threonine		0.974	g/100 g
Hydroxyproline		<0.05 (LOQ)	g/100 g
Ornithine		<0.05 (LOQ)	g/100 g
DJ009	**Tryptophane**		
Method :	EU 152/2009, , IC-UV		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Tryptophan (Total)		0.257	g/100 g
A7273	**Vitamin B1 - Thiamine base**		
Method :	EN 14122:2003, mod., , LC-FLD		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Thiamine (vitamin B1)		3.20	mg/100 g
A7289	**Vitamin B12, microbiological**		
Method :	AOAC 952.20, , Nephelometry		
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.			
Vitamin B12 (cyanocobalamin)		0.0477	µg/100 g

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Analytical report AR-18-JK-093780-01
Sample Code 703-2018-00856648

A7274	**Vitamin B2 - riboflavin**			
Method :	EN 14152:2003, mod., 852, LC-FLD			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Riboflavin (vitamin B2)		0.587		mg/100 g
DJB05	**Vitamin B3 (Total Niacin) EN-HPLC**			
Method :	EN 15652:2009, , LC-FLD			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Niacin (vitamin B3)		4.80		mg/100 g
A7251	**Vitamin B6**			
Method :	EN 14164, , LC-FLD			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Pyridoxine (vitamin B6)		0.813		mg/100 g
A7284	**Vitamin B8 - biotin, microbiological**			
Method :	analog. to FDA method, LST AB 266.1,1995, 866, Nephelometry			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Biotin (vitamin B8)		19.0		µg/100 g
A7286	**Vitamin B9 - Total folate, microbiological**			
Method :	NMKL 111:1985, 870, Nephelometry			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Folate (vitamin B9)		358		µg/100 g
A7291	**Vitamin C (Ascorbic acid + dehydroascorbic acid)**			
Method :	Food Chemistry, 94 626-631, , LC-DAD			
Subcontracted to Eurofins Vitamin Testing Denmark A/S, Vejen, which is accredited for this test.				
Ascorbic acid (vitamin C)		1620		mg/100 g
J8306	**Lead (Pb)**			
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS			
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)				
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.				
Lead (Pb)		<0.05	*	mg/kg
J8308	**Cadmium (Cd)**			
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS			
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)				
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.				
Cadmium (Cd)		0.14		mg/kg
JCHG2	**Mercury (Hg)**			
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS			
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)				
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.				
Mercury (Hg)		<0.005	*	mg/kg
J8312	**Arsenic (As)**			
Method :	DIN EN 15763:2010 (2010-04), mod., CON-PV 01274 (2017-12), ICP-MS			
(Modification: incl. ICP-MS/MS, extension of the analysis parameters, extension of the application scope to feed and tabacco/-products)				
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.				
Arsenic (As)		<0.1	*	mg/kg
GFL05	**Dioxins and Furans (17 PCDD/F)**			
Method :	Internal, GLS DF 110, GC-MS/MS			
Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.				
2,3,7,8-TetraCDD		< 0.0123		pg/g
1,2,3,7,8-PentaCDD		< 0.0162		pg/g
1,2,3,4,7,8-HexaCDD		< 0.0246		pg/g
1,2,3,6,7,8-HexaCDD		< 0.0336		pg/g
1,2,3,7,8,9-HexaCDD		< 0.0317		pg/g
1,2,3,4,6,7,8-HeptaCDD		< 0.0517		pg/g

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Analytical report AR-18-JK-093780-01
Sample Code 703-2018-00856648

OctaCDD	< 0.375		pg/g
2,3,7,8-TetraCDF	< 0.0336		pg/g
1,2,3,7,8-PentaCDF	< 0.0233		pg/g
2,3,4,7,8-PentaCDF	< 0.0362		pg/g
1,2,3,4,7,8-HexaCDF	< 0.0381		pg/g
1,2,3,6,7,8-HexaCDF	< 0.0349		pg/g
1,2,3,7,8,9-HexaCDF	< 0.0259		pg/g
2,3,4,6,7,8-HexaCDF	< 0.0317		pg/g
1,2,3,4,6,7,8-HeptaCDF	< 0.0362		pg/g
1,2,3,4,7,8,9-HeptaCDF	< 0.0252		pg/g
OctaCDF	< 0.0776		pg/g
WHO(2005)-PCDD/F TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCDD/F TEQ (medium-bound)	0.0333		pg/g
WHO(2005)-PCDD/F TEQ (upper-bound)	0.0667		pg/g

GFL11 polychlorinated biphenyls (12 WHO PCB + 6 ICES PCB)

Method : Internal, GLS DF 110, GC-MS/MS

Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.

PCB 77	< 1.16		pg/g
PCB 81	< 0.175		pg/g
PCB 105	< 2.52		pg/g
PCB 114	< 0.343		pg/g
PCB 118	< 9.05		pg/g
PCB 123	< 0.259		pg/g
PCB 126	< 0.162		pg/g
PCB 156	< 1.42		pg/g
PCB 157	< 0.265		pg/g
PCB 167	< 0.711		pg/g
PCB 169	< 0.776		pg/g
PCB 189	< 0.259		pg/g
WHO(2005)-PCB TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCB TEQ (medium-bound)	0.0200		pg/g
WHO(2005)-PCB TEQ (upper-bound)	0.0400		pg/g
PCB 28	< 0.0646		ng/g
PCB 52	< 0.0646		ng/g
PCB 101	< 0.0646		ng/g
PCB 138	< 0.0646		ng/g
PCB 153	< 0.0646		ng/g
PCB 180	< 0.0646		ng/g
Total 6 ndl-PCB (lower-bound)	ND		ng/g
Total 6 ndl-PCB (medium-bound)	0.194		ng/g
Total 6 ndl-PCB (upper-bound)	0.388		ng/g

GFTE1 TEQ-Totals WHO-PCDD/F and PCB

Method : Internal, GLS DF 110, 120, 130, 140, Calculation

Subcontracted to Eurofins GfA Lab Service GmbH, Hamburg, which is accredited for this test.

WHO(2005)-PCDD/F+PCB TEQ (lower-bound)	ND		pg/g
WHO(2005)-PCDD/F+PCB TEQ (medium-bound)	0.0534		pg/g
WHO(2005)-PCDD/F+PCB TEQ (upper-bound)	0.107		pg/g

JC00U PAH 4

Method : Internal, CON-PV 01176-(2018-07), GC-MS

Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Benz(a)anthracene	<0.5	*	µg/kg
Benzo(a)pyrene	<0.5	*	µg/kg
Benzo(b)fluoranthene	<0.5	*	µg/kg
Chrysene	<0.5	*	µg/kg
Sum PAH 4	Inapplicable		µg/kg

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Analytical report AR-18-JK-093780-01
Sample Code 703-2018-00856648

JJ0ES Citrinin (rice, cereals)
Method : Internal, CON-PV 01126 (2017-08), LC-MS/MS
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Citrinin	<20	*	µg/kg

SP205 Organonitrogen Pesticides and others (GC-MS)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected

SP206 Pesticides NCI-GHT
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-NCI-MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected

SP201 Organochlorine Pesticides and Pyrethroids (GC-ECD)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-ECD
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected

SP203 Organophosphorus Pesticides (GC-FPD)
Method : ASU L 00.00-34:2010-09, DFG-S19, GC-FPD
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected

SP914 Pesticide Screening LC-GHT
Method : DIN EN 15662:2009-02, P-14.141, LC-MS/MS
Subcontracted to Eurofins | Dr. Specht Laboratorien GmbH, Hamburg, which is accredited for this test.

Screened pesticides	Not Detected

JJ0F0 Aflatoxins B1, B2, G1, G2 (spices, special matrix) low LOQ
Method : internal method based on EN 14123, CON-PV 00873 (2017-06), IAC-LC-FLD
(Modification: sample weight, extraction solvent, IAC-volumina and buffer, extension of the scope to other food and feed)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Aflatoxin B1	<0.1	*	µg/kg
Aflatoxin B2	<0.1	*	µg/kg
Aflatoxin G1	<0.1	*	µg/kg
Aflatoxin G2	<0.1	*	µg/kg
Sum of all positive Aflatoxins	<0.4	*	µg/kg

JJ0FH Ochratoxin A (spices, special matrix) low LOQ
Method : DIN EN 14132, mod., CON-PV 00850 (2017-05), IAC-LC-FLD
(Modification: sample weight, extraction solvent, IAC-volumina and buffer, postcolumn derivatization, extension of the scope to other food and feed)
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Ochratoxin A (OTA)	<0.2	*	µg/kg

J5012 Deoxynivalenol (DON)
Method : Internal, CON-PV 01126 (2017-08), LC-MS/MS
Subcontracted to Eurofins WEJ Contaminants GmbH, Hamburg, which is accredited for this test.

Deoxynivalenol (Vomitoxin)	140	µg/kg

Molecularbiological Analysis

JJ604 Detection of gluten (#)
Method : r-biopharm Test-Combination R7001, mod., PV 01193, ELISA [Sandwich ELISA]
(Modification: apply also on equipment and commodities from the food production as well as cleaning water)

Gluten	>50	mg/kg

* = Below indicated quantification level

(#) = Eurofins Analytik GmbH is accredited for this test.

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Analytical report AR-18-JK-093780-01
Sample Code 703-2018-00856648

Remark: For this matrix complete validation data for each test (fibre) are not available.

Signature [redacted]

Analytical Service Manager (Nancy Heckert)

GRAS Notification for spermidine rich wheat germ extract (SpermidineLife®)

TLL The Longevity Labs, GmbH, Austria

Appendix V:

Analytical Results of SpermidineLife ®
(HYGIENICUM)

Cover page + 9 pages

HYGIENICUM®
INSTITUT FÜR MIKROBIOLOGIE & HYGIENE-CONSULTING GMBH

Institut für Molekulare Biowissenschaften
[redacted]
Humboldtstraße 50/EG (MIKROBIOLOGIE - EG)
8010 Graz

report no.:	**P2018/20501**
date of receipt:	13.03.2018 08:10
sampled by:	client
sample transmission:	Spedition I-Log

analysis report

[redacted] Weizenkeim Extrakt SD - Ch-Nr: [redacted] MHD: 08-09-2018 - Netto: 250g
sample image: see end of report
number of packages: 1
sample weight (including packaging): 303g
package description: Aluminiumbeutel mit Klebeband verschlossen, mit Etikett
entry temperature: +8,3 °C (surface temperature)
inspection order: Deoxynivalenol (ordert on 02.08.2018)
begin of analysis: 13.03.2018
end of analysis: 13.08.2018

chemical analysis

[redacted] Weizenkeim Extrakt SD - Ch-Nr: [redacted] MHD: 08-09-2018 - Netto: 250g

parameter	result
deoxynivalenol (NA*)(SC)	211 µg/kg

legend:
Test location Unterauftragnehmer (Fremdleister)
(NA) not accredited (SC) subcontractor (NA*) not accredited within the scope of the laboratory but accredited method of subcontractor. (n.b.) determination not possible
<: below the limit of quantification(LOQ). Please mind that accreditation is only valid for the matrices indicated in the titles of the method. (n.d.) not detected.
deoxynivalenol | HM-MA-M 02-008, LC-MS/MS

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E-mail: office@hygienicum.at, www.hygienicum.at

Graz, 16th August 2018

DI Dr. Gregor Fiechter

authorized signatory for chemistry

Notes: (1) Sampling is not covered by accreditation. (2) The results exclusively refer to tested matter. (3) This report may not be copied in parts without written permission of the laboratory.

Document created by Katharina Resch, BSc

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E-mail: office@hygienicum.at, www.hygienicum.at

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TLL
The Longevity Labs GmbH
[redacted]
Kratkystraße 2
8020 Graz

report no.: **P2019/6254**
date of receipt: 24.01.2019 15:00
sampled by: client
sample transmission: client

analysis report

[redacted] Longevity Labs+, It's Natural to be healthy - Ch-Nr: [redacted] - MHD: 01-12-2019
sample image: see end of report
number of packages: 1
sample weight (including packaging): 515g
package description: see picture in the test report
entry temperature: +15,6 °C (surface temperature)
inspection order: Mikrobiologische Untersuchung, chemische Untersuchung auf Schwermetalle (Arsen, Blei, Cadmium, Quecksilber), PAKs (Benzo(a)anthracen, Benzo(a)pyren, Benzo(b)fluoranthen, Chrysen, PAKs Summe), Toxine (Aflatoxin, Deoxynivalenol)
begin of analysis: 24.01.2019
end of analysis: 06.02.2019

microbiological analysis

[redacted] Longevity Labs+, It's Natural to be healthy - Ch-Nr: [redacted] - MHD: 01-12-2019
begin of microbiological analysis: 28.01.2019

parameter	result
Aerobic colony count 30°C	$2{,}6 * 10^3$ cfu/g
Enterobacteriaceae	<10 cfu/g
Escherichia coli	<10 cfu/g
Yeasts	<100 cfu/g
Coagulase-positive staphylococci	<10 cfu/g
Listeria monocytogenes detection	n.d. /25g
Salmonella spp.	n.d. /25g
Moulds	<100 cfu/g

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E-mail: office@hygienicum.at, www.hygienicum.at

legend:
Test location 8055 Graz, Robert-Viertl-Straße 7
cfu = colony forming units
n.d. = not detected
n.a. = not evaluable
NA = non accredited method, SC = Subcontractor, NA* = not accredited within the scope of the laboratory but accredited method of subcontractor
Aerobic colony count 30°C | EN ISO 4833-2 (Horizontal method)
Coagulase-positive staphylococci | EN ISO 6888-1 (Horizontal method for the enumeration of coagulase-positive staphylococci (Staphylococcus aureus and other species))
Enterobacteriaceae | ISO 21528-2 (Horizontal method, incubation temperature 30°C)
Escherichia coli | ISO 16649-2 (Horizontal method)
Listeria monocytogenes detection | § 64 LFGB L 00.00-95(V), Real-time PCR method for specific detection of Listeria spp. or Listeria monocytogenes in specific pre-enrichments; confirmation of positive results according to EN ISO 11290-1
Moulds | ISO 21527-2 (Horizontal methode, DG18 Agar)
Salmonella spp. | SOP G008, real-time PCR method for specific detection of salmonella spp. in pre-enrichments, according to § 64 LFGB L 00.00.98
Yeasts | ISO 21527-2 (Horizontal methode, DG18 Agar)

Storage of the sample:
The analysed sample was stored at +22 °C until the beginning of the microbiological analysis.

chemical analysis

[redacted] - Longevity Labs+, It's Natural to be healthy - Ch-Nr: [redacted] - MHD: 01-12-2019

aflatoxins (NA)(SC)*

parameter	result
aflatoxin B1	<LOQ (0,50 µg/kg)
aflatoxin B2	<LOQ (0,50 µg/kg)
aflatoxin G1	<LOQ (0,50 µg/kg)
aflatoxin G2	<LOQ (0,50 µg/kg)

element analytic (heavy metals, minerals and trace elements) (NA)(SC)*

parameter	result
arsenic	<LOQ (0,040 mg/kg)
lead	<LOQ (0,020 mg/kg)
cadmium	0,20 mg/kg
mercury	<LOQ (0,010 mg/kg)

polycyclic aromatic hydrocarbons (PAH) (NA)(SC)*

parameter	result
benzo(a)anthracene	<LOQ (1,0 µg/kg)
benzo(a)pyrene	<LOQ (1,0 µg/kg)
benzo(b)fluoranthen	<LOQ (1,0 µg/kg)
chrysene	<LOQ (1,0 µg/kg)
sum of PAH	n.d.

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E-mail: office@hygienicum.at, www.hygienicum.at

parameter	result
parameter	result
deoxynivalenol (NA*)(SC)	213 µg/kg

legend:
Test location Unterauftragnehmer (Fremdleister)
(NA) not accredited (SC) subcontractor (NA*) not accredited within the scope of the laboratory but accredited method of subcontractor. (n.b.) determination not possible
<: below the limit of quantification(LOQ). Please mind that accreditation is only valid for the matrices indicated in the titles of the method. (n.d.) not detected.
aflatoxins | § 64 LFGB L15.00-2 (Aflatoxine B1, B2, G1, G2)
deoxynivalenol | HM-MA-M 02-008, LC-MS/MS
element analytic (heavy metals, minerals and trace elements) | DIN EN 15763, ICP-MS
polycyclic aromatic hydrocarbons (PAH) | HH-MA-M 02105, HPLC-FLD

Graz,11th March 2019

DI Dr. Gregor Fiechter
authorized signatory for chemistry

Stefanie Mussger, BSc
authorized signatory for microbiology

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E-mail: office@hygienicum.at, www.hygienicum.at

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TLL
The Longevity Labs GmbH
[redacted]
Kratkystraße 2
8020 Graz

report no.: **P2019/6325**
date of receipt: 16.03.2017 15:10
sampled by: client
sample transmission: Spedition FedEx

analysis report

[redacted] **- Extrakt - 0,65kg -** [redacted]
sample image: see end of report
number of packages: 1
sample weight (including packaging): 626g
package description: Plastic bag, labeled; bag was in good order upon arrival
entry temperature: +21,7°C (surface temperature)
inspection order: aerobe Keimzahl 30°C, Enterobacteriaceae, Escherichia coli, Hefen / Schimmelpilze, koagulase-positive Staphylokokken, Listeria monocytogenes qualitativ, Salmonella spp.
begin of analysis: 16.03.2017
end of analysis: 22.03.2017

microbiological analysis

[redacted] **Extrakt - 0,65kg -** [redacted]
begin of microbiological analysis: 17.03.2017

parameter	result
Aerobic colony count 30°C	<1000 cfu/g
Enterobacteriaceae	<10 cfu/g
Escherichia coli	<10 cfu/g
Yeasts	<100 cfu/g
Coagulase-positive staphylococci	<10 cfu/g
Listeria monocytogenes detection	n.d. /25g
Salmonella spp.	n.d. /25g
Moulds	<100 cfu/g

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E-mail: office@hygienicum.at, www.hygienicum.at

legend:
Test location 8055 Graz, Robert-Viertl-Straße 7
cfu = colony forming units
n.d. = not detected
n.a. = not evaluable
NA = non accredited method, SC = Subcontractor, NA* = not accredited within the scope of the laboratory but accredited method of subcontractor
Aerobic colony count 30 °C | EN ISO 4833-2 (Horizontal method)
Coagulase-positive staphylococci | EN ISO 6888-1 (Horizontal method for the enumeration of coagulase-positive staphylococci (Staphylococcus aureus and other species))
Enterobacteriaceae | ISO 21528-2 (Horizontal method, incubation temperature 30 °C)
Escherichia coli | ISO 16649-2 (Horizontal method)
Listeria monocytogenes detection | § 64 LFGB L 00.00-95(V), Real-time PCR method for specific detection of Listeria spp. or Listeria monocytogenes in specific pre-enrichments; confirmation of positive results according to EN ISO 11290-1
Moulds | ISO 6611 (Accreditation limited to milk and diary products)
Salmonella spp. | SOP G008, real-time PCR method for specific detection of salmonella spp. in pre-enrichments, according to § 64 LFGB L 00.00.98
Yeasts | ISO 6611 (Accreditation limited to milk and diary products)

Storage of the sample:
The analysed sample was stored at +22 °C until the beginning of the microbiological analysis.

Graz, 11th March 2019

Jennifer Michou

authorized signatory for microbiology

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E-mail: office@hygienicum.at, www.hygienicum.at

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Institut für Molekulare Biowissenschaften
[redacted]
Humboldtstraße 50/EG (MIKROBIOLOGIE - EG)
8010 Graz

report no.: **P2019/6328**
date of receipt: 11.10.2017 11:45
sampled by: client
sample transmission: Spedition Global Express

analysis report

[redacted] **Pflanzenextrakt - Trockengut -** [redacted] **- Datum: 03.10.2017 - Zeit: 09:30**
sample image: see end of report
number of packages: 1
sample weight (including packaging): 140g
package description: aluminium-bag, sealed, with a lable
entry temperature: +23,0 °C (surface temperature)
inspection order: aerobe Keimzahl 30 °C (inkl. Differenzierung auf Präsumtive Bacillus cereus, am 18.10.2017 in Auftrag gegeben), Enterobacteriaceae, Escherichia coli, Hefen / Schimmelpilze, koagulase-positive Staphylokokken, Listeria monocytogenes qualitativ, Salmonella spp.
begin of analysis: 11.10.2017
end of analysis: 20.10.2017

microbiological analysis

[redacted] **- Pflanzenextrakt - Trockengut -** [redacted] **- Datum: 03.10.2017 - Zeit: 09:30**
begin of microbiological analysis: 11.10.2017

parameter	result
Aerobic colony count 30 °C	$5{,}0 * 10^3$ cfu/g *
Enterobacteriaceae	<10 cfu/g
Escherichia coli	<10 cfu/g
Yeasts	<100 cfu/g
Coagulase-positive staphylococci	<10 cfu/g
Listeria monocytogenes detection	n.d. /25g
Salmonella spp.	n.d. /25g
Moulds	<100 cfu/g

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E-mail: office@hygienicum.at, www.hygienicum.at

legend:
Test location 8055 Graz, Robert-Viertl-Straße 7
cfu = colony forming units
n.d. = not detected
n.a. = not evaluable
NA = non accredited method, SC = Subcontractor, NA* = not accredited within the scope of the laboratory but accredited method of subcontractor
Aerobic colony count 30°C | EN ISO 4833-2 (Horizontal method)
Coagulase-positive staphylococci | EN ISO 6888-1 (Horizontal method for the enumeration of coagulase-positive staphylococci (Staphylococcus aureus and other species))
Enterobacteriaceae | ISO 21528-2 (Horizontal method, incubation temperature 30°C)
Escherichia coli | ISO 16649-2 (Horizontal method)
Listeria monocytogenes detection | § 64 LFGB L 00.00-95(V), Real-time PCR method for specific detection of Listeria spp. or Listeria monocytogenes in specific pre-enrichments; confirmation of positive results according to EN ISO 11290-1
Moulds | ISO 6611 (Accreditation limited to milk and diary products)
Salmonella spp. | SOP G008, real-time PCR method for specific detection of salmonella spp. in pre-enrichments, according to § 64 LFGB L 00.00.98
Yeasts | ISO 6611 (Accreditation limited to milk and diary products)

Annotation on the parameter Aerobic colony count 30°C:
* The detected bacteria species are aerobic spore-forming bacteria, including 1,6 * 10^3 cfu/g Presumptive Bacillus cereus.

Graz,12th March 2019

Jennifer Michou

authorized signatory for microbiology

Notes: (1) Sampling is not covered by accreditation. (2) The results exclusively refer to tested matter. (3) This report may not be copied in parts without written permission of the laboratory.

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GRAS Notification for spermidine rich wheat germ extract (SpermidineLife®)

TLL The Longevity Labs, GmbH, Austria

Appendix VI:

Analytical Results of SpermidineLife ®
(JOANNEUM RESEARCH)

Cover page + 4 pages

JOANNEUM RESEARCH HEALTH
Neue Stiftingtalstraße 2
8010 Graz, Austria
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Certificate of Analysis

Graz, 04-Apr-2019

Date of analysis: 26-Feb-2019

Method: M05

Operator: Ing. Markus Hausl

Sample: SpermidinLIFETLL[redacted]

Results for **19-02-11TLL 7**

Analyte	Value	Unit	Comment
Putrescine	0,1189	mg/g	--
Spermidine	1,2850	mg/g	--
Spermine	0,3758	mg/g	--

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Certificate of Analysis

Graz, 04-Apr-2019

Date of analysis: 26-Feb-2019

Method: M05

Operator: Ing. Markus Hausl

Sample: SpermidinLIFETLL [redacted]

Results for **19-02-11TLL 8**

Analyte	Value	Unit	Comment
Putrescine	0,1237	mg/g	--
Spermidine	1,1716	mg/g	--
Spermine	0,2865	mg/g	--

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Certificate of Analysis

Graz, 04-Apr-2019

Date of analysis: 26-Feb-2019

Method: M05

Operator: Ing. Markus Hausl

Sample: SpermidinLIFETLL; [redacted]

Results for **19-02-11TLL 9**

Analyte	Value	Unit	Comment
Putrescine	0,1142	mg/g	--
Spermidine	1,3409	mg/g	--
Spermine	0,3237	mg/g	--

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Certificate of Analysis

Graz, 04-Apr-2019

Date of analysis: 26-Feb-2019

Method: M05

Operator: Ing. Markus Hausl

Sample: SpermidinLIFETLL [redacted]

Results for **19-02-11TLL 10**

Analyte	Value	Unit	Comment
Putrescine	0,1856	mg/g	–
Spermidine	1,3088	mg/g	–
Spermine	0,3437	mg/g	–