Statement on TSE/BSE Safety Framework

Capsugel® empty gelatin-based capsule products

As a global supplier of empty capsules, Lonza strives to maintain broad compliance with worldwide applicable regulations for our finished products and when sourcing our raw materials. For our Capsugel® hard empty gelatin capsules, Lonza can use blends of several high-quality gelatin sources of bovine and/or porcine origin in compliance with a broad set of pharmaceutical and/or food regulatory statutes.

More specifically, regarding the gelatin of bovine origin, Lonza has closely followed worldwide BSE (Bovine Spongiform Encephalopathy) regulatory evolutions since initial legislative publications as a critical selection criterium in bovine gelatin sourcing strategies.

The vast majority of worldwide regulators in Europe, the US, and Asia Pacific have adopted the international guidance for BSE safety outlined by the WOAH (World Organization for Animal Health) Terrestrial Animal Health Code in their specific regulations aiming to secure TSE/BSE safety.

Lonza's gelatin suppliers source their bovine gelatin starting materials from any geographical origin listed on their granted Certificates of Suitability and apply the alkaline treatment during bovine gelatine manufacturing under conditions required by the respective BSE safety regulations.

As such, Lonza sources bovine gelatin complying as a minimum with the below legal requirements as set out by food and/or pharmaceutical regulatory bodies:

International Guidance:

- WOAH – Terrestrial Animal Health Code – Chapter 11.4 BSE.

Europe – Pharma:

- 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.
- This Directive requires 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).

Europe – Food:

- 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."

In accordance with 21 CFR 189.5, the bovine gelatin used in Capsugel® empty hard gelatin capsules meets the definition of materials permitted for human use and is therefore considered out of scope for this regulation. The gelatin is manufactured using industry-standard processes shown to significantly reduce potential BSE infectivity, and does not contain prohibited cattle materials as defined by FDA.

- United States Department of Agriculture (USDA) – 9 CFR 94.23 Importation of Gelatin Derived from Bovines.

For U.S.-bound capsules, Lonza further confirms that our bovine gelatin suppliers:

1. Source bones from cattle that have passed ante-mortem and post-mortem inspection
2. Do not include skulls or vertebral column from cattle 30 months of age or older
3. Apply a validated gelatin manufacturing process that includes:
    - Degreasing
    - Acid demineralization
    - Acid or alkaline treatment
    - Filtration
    - Sterilization at 138°C or higher for at least 4 seconds
4. Ensure the final gelatin is not commingled with any ineligible materials for U.S. entry

This sourcing approach supports compliance with 9 CFR Part 94.23, which governs the importation of bovine-derived gelatin intended for human use in the United States.

Japan – Food:

- 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.

Lonza acknowledges that there may be specific countries and/or target markets that require more stringent measures in bovine animal geographical sourcing and/or tissues used and will continue to foresee the availability of Capsugel® empty capsule supplies in compliance with these more restrictive bovine gelatin sourcing requirements of these countries upon request.

The specific BSE safety compliance declaration for your specific capsule products is available on your batch Certificates of Analysis.

Lonza is dedicated to ensuring that you receive the highest-quality products and services. If you have additional questions or would like additional information, please contact your local Lonza representative.

Revision History

Last update	Update description
June 2025	Updated U.S. section to align with 21 CFR 189.5 and 9 CFR 94.23; clarified regulatory scope and removed importer-specific documentation language.
July 2023	Initial issue – BSE safety declaration based on minimum requirements

The information contained herein corresponds to Lonza's knowledge on the subject at the date of publication and is, to the best of our knowledge, accurate. However, Lonza refuses any liability for the application and use of further processed material containing our products. According to the relevant regulations, the manufacturer of the final product is solely responsible for the use and commercialization of the Lonza product and the information contained herein.

For further information, please contact your Lonza account representative.

Products: Hard Gelatin
Sites: Bornem BELGIUM, Colmar FRANCE, Greenwood USA, Puebla MEXICO

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