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Certified Quality System
ISO 13485:2021
Cert. n° D2001500016
ISO 9001:2015
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Cert. n° AQS/A/104002023

TSE STATEMENT FOR MINIMIZING THE RISK OF TSE IN ANIMAL DERIVATIVES

MANUFACTURER: Biolife Italiana Srl, Viale Monza 272, 20128 Milan, Italy

NAME OF THE PRODUCTS: Dehydrated Microbiological Culture Media; Ready-to-use culture media in plates, tubes and bottles.

DESCRIPTION OF THE PRODUCTS

Microbiological Culture Media in powder form and ready-to-use in plates, tubes and bottles, manufactured by Biolife Italiana S.r.l., are composed of a mixture of peptones, organic/inorganic salts and purified water (in ready to use media) to be used for diagnostic and/or laboratory purposes, in fermentation process and for general microbiological applications.
Formulations of the products are reported in product labels and in technical sheets.

QUALITY ASSURANCE SYSTEM

Biolife Italiana S.r.l. is certified according to ISO 9001:2015, ISO 13485:2016 and ISO 14001:2015 for design, production control and distribution of in vitro diagnostic products.

REGISTRATION

Biolife Italiana S.r.l has been registered by ASL Milano, Sanità Pubblica Veterinaria, according to Reg. (EC) n° 1069/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 21 October 2009, laying down health rules as regards animal by-products and derived products not intended for human consumption and repealing EC Regulation EC No 1774/2002 (Animal by-products Regulation). Registration n° 1144PT of 23/05/2011, according to Article 23.

REFERENCES

1. **EMA/410/01 rev.3**: “Note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products;
2. **Chapter 5.2.8. of European pharmacopoeia rev. 1** “Minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products”;
3. **FDA CFR 94.18** “Bovine spongiform encephalopathy; importation of edible products derived from bovines”;
4. **WHO/EMC/ZOO 097.3** “Report of a WHO Consultation on Medicinal and other Products in Relation to Human and Animal Transmissible Spongiform Encephalopathies”;
5. **REGULATION (EC) No 1069/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL** of 21 October 2009 laying down health rules as regards animal by-products and derived products not intended for human consumption and repealing Regulation (EC) N 1774/2002 (Animal by-products Regulation).

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MANUFACTURING

The ingredients of animal origin used by Biolife Italiana S.r.l. for manufacturing of Microbiological Culture Media in powder form, ready-to-use in plates, tubes, bottles and ancillary products are reported in the table below:

N°	INGREDIENT/ BIOLIFE REF	TISSUE/ MATERIAL°	COUNTRY OF ORIGIN OF ANIMALS °	CATEGORY	NOTES	EDQM CERTIFICATE OF SUITABILITY
1	**Meat peptone** BL2BEP039	Beef lung	New Zealand	IB*/III**	1	R1-CEP 2001-291-Rev 04
2	**Meat Peptone** BL2BEP011	Bovine tissues	New Zealand	IC*	2	
3	**Meat Peptone** BL2BEP051	Bovine tissues	Switzerland New Zealand Spain	N/A	3	
	Meat Peptone BL2BEP045	Bovine tissues	India	IB*/III	36	
4	**Meat Extract** BL2BEP037	Bovine tissue Porcine tissue	New Zealand	IB* NA	4	
5	**Beef Extract** BL2BEP017	Bovine bones excluding skulls, vertebrae and spinal cord	USA	IC*	5	R1-CEP 2000-163-REV. 00
6	**Beef Extract** BL2BEP038	Bovine skeletal muscle and marrow	New Zealand	III/IV**/IB*	6	R1-CEP 2001-299-Rev 03
7	**Beef Extract** BL2BEP050	Pork gelatin Bovine Milk Casein Bovine cheek meat	Italy New Zealand Spain	NA IB* -	7	
8	**Proteose Peptone** BL2BEP040	Porcine tissue	USA		8	
9	**Proteose Peptone** BL2BEP041	Bovine skeletal muscle and marrow	USA	IB */III/IV**	9	
10	**Proteose Peptone** BL2BEP042	Bovine: bones and milk casein Porcine: stomach and bones	USA New Zealand USA/Canada	IC* IB*	10	R1-CEP 2001-112 Rev.00
11	**Mycological Peptone** BL2BEP043	Bovine Liver Porcine Pancreatic Extract	New Zealand USA/Canada	IB* -	11	
12	**Mycological Peptone** BL2BEP043S	Pork liver	Italy		12	
13	**Bile Salts n° 3** BL2BEU002	Bovine and ovine bile	New Zealand and other countries	IB*	13	R1-CEP 2000-383 REV. 03

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14	**Bile Salts n° 3** BL2BEU001	Bovine bile salts	New Zealand and other countries	IC*	14	
15	**Acid Hydrolysate of Casein** BL2BEP001	Bovine Milk	New Zealand	IB*	15	
16	**Acid digest of casein** BL2BEP002	Bovine Milk	USA	IC*	16	
17	**Casein peptone** BL2BEP009	Bovine Milk	New Zealand	IV**	17	
18	**Casein peptone** BL2BEP010	Bovine Milk	New Zealand	IV**	18	
19	**Casein peptone** BL2BEP010S	Bovine Milk	New Zealand	IB*	19	
20	**Peptonized Milk** BL2BEP021	Bovine Milk, Porcine pancreas	USA USA	IB* NA	20	
21	**Oxgall** BL2BEU006	Bovine bile ovine bile	New Zealand and other countries	IB* NA	21	R1-CEP 2000-383-REV. 03
22	**Sodium Cholate** BL2BAU007	Bovine bile	Argentina, India Colombia, USA, Paraguay, Uruguay, Brazil, Australia	IB*	22	*R1-CEP 2000-334 REV 04*
23	**Sodium Desoxycholate** BL2BAU006	Bovine bile	USA, Argentina, Paraguay, Uruguay	IB*	23	*R1-CEP 2000-335 REV 03*
24	**Skim Milk** BL2BEP022	Bovine milk	Not declared by the Supplier	NA	24	
25	**Brain Heart Infusion Pork** BL2BEP005P	Pork brain and heart	USA	NA	25	
26	**Pork Gelatin** BL2BEX003	Pig skin	Countries approved by European commission	NA	26	
27	**Gelatin Peptone** BL2BEP033	Pork skin	USA	NA	27	
28	**Gelatin Peptone** BL2BEP034	Pork gelatin	Not declared	NA	28	
		Pork gelatin	Mexico U.S.A.	NA	35	
29	**Liver Extract** BL2BEP006	Pork liver	Italy	NA	29	
30	**Tryptose** 4122602	Bovine Milk	Australia or New Zealand	IC*	18, 19	

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31	**Peptocomplex** 4123102	Beef lung, Bovine Milk	New Zealand	IB* III**	1, 18	
32	**Defibrinated Sheep Blood** BL2MAZ001	Sheep blood	Italy	NA	30	
33	**Defibrinated Horse Blood** BL2MAZ003	Horse blood	Italy	NA	30	
34	**Lysed Horse Blood** BL2MAZ007	Horse blood	Italy	NA	30	
35	**Rabbit Plasma** BL2BEB058-BL2BEB059	Rabbit blood	Italy	NA	30	
36	**Horse Serum** BL2MAZ015	Horse blood	Italy	NA	30	
37	**Chicken Eggs** BL2FAU007	Chicken eggs	Italy	NA	31	
38	**Acid Hydrolysate of Casein** BL2BEP003	Bovine Milk	New Zealand	NA	32	
39	**Bovine Fibrinogen + Soybean Typsin Inhibitor – 5% frozen solution** BL2EAF055X	Bovine plasma	French	N/A	33	
40	**Beef heart infusion** BL2BEP060	Bovine heart	New Zealand	IV**/IB*	34	*R1-CEP 2007-139 REV.01*

°Tissue/material, Country of origin, Category: as declared by the manufacturer
*as defined in EMA/410/01 rev 3 - ** as defined according to WHO/EMC/ZOO 097.3
NA: the risk classification is not applicable .

NOTES

N° 1 - Note 1

Meat Peptone (Biolife REF: BL2BEP039) has been certified by Directorate for Quality Medicines (Certification of Suitability n° R1-CEP 2001-291 Rev 04). Each batch is supplied with the Sanitary Certificate declaring that:

- The mentioned product consists exclusively of hydrolyzed protein not intended for human consumption.
- The mentioned product has been prepared and stored in a plant approved validated and supervised by the competent authority in accordance with article 24 and where appropriate article 14 of Reg. (EC) n°1069/2009 in order to kill pathogenic agents.
- The country of origin of animals is New Zealand, the country of born, raise and slaughter is New Zealand the country of manufacture of the finished product is Mexico.
- The country of origin of enzyme from porcine pancreas is USA
- Part of animals: lung
- According to WHO/EMC/ZOO 097.3 the risk category (IES) of the main component is class III; according to EMA/410/01 rev 3 the risk category of the main component is class “IB”.
- The processing facility does not receive, store, process ruminant material from any BSE country listed in CFR 94.18 (a) (Europe, Oman, Israel, Canada and Japan) except milk products.

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- These animals were slaughtered in authorized establishments and were subjected to permanent veterinary inspection. The said animals were ascertained to be in good health before and after slaughtering and were considered fit for human consumption. The animals did not show any pathological condition.
- The animals did not show any pathological condition.
- The animals were prepared, handled and dispatched according to hygienic requirements.
- The product has been heated to a minimum of 80 °C for a minimum of 1 hour, followed by a minimum of 30 minutes at a minimum of 105 °C after the addition of enzymes
- During processing are avoided commingling or mixing with other animal materials.
- The product has been dried at a minimum of 140 °C.
- Before, during and after completion of drying process, every precaution has been taken to prevent contamination of the product.
- The final product has been packed in new containers
- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 2 - Note 2

Meat Peptone (Biolife REF: BL2BEP011): each batch is supplied with a Sanitary Certificate declaring that:

- Among the raw materials and auxiliaries used in the preparation the bovine animal tissues belong the category IC according the classification of the “Note for Guidance EMA/410/01 rev 3.
- The bovine tissues are sourced in New Zealand and come from herd free from Bovine Spongiform Encephalopathy and foot-and-mouth disease after examination by Veterinary Authorities.
- The manufacturing process includes boiling at 100°C for 15 minutes and a step of 30 minutes at 98°C and instantaneous heating at 160°C on spray drying.

N° 3 - Note 3

Meat Peptone (Biolife REF BL2BEP051): each batch is supplied with the Health declaration, released by the official inspector Veterinary, declaring that:

- Goods for technical/industrial use, produced in a facility authorized according to the Reg. (EC) No 1069/2009 for the manufacturing of intermediate and pharmaceutical products, under official control by the local Health Authority.
- Adequate precautions have been taken to avoid contamination of raw materials or their derivates by pathogens
- The products have been prepared from organs coming from animals declared suitable for human consumption
- New Zealand is an OIE listed country as being free from BSE.
- The products is treated at 123°C for 30 minutes.

N° 4 - Note 4

Meat Extract (Biolife REF: BL2BEP037): each batch is supplied with the Sanitary Certificate and with a Manufacturer’s certificate declaring that:

- among the raw material and auxiliaries used in its preparation the bovine constituents belong to category IB according the classification of the “Note for guidance EMA/410/01 Rev. 3”;
- the bovine raw materials are sourced in New Zealand, and come from herds free from Bovine Spongiform Encephalopathy and foot-and-mouth disease after examination by Veterinary Authorities;
- the manufacturing process includes boiling at 100°C for a minimum of 5 minutes and instantaneous heating at 170°C minimum on spray drying.

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N° 5 - Note 5

Beef Extract (Biolife REF: BL2BEP017): has been certified by Council of Europe, European Directorate for the Quality of Medicines (Certification of Suitability n° R1-CEP 2000-163 Rev.00).
Each batch is supplied with a Manufacturer's TSE/BSE Certificate declaring that:

- Animal material: bone stock
- Animal source: bovine bones, excluding skull, vertebrae and spinal cord
- Country of origin: USA
- Category as defined EMA/410/01 rev 3: IC

The supplier declares that the country of origin is Geographical BSE risk III and that the product is processed at 133°C, 30 psi for 20 minutes.

N° 6 - Note 6

Beef Extract (Biolife REF: BL2BEP038): has been certified by Directorate for Quality Medicines (Certification of suitability n° R1-CEP 2001-299 Rev 03).
Each batch is supplied with the Sanitary Certificate and a manufacturer's certificate declaring that:

- The mentioned product consists exclusively of hydrolyzed protein not intended for human consumption.
- The mentioned product has been prepared and stored in a plant approved, validated and supervised by the competent authority in accordance with article 24 and where appropriate article 14 of Reg. (EC) n°1069/2009 in order to kill pathogenic agents.
- The country of origin of animals is New Zealand, the country of manufacture of the finished product is Mexico.
- Part of animals: skeletal muscle and marrow.
- According to WHO/EMC/ZOO 097.3 the risk category (IES) of the main component is (are) class III/IV; according to EMA/410/01 rev 3 the risk category of the main component is class "IB".
- The processing facility does not receive, store, process ruminant material from any BSE country listed in CFR 94.18 (a) (Europe, Oman, Israel, Canada and Japan) except milk products.
- These animals were slaughtered in authorized establishments and were subjected to permanent veterinary inspection. The said animals were ascertained to be in good health before and after slaughtering and were considered fit for human consumption.
- The animals did not show any pathological condition.
- The animals were prepared handled and dispatched according to hygienic requirements.
- The product has been heated to a minimum of 80°C for a minimum of 1 hour including a minimum of 30 minutes at a minimum of 105°C
- During processing no commingling or in any manner mixing with any animal material does occur
- The product has been dried at a minimum of 140°C.
- Before, during and after completion of drying process every precaution has been taken to prevent contamination of the product.
- The final product has been packed in new containers
- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 7 - Note 7

Beef Extract (Biolife REF: BL2BEP050): each batch is supplied with the Sanitary Certificate and with a Manufacturer's certificate declaring that:

- The mentioned product is good for technical/industrial use produced in a factory registered according to Reg. (EC) n°1069/2009 for the manufacturing of intermediate and pharmaceuticals products, under official control by the local Health Authority;

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- adequate precautions have been taken to avoid contamination of raw materials or their derivatives by pathogens;
- the mentioned product has been prepared from organs coming from animals declared suitable for human consumption.

N° 8 - Note 8

Proteose Peptone (Biolife REF: BL2BEP040): every batch is supplied with the Manufacturer's certificate declaring the country of origin and the tissue category.

N° 9 - Note 9

Proteose Peptone (Biolife REF: BL2BEP041): each batch is supplied with the Sanitary Certificate and with a Manufacturer's certificate declaring that:

- The mentioned product consists exclusively of hydrolyzed protein not intended for human consumption.
- The mentioned product has been prepared and stored in a plant approved validated and supervised by the competent authority in accordance with article 24 and where appropriate article 14 of Reg. (EC) n° 1069/2009 in order to kill pathogenic agents.
- The country of origin of animals is USA, the country of born, raised and slaughtered is USA, the country of manufacture of the finished product is Mexico.
- The country of origin of enzyme from porcine pancreas/stomach is USA.
- Part of animal: skeletal muscle and marrow.
- According to WHO/EMC/ZOO 097.3 the risk category (IES) of the main component is (are) class III/IV; according to EMA/410/01 rev 3 the risk category of the main component is class "IB".
- The processing facility does not receive, store, process ruminant material from any BSE country listed in CFR 94.18 (a), with the exception of milk products (Europe, Oman, Israel, Canada and Japan)
- These animals were slaughtered in authorized establishments and were subjected to permanent veterinary inspection. The said animals were ascertained to be in good health before and after slaughtering and were considered fit for human consumption.
- The animals did not show any pathological condition.
- The animals were prepared handles and dispatched according to hygienic requirements.
- The product has been heated to a minimum of 80°C for a minimum of 1 hour including a minimum of 30 minutes at a minimum of 105°C after addition of enzymes
- During processing no commingling or in any manner mixing with any animal material does occur
- The product was dried at a minimum of 140°C.
- Before, during and after completion of drying process every precaution was taken to prevent contamination of the product.
- The final product was packed in new containers
- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 10 - Note 10

Proteose Peptone (Biolife REF: BL2BEP042) has been certified by Council of Europe, European Directorate for the Quality of Medicines (Certification of Suitability n° R1-CEP 2001-112 REV.00). Each batch is supplied by the Manufacturer with the BSE/TSE Certificate.
The following materials have been sourced from countries with a "Negligible BSE Risk" or "Controlled BSE Risk" in accordance with chapter 11.4 of the Terrestrial Code, as set forth in the World Organisation for Animal Health, Office Internationale des Epizooties (OIE).

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Material	Country of Origin	Species	Processing	Tissue / Fluid*	Category**
Casein	New Zealand	Bovine	≥ 72˚C for ≥ 15 seconds	Milk	IB
Beef Stock	USA	Bovine	> 133°C, 30psi for > 20 minutes	Bones, excluding skulls, vertebrae and spinal cord	IC

* Milk, when listed above, is sourced from healthy animals in the same conditions as milk collected for human consumption and no other ruminant materials, with the exception of calf rennet, are used in the preparation of such derivatives (e.g. pancreatic enzyme digests of casein).
** As defined in European Pharmacopeia general chapter 5.2.8.

Other Materials of Animal Origin

Material	Country of Origin	Species	Processing	Tissue / Fluid
Pancreatic Extract	USA, Canada	Porcine	Washed with Isopropyl alcohol; vacuum dried for ≥ 38 hours with final temperature of 49°C	Pancreas
Dried Pork Stock	USA	Porcine	> 133°C, 30psi for > 20 minutes	Bone
Pancreatic Extract	USA, Canada	Porcine	Washed with Isopropyl alcohol; vacuum dried for ≥ 38 hours with final temperature of 49°C	Pancreas
Pepsin Powder	USA, Canada	Porcine	Acid Hydrolysis at < pH 2.0 for 30 minutes and pH 2-3 for 4 hours	Stomach
Peptone	USA	Porcine	Heated to 80°C for 2 hours; pH at 2.0-3.0 for > 48 hours	Stomach
Pancreatin	USA, Canada	Porcine	> 77°C for ≥ 30 seconds	Pancreas

N° 11 - Note 11

Mycological Peptone (Biolife REF: BL2BEP043): each batch is supplied by the Manufacturer with the BSE/TSE Certificate declaring that Mycological Peptone contains the following materials of bovine/porcine origin

MATERIAL	COUNTRY OF ORIGIN	ANIMAL SOURCES	CATEGORY (EMA/410/01 REV 3)
Liver	New Zealand	Bovine	IB
Pancreatic extract	USA/ Canada	Porcine	NA

N° 12 - Note 12

Mycological Peptone (Biolife REF: BL2BEP043S) contains Liver Extract.
Liver Extract (Biolife REF: BL2BEP006) is supplied with a Health Declaration stating that:

- The country of origin and manufacturing is Italy.

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- The product is for technical use and produced in a factory registered according to Reg. (EC) N°1069/2009 for the manufacturing of intermediate and pharmaceutical products under official control by the local Health Authority.
- Adequate precautions have been taken to avoid contamination of raw materials or their derivatives by pathogens and cross-contamination between different typology of products.
- Liver is a Category 3 by products coming from animals submitted to ante and post mortem inspection, found healthy and free from infectious diseases in act as for the Veterinary Certificate of raw material.

N° 13 - Note 13
Bile Salts n° 3(Biolife REF: BL2BEU002) has been certified by Council of Europe, European Directorate for the Quality of Medicines (Certification of Suitability n° R1-CEP 2000-383 Rev. 03) declaring the countries of origin of source materials for manufacturing of bile acids and derivatives: Argentina, Australia, Belgium, Brazil, Canada, Chile, Colombia, Denmark, Ecuador, France, Germany, India, Ireland, Italy, Mexico, Netherlands, New Zealand Panama, Paraguay, South Africa, Spain, Uruguay, USA, Venezuela.
Each batch is supplied with the Sanitary Certificate and a manufacturer's Declaration declaring that:

- Bile salts n° 3 is a product derived from Category 3 material intended for the manufacture of medical devices, in vitro diagnostics or laboratory reagents.
- It is already highly purified and is used without further purification to manufacture medical devices, in-vitro diagnostics and laboratory reagents
- It is derived from material sourced from only healthy animals which have passed ante- and post-mortem inspection in government approved slaughterhouses and have been found free of contagious diseases of quarantine concern and therefore fit for human consumption (i.e. category 3).
- It is derived from bovine bile sourced from following countries: Argentina, Australia, Brazil, India, New Zealand, USA as well as ovine bile sourced from New Zealand. According to EMA/410/01 rev 3 bile has been classified under the lowest risk category IC "Tissue with no detectable infectivity".
- Bile is therefore not expected to contain infectivity even in infected animals showing clinical signs, indicating that bile is not considered to be a TSE risk material.
- It is manufactured using extremely aggressive processing conditions including an alkaline hydrolysis at high temperature (>6% w/v NaOH at > 120°C for >hours). A combination of sodium hydroxide at high temperature is known to be most effective at completely inactivating BSE causative agent and such an exposure for only 30-90 minutes achieves reduction of 100 million-fold. Subsequent purification steps involve prolonged boiling in organic solvents, the addition of aqueous sodium hydroxide and boiling of the solution and spry drying (inlet temp. >140°C, outlet temp >90°C).

N° 14 - Note 14
Bile Salts n° 3 (**Biolife REF: BL2BEU001**): each batch is supplied with a Manufacturer's TSE/BSE Certificate declaring that:

- Animal material and sources: bovine bile salts
- Country of origin: New Zealand (New Zealand may use the following countries as a source: Australia, USA, Brazil, Colombia, Ecuador, Paraguay, Uruguay, Mexico, South Africa).
- Geographical BSE risk: III
- Process: 6% sodium hydroxide at 125°C for more than 8 hours; spray dried, inlet temperature >140°C, outlet temperature >90°C
- Category as defined in chapter 5.2.8 of European pharmacopoeia: IC

N° 15 - Note 15
Acid Hydrolysate of Casein (Biolife REF: BL2BEP001): each batch is supplied with the Sanitary and Origin Certificate declaring that:

- The product does not contain and is not derived from specified risk material as defined in Commission Decision 2000/418/EC.

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- The product has been prepared from raw materials of bovine origin which are classified in category B (tissue with no detected infectivity) according to EMA/410/01 rev.3.
- The raw materials were collected in New Zealand.
- The raw materials come from animals not showing clinical signs of a disease that can be transmitted through the milk.
- The manufacturing process includes heat treatment of at least 30 minutes at a minimum temperature of 95°C.
- The official veterinarian, in accordance with the information supplied by the manufacturer, attests that there is no commingling with any other animal material during processing and that all animal raw materials present in the plant are issued from animal free of foot-and-mouth disease.

N° 16 - Note 16
Acid Hydrolysate of Casein (Biolife REF: BL2BEP002): each batch is supplied with the Health Certificate for dairy products derived from milk cows, ewes, goats, and buffaloes for human consumption from third countries or parts thereof authorized in column B of Annex I to Reg. (EU) n° 605/2010 intended for importation into European Union, including health information, Public Health attestation, notes.

N° 17 - Note 17
Casein Peptone (Biolife REF: BL2BEP009): each batch is supplied with the Sanitary Certificate declaring that:
- The mentioned product consists exclusively of hydrolyzed protein not intended for human consumption.
- The mentioned product has been prepared and stored in a plant approved validated and supervised by the competent authority in accordance with article 24 and where appropriate article 14 of Reg. (EC) n° 1069/2009 in order to kill pathogenic agents.
- The country of origin of animals is New Zealand, the country of born, raise and slaughter is New Zealand, the country of manufacture of the finished product is Mexico.
- The country of origin of enzyme from porcine pancreas is USA.
- Animal product: milk.
- According to WHO/EMC/ZOO 097.3 the risk category (IES) of the main component is class IV; according to EMA/410/01 rev 3 the risk category of the main component is class “IB”.
- The processing facility does not receive, store, process ruminant material from any BSE country listed in CFR 94.18 (a), with the exception of milk products (Europe, Oman, Israel, Canada and Japan).
- The raw material was obtained from healthy animals from registered establishments and was fit for human consumption.
- The product has been heated to a minimum of 80°C for a minimum of 1 hour including a minimum of 5 minutes at a minimum of 105°C after addition of enzymes
- During processing no commingling or in any manner mixing with any animal material does occur
- The product was dried at a minimum of 140°C.
- Before, during and after completion of drying process every precaution was taken to prevent contamination of the product.
- The final product was packed in new containers
- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 18 - Note 18
Casein peptone (Biolife REF: BL2BEP010): each batch is supplied with the Sanitary Certificate declaring that:
- Among the raw materials and auxiliaries used in the preparation, the milk casein is of bovine origin, it belongs to the category IV of the WHO classification. It is sourced in New Zealand, under veterinary control.

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- Pancreatin used is issued from pigs' pancreas coming from France. Enzyme is issued from pigs coming from holdings free from foot-and-mouth disease and not subjected to sanitary restrictions linked to infectious diseases of the species.
- Furthermore, the manufacturing process includes boiling at 100°C for a minimum of 5 minutes and instantaneous heating at 160°C on spray drying.

N° 19 - Note 19
Casein peptone (Biolife REF: BL2BEP010S): each batch is supplied with the Sanitary Certificate declaring that:

- The product does not contain and is not derived from specified risk material as defined in Commission Decision 2000/418/EC.
- The product has been prepared from raw materials of bovine origin which are classified in category IB (lower infectivity tissue) according to the EMA/410/01 rev.3.
- The raw materials were collected in New Zealand.
- The raw materials come from animals not showing clinical signs of a disease that can be transmitted through the milk.
- There is no validated procedure during the manufacturing process in order to eliminate or inactivate infectious agents. The procedure recommended in EEC Note for Guidance III/3298/9EN would adulterate the product. However, the manufacturing process includes a 30 minutes heat treatment at 95± 5°C.
- The product contains no genetically modified vegetable raw materials, enzymes or other additives.
- The enzymes used during the manufacturing process are obtained from pork pancreas: The country of origin of the animals is France. The pancreatin used in production is subjected to heating at 80°C for a minimum of 4 hours.
- Raw materials are issued from animals coming from holdings free from foot-and-mouth disease and not subjected to sanitary restrictions linked to infectious diseases of the species.
- The casein used on manufacturing is obtained via acid precipitation
- The official veterinarian, in accordance with the information supplied by the manufacturer, attests that there is no commingling with any other animal material during processing and that all animal raw materials present in the plant are issued from animal free of foot-and-mouth disease.

N° 20 - Note 20
Peptonized milk(Biolife REF: BL2BEP021): each batch is supplied with the Health Certificate for dairy products derived from milk cows, ewes, goats, and buffaloes for human consumption from third countries or parts thereof authorized in column B of Annex I to Reg. (EU) n° 605/2010 intended for importation into European Union, including health information, Public Health attestation, notes.

N° 21 - Note 21
Oxgall (Biolife REF: BL2BEU006) has been certified by Council of Europe, European Directorate for the Quality of Medicines (Certification of Suitability n° R1-CEP 2000-383 Rev.03), declaring the countries of origin of source materials for manufacturing bile acids and derivatives: Argentina, Australia, Belgium, Brazil, Canada, Chile, Colombia, Denmark, Ecuador, France, Germany, India, Ireland, Italy, Mexico, Netherlands, New Zealand Panama, Paraguay, South Africa, Spain, Uruguay, USA, Venezuela.
Each batch is supplied with a Manufacturer's Declaration for Intermediate Products declaring that Bile Salts is a product:

- already highly purified and is used without further purification to manufacture medical devices, in-vitro diagnostics and laboratory reagents.
- derived from material sourced from only healthy animals which have passed ante- and post-mortem inspection in government approved slaughterhouses and have been found free of contagious diseases of quarantine concern and therefore fit for human consumption (i.e. category 3)

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- derived from bovine bile sourced from USA as well as ovine bile sourced from New Zealand.
- According to EMA/410/01 rev 3, bile has been classified under the lowest risk category IC "Tissue with no detectable infectivity". Bile is therefore not expected to contain infectivity even in infected animals showing clinical signs, indicating that bile is not considered to be a TSE risk material.
- manufactured using aggressive processing conditions including an alkaline heat treatment at pH >11 and 95-100°C for >45 minutes before being filtered at approx. 90°C (approx. 3 hours). The clarified bile is then acidified and heated to 95-100°C for 30-45 minutes and filtered (approx. 3 hours). After decolorization with a second oxidizing agent, the product is spry dried using an inlet temperature >105°C and outlet temperature >90°C.

N° 22 - Note 22
Sodium Cholate (Biolife REF: BL2BAU007) *has been certified by Council of Europe, European Directorate for the Quality of Medicines (Certification of Suitability n° R1-CEP 2000-334 REV 04).*
It is supplied with a "Health Certificate" released by the Italian Public Health Authority declaring that the product:
- Has been obtained by raw deoxycholic acid derived from ox bile
- Derives from animals free from BSE
- Derives from animals which were found healthy before and after slaughtering
- Derives from animal which were not fed with animal proteins
- Has been submitted to a thermic process for at least 8 hours to a minimum temperature of 140°C.

The Health certificates of the supplied batches, declare the country/countries of origin of the product.

N° 23 - Note 23
Sodium Desoxycholate (Biolife REF: BL2BAU006) *has been certified by Council of Europe, European Directorate for the Quality of Medicines (Certification of Suitability n° R1-CEP 2000-335 REV 03).*
It is supplied with a "Health Certificate" released by the Italian Public Health Authority declaring that the product:
- Has been obtained by raw deoxycholic acid derived from ox bile
- Derives from animals free from BSE
- Derives from animals which were found healthy before and after slaughtering
- Derives from animal which were not fed with animal proteins
- Has been submitted to a thermic process for at least 8 hours to a minimum temperature of 140°C.

The Health Certificates of the supplied batches, declare the country/countries of origin of the product.

N° 24 - Note 24
Skim Milk (Biolife REF: BL2BEP022) is a powdered milk intended for human consumption. The risk classification is not applicable.

N° 25 - Note 25
Brain Heart Infusion Pork (Biolife REF BL2BEP005P): each batch is supplied with the Sanitary Certificate declaring that:
- The mentioned product consists exclusively of hydrolyzed protein not intended for human consumption.
- The mentioned product has been prepared and stored in a plant approved validated and supervised by the competent authority in accordance with article 24 and where appropriate article 14 of Reg. (EC) n° 1069/2009 in order to kill pathogenic agents.
- Animal species: porcine
- The country of origin of animals is USA, the country of born, raised and slaughtered is USA, the country of manufacture of the finished product is Mexico.
- The country of origin of enzyme from porcine pancreas is USA.
- Part of animals: brain and heart.
- The processing facility does not receive, store, process ruminant material from any BSE country listed in CFR 94.18 (a), with the exception of milk products (Europe, Oman, Israel, Canada and Japan).

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- These animals were slaughtered in authorized establishments and were subjected to permanent veterinary inspection. The said animals were ascertained to be in good health before and after slaughtering and were considered fit for human consumption.
- The animals did not show any pathological condition.
- The animals were prepared handles and dispatched according to hygienic requirements.
- The product has been heated to a minimum of 80°C for a minimum of 1 hour including a minimum of 30 minutes at a minimum of 105°C
- During processing no commingling or in any manner mixing with any animal material does occur
- The product was dried at a minimum of 140°C.
- Before, during and after completion of drying process every precaution was taken to prevent contamination of the product.
- The final product was packed in new containers
- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 26 - Note 26
Pork Gelatin (Biolife REF: BL2BEX003): the manufacturer of pork gelatin declares the following:

- Pork gelatin is obtained from pig skin raw material for the production of edible and pharmaceutical gelatin.
- Raw materials are bought from meat-cutting plants situated in countries approved by the European Commission.
- Pigskins originate from animals inspected and approved for human consumption.
- Raw materials transports, handling and processing comply with applicable regulations.
- Reception of raw materials, production facilities and laboratory are kept under continuous control by an official veterinary appointed by National Food Agency.

N° 27 - Note 27
Gelatin Peptone (Biolife REF: BL2BEP033): each batch is supplied with the Sanitary Certificate declaring that:

- The mentioned product consists exclusively of hydrolyzed protein not intended for human consumption
- The mentioned product has been prepared and stored in a plant approved validated and supervised by the competent authority in accordance with article 24 and where appropriate article 14 of Reg. (EC) n° 1069/2009 in order to kill pathogenic agents.
- For gelatin, animal species of raw material: porcine. The country of origin of animals is USA the country of born, raised and slaughtered is USA; the country of manufacture of the finished product is Mexico.
- The country of origin of enzyme from porcine pancreas is USA
- Part of animals: pork skin
- The processing facility does not receive, store, process ruminant material from any BSE country listed in CFR 94.18 (a), with the exception of milk products (Europe, Oman, Israel, Canada and Japan)
- These animals were slaughtered in authorized establishments and were subjected to permanent veterinary inspection. The said animals were ascertained to be in good health before and after slaughtering and were considered fit for human consumption.
- The animals did not show any pathological condition.
- The animals were prepared handles and dispatched according to hygienic requirements.
- The product has been heated to a minimum of 80°C for a minimum of 1 hour including a minimum of 5 minutes at a minimum of 105°C after addition of enzymes
- During processing no commingling or in any manner mixing with any animal material does occur
- The product was dried at a minimum of 140°C.
- Before, during and after completion of drying process every precaution was taken to prevent contamination of the product.
- The final product was packed in new containers

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- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 28 - Note 28
Gelatin Peptone (Biolife REF: BL2BEP034): each batch is supplied by the manufacturer with a Sanitary certificate declaring that:
- None of the raw materials and auxiliaries used in its preparation is of bovine origin.
- The raw material is of porcine origin.
- The manufacturing process includes boiling at 100 °C for a minimum of 5 minutes and instantaneous heating at 160°C on spry drying.

N° 29 - Note 29
Liver Extract (Biolife REF: BL2BEP006): each batch is supplied with a Health Declaration stating that:
- The country of origin and manufacturing is Italy.
- The product is for technical use and produced in a factory registered according to Reg. (EC) n°1069/2009 for the manufacturing of intermediate and pharmaceutical products under official control by the local Health Authority.
- Adequate precautions have been taken to avoid contamination of raw materials or their derivatives by pathogens and cross-contamination between different typology of products.
- Liver is a Category 3 by product coming from animals submitted to ante and post mortem inspection, found healthy and free from infectious diseases in act as for the Veterinary Certificate of raw material.

N° 30 - Note 18 or 19
Tryptose (Biolife REF: 412260): Tryptose is a mixture of peptones of animal and non-animal origin. It contains casein peptone and the notes 15 or 16 are applicable.

N° 31 - Note 1 and 18
Peptocomplex (Biolife REF: 412310): Peptocomplex is a mixture of peptones of animal and non-animal origin. It contains casein peptone and meat peptone and the notes 1 and 15 are applicable.

N° 32 to 36 - Note 30
Animal Blood derivatives (Biolife REF: BL2MAZ001, BL2MAZ003, BL2MAZ007, BL2BEB058, BL2BEB059): the facility where the blood is collected has been authorized by the local municipality and by Ministry of Health for the production of blood, serum and plasma for IVDs and microbiological culture media applications. The facility is under the supervision of a Veterinary and the responsible of animal welfare.

N° 37 - Note 31
Chicken eggs (Biolife REF: BL2FAU007): the facility of the supplier is authorized by Regione Lombardia USL n° 65 and by Ministry of Agriculture for classification and packaging of chicken eggs. Each batch is supplied with a Document of Regione Lombardia concerning the transport of animal derivatives according to Reg. (EC) n° 1069/2009.

N° 38 - Note 32
Acid Hydrolysate of Casein (Biolife REF: BL2BEP003): each batch is supplied with the Certificate of Origin according to EU1069/2009 (Category –Intermediary Product) stating that the country of manufacturing is New Zealand, the country of origin is United States.
The protein source comes from bovine milk (casein), obtained from healthy cows for human consumption. Milk is classified as a Category C material (no detectable infectivity). No other ruminant derived materials were used in the manufacture. The protein is chemically hydrolyzed. No enzymes are used it the manufacture of this product.

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N° 39 - Note 33
Bovine Fibrinogen + Soybean Typsin Inhibitor – 5% frozen solution(Biolife REF: BL2EAF055X): each batch is supplied with the Certificate of origin stating that:

- The product is made in France. Registration of the establishment controlled by the veterinary authority: FR 51424377300017
- The product is obtained from bovine plasma.
- The product is from animals that have been slaughtered in an authorized slaughterhouse and, following and ante-mortem inspection, which have not shown any sign of disease transmissible to humans or animals
- The product has been handled in a way to prevent contamination
- The product only intended for scientific purposes (not for drug, human, veterinary use)

N°40 – Note 34
Beef heart infusion (Biolife REF: BL2BEP060): *has been certified by Directorate for Quality Medicines (Certification of Suitability n° R1-CEP 2007-139 REV.01).*
Each batch is supplied with the certificate, released by the authorized veterinarian inspector, stating that:

- The product consists of hydrolyzed protein that satisfied the health requirement
- The product consists exclusively of hydrolyzed protein not intended for human consumption
- The product has been prepared and stored in a plant approved, validated and supervised by the competent authority in accordance with article 24 and were appropriate article 14 of regulation (EC) N° 1069/2009, in order to kill pathogenic agents.
- For meat, animal species of raw material: bovine; country of origin of animals: New Zealand; Country of born, raised and slaughtered: New Zealand
- Part of animal: heart
- Country of manufacture of the finished product: Mexico
- According to WHO/EMC/ZOO97.3 category, the risk category of the main component is class IV
- According to EMA/410/01 Rev.3, the risk category of the main component is class IB
- The processing facility does not receive, store, process ruminant material from any BSE country listed in CFR 94.18 (a), with the exception of milk products (Europe, Oman, Israel, Canada and Japan).
- These animals were slaughtered in authorized establishments and were subjected to permanent veterinary inspection. The said animals were ascertained to be in good health before and after slaughtering and were considered fit for human consumption.
- The animals did not show any pathological condition.
- The animals were prepared handles and dispatched according to hygienic requirements.
- The product has been heated to a minimum of 80°C for a minimum of 1 hour including a minimum of 30 minutes at a minimum of 105°C
- During processing no commingling or in any manner mixing with any animal material does occur
- The product was dried at a minimum of 140°C.
- Before, during and after completion of drying process every precaution was taken to prevent contamination of the product.
- The final product was packed in new containers
- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 28 - Note 35
Gelatin Peptone (Biolife REF: BL2BEP034): each batch is supplied by the manufacturer with the certificate, released by the authorized veterinarian inspector, stating that:

- The product consists of hydrolyzed protein that satisfied the health requirement
- The product consists exclusively of hydrolyzed protein not intended for human consumption

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- The product has been prepared and stored in a plant approved, validated and supervised by the competent authority in accordance with article 24 and were appropriate article 14 of regulation (EC) N° 1069/2009, in order to kill pathogenic agents.
- For gelatin, animal species of raw material: porcine; country origin of animals: USA; country of born and raised: USA; country of slaughtered: USA
- Enzyme animal species: porcine (derived from pancreas); country of origin: USA
- Part of animal: skin
- Country of manufacture of the finished product: Mexico
- The processing facility does not receive, store, process ruminant material from any BSE country listed in 9 CFR 94.18 (a), with the exception of milk products (Europe, Oman, Israel, Canada and Japan).
- These animals were slaughtered in authorized establishments and were subjected to permanent veterinary inspection. The said animals were ascertained to be in good health before and after slaughtering and were considered fit for human consumption.
- The animals did not show any pathological condition.
- The animals were prepared, handles and dispatched according to hygienic requirements.
- The product has been heated to a minimum of 80°C for a minimum of 1 hour including a minimum of 5 minutes at a minimum of 105°C after addition of enzymes.
- During processing no commingling or in any manner mixing with any animal material does occur
- The product was dried at a minimum of 140°C.
- Before, during and after completion of drying process every precaution was taken to prevent contamination of the product.
- The final product was packed in new containers
- The product was tested s per BIOTECNICA INTERNATIONAL, S.A. DE C.V. test procedures and conformed to specifications.
- Mexico does not have BSE, rinderpest, foot and mouth disease, African swine fever, swine vesicular disease.

N° 3 - Note 36
Meat Peptone (Biolife REF BL2BEP045): each batch is supplied with the Veterinary Certificate to EU released by Regional Office3NR Animal Quarantine and Sanitary Certification Service, Ministry of Agriculture & FW, Government of India.

PROCESS VALIDATION
Biolife Italiana Srl has no information regarding prion inactivation studies.
However, Biolife Italiana Srl purchases ruminant origin materials from countries with no endemic cases of BSE.

The information provided in this document is the best of our knowledge at the moment and should be used only for regulatory purposes.

Revision n° 30 prepared by: Valentina Surace
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Biolife Italiana Srl

Date: 21st December 2023