TO THE ATTENTION OF:

Capsugel
A Lonza Company

CERTIFICATE OF ANALYSIS

The capsules are produced under carefully controlled conditions. Controls are performed continuously throughout the process and guarantee that capsules conform to the highest quality standards. The capsules described below conform to the specifications as defined in the current edition of the Capsugel "Technical Reference File".

PRODUCT DESCRIPTION Empty Hard Gelatin Capsules - Coni-Snap® (Bovine and/or Porcine Origin)

Customer:	Acofarma Distribución, S.A.	Lot Number:	3641572
Product Name:	CAPS GEL 0 BLANCAS	Customer Reference:	2576
Product Code:	M0012380	Product Size:	Size 0, Coni-Snap, Standard
Manufacturing Date:	06-Nov-2022		
Expiration Date:	05-Nov-2027		

BODY

Code:	44.000
Name:	WHITE OP.
Print Type:	Non-Print

CAP

Code:	44.000
Name:	WHITE OP.

Body Composition		Cap Composition	
Titanium dioxide	2.0000 %	Titanium dioxide	2.0000 %
GELATIN	qsp 100 %	GELATIN	qsp 100 %

Due to the nature of raw materials, their sourcing, and technology improvements, the colorant composition data indicated are target values and actual values may vary to insure the consistency of lot color. Capsugel supports the expiry date if precautions for warehousing and transportation are observed (recommended: 15°C - 25°C and 35% - 65% relative humidity).

Ingredient / Reference	E Nr	C.I. Nr	Function	Regulatory References
Titanium dioxide	E171	77891	Opacifier	(EU) 231/2012, 21 CFR, EP, JP, USP/NF
GELATIN			Structure	EP, JP, USP/NF, CHP

ANALYTICAL DATA

Characteristics	Test Method	Units	Specifications	Results
Identification of gelatin	TRF 001A		Positive	pass *
Identification of TiO2	TRF 007A		Conforms to composition	pass *
Sulphated ash	TRF 200A	%	Less than 7	pass *
Lubricant content (Soxtherm)	TRF 202B	%	Less than 0.5	0.02 *
Sulphur dioxide	TRF 201A	ppm	Not more than 10	I *
Disintegration time	TRF 300A	min/sec	Less than 10:00	02:08 *
Loss on drying	TRF 101A	%	13.0 to 16.0	14.8
Average weight	TRF 100A	mg	90.0 to 102.0	94.8
Total Aerobic Microbial Count	TRF 500A	cfu / g	Less than 1000	< 10
Escherichia coli	TRF 520A		Absence in 1 gram	pass *
Salmonella	TRF 550A		Absence in 10 gram	pass *
Staphylococcus aureus	TRF 530A		Absence in 1 gram	pass *
Pseudomonas aeruginosa	TRF 540A		Absence in 1 gram	pass *
Total Yeasts/Moulds Count	TRF 510A	cfu / g	Less than 100	< 10 *

*** Reduced frequency testing**

Elemental Impurities / Heavy Metals

With reference to ICH Q3D and other applicable standards controlling levels of elemental impurities in drug products and food supplements, Capsugel empty capsule products are meeting below levels of applicable elements. Monitoring testing is in place under validated methods, as described in the current edition of Capsugel's applicable Technical Reference File. A documented risk assessment based on the ICH Q3D principles is available on www.mycapsugel.com.

Element	Unit	Acceptance Level
Arsenic	ppm	Not more than 1
Lead	ppm	Not more than 1
Cadmium	ppm	Not more than 0.5
Mercury	ppm	Not more than 0.1
Cobalt	ppm	Not more than 5
Vanadium	ppm	Not more than 10
Nickel	ppm	Not more than 20
Chromium	ppm	Not more than 2

METAPHARMACEUTICAL

N DE LOTE:
0230923

25 ABR. 2023

Nº lote ACOFARMA:
226624

Firma y fecha: 29/11/22

CERTIFICATE OF ANALYSIS

Customer Name: Acofarma Distribución, S.A.

Lot Nr: 3641572

Residual Solvent Statement

In accordance with ICH Q3C residual solvent guideline, Class 3 solvents may be used according to good manufacturing practices such that their cumulative value does not exceed 5000ppm or 0.5%, under option 1 as defined in ICH Q3C, USP<467>, and EP General Text 5.4.

Physical Characteristics

Defect levels are in conformance with the Coni-Snap® specification for Visual attributes, as defined in the table below.

Defect Group	Class I	Class II	Class III
	Visual	Visual	Visual
Sigma Level	4.9	4.7	4.2
PPM	<290	<670	<3600

Appearance - Clean empty capsules, meeting the specified requirements of color and size.
Odor - Free of disagreeable odor.
The reported disintegration time is subjective, and is provided to indicate Pass/Fail status for 10 minutes.
Empty hard gelatin capsules are conform with the Japanese Pharmacopoeia monograph for capsules.

Nº lote ACOFARMA:
226624
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CERTIFICATE OF ANALYSIS

Customer Name: Acofarma Distribución, S.A.

Lot Nr: 3641572

TSE/BSE Regulations

For this empty capsule product, Lonza can use blends of several gelatins of bovine and/or porcine origin. Related to the specific regulations aiming to secure the TSE/BSE safety, Lonza sources bovine gelatin fully complying with the following:
International Guidance
OIE – Terrestrial Animal Health Code – Chapter 11.4 BSE.
Europe:
Note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (EMA/410/01 rev.3), which is published by the European Commission following Commission Directive 2003/63/EC, (amending Directive 2001/83/EC on the Community code relating to medicinal products for human use), Annex I, Part I, paragraph 3.2.2.4. Control of excipients.
These Directives require that applicants for Marketing Authorization must demonstrate that medicinal products are manufactured in accordance with the latest version of this Note for Guidance and compliance is demonstrated by the "Certificate of Suitability" issued to the manufacturer of the bovine gelatin by the European Directorate for the Quality of Medicines (EDQM). As such, from January 2022, Lonza manufactures capsules under any (or all) of the following Certificates of Suitability:

- Rousselot R1-CEP 2000-029-Rev 05
- Rousselot R1-CEP-2010-043-Rev 00
- Tessenderlo Group R1-CEP 2000-045-Rev 04
- Gelita Group R1-CEP 2001-424-Rev 03
- Sterling Gelatin R1-CEP 2001-211-Rev 01
- Nitta Gelatin R1-CEP 2000-344-Rev 03
- Nitta Gelatin R1-CEP 2005-217-Rev 02

Regulation (EC) No 853/2004 laying down specific hygiene rules for food of animal origin.
Regulation (EC) No 999/2001 laying down rules for the prevention, control and eradication of certain transmissible spongiform encephalopathies.
US:
United States Food and Drug Administration - 21 CFR Part 189 – "Substances Prohibited from Use in Human Food: Prohibited Cattle Materials.
United States Department of Agriculture (USDA) – 9 CFR 94.23 Importation of Gelatin Derived from Bovines.
Japan:
Japanese Ministry of Health, Labor Welfare (MHLW) - "Food Sanitation Law", Chapter 2, Article 7 and Article 10 "Specifications and Standards for Food or additives" revised and announced by MHLW Notice No.0327-2 of March 27, 2015.
Japanese Ministry of Health, Labor and Welfare - Notification No. 210 of the MHLW issued on May 20, 2003 and the latest version by Notification No. 1002-27 about the partial amendment of the criteria eliminating source country restrictions, applicable from November 25th 2014.
The bovine bone starting material is derived from healthy animals that were slaughtered in a slaughterhouse and that passed an ante-mortem and post-mortem inspection by an official veterinarian.
For what concerns specified risk materials (SRMs), next to the removal of skulls and spinal cords, Lonza's bovine bone gelatin suppliers certify vertebrae removal independent from the geographical origin and/or age of the animals.
Lonza continuously monitors all regulatory activities; please let us know if there are further questions or clarification needed.
Revision history:
September 2015: Actualization of list of applicable CEPs and legislative references
November 2016: Actualization of US Interim Final Rule to Final Rule
July 2017: Introduction R1-CEP-2010-043 and discontinuation R1-CEP 2001-332, R1-CEP 2003-172, R1-CEP 2000-027 and R1-CEP 2002-110 as from October 1st, 2017
June 2019: Update of R1-CEP-2000-045 from Rev03 to Rev04, Update from R1-CEP-2005-217 from Rev00 to Rev01. Discontinuation of R1-CEP-2004-247 and R1-CEP-2004-320
July 2019: Update of R1-CEP-2005-217 from Rev01 to Rev02
October 2019: Update of R1-CEP 2000-344 from Rev02 to Rev03
January 2020: New LONZA template
September 2021: CEPs in attachment replaced by recently signed versions

Manufacturing Processes:

No Addition of Preservatives
No Ethylene Oxide Treatment
No Irradiation Treatment

Nº lote ACOFARMA: 226624
Firma y fecha: 29/11/22

Capsugel Belgium NV
Sophie De Keersmaeker - Quality Assurance
Rijksweg 11 - 2880 Bornem -Belgium
Tel: +32 (0)3 8900588

Digitally approved by Roel Moernaut (Nov 21 2022, 12:28:51)
Authorized Signer