CERTIFICATE OF ORIGIN

Collagenase HA

Version Aug 2025

COUNTRY OF ORIGIN

Collagenase HA, Catalogs #001-1000, #001-1050 and #001-1070 are manufactured entirely within the United States by VitaCyte, LLC.

STATEMENT OF ANIMAL ORIGIN

The only animal sourced material used in the manufacture of Collagenase HA is porcine gelatin peptone during the fermentation of the *Clostridium histolyticum* organism to stimulate collagenase biosynthesis. Prior to inoculation with the organism, the culture media is sterilized for 30 minutes at 121°C, a process shown to inactivate many viruses.[1,2] The subsequent purification process largely removes culture media components. The rest of the manufacturing process is entirely animal free.

RISK OF TRANSMISSIBLE SPONGIFORM ENCEPHALOPAHTY

None of the components used in the Collagenase HA product use or come into contact with any material of bovine origin during the manufacturing process. The use of porcine derived components represents a minimal risk of Transmissible Spongiform Encephalopathy (TSE). No evidence exists for naturally occurring TSE in pigs or transmission to pigs from infected tissue.[3] In addition, 'Note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products' (EMA410/01 rev.3) and European Pharmacopeia Chapters 5.2.8 indicates that pigs are not defined as 'TSE-relevant animal species'.

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1 International Federation for Animal Health Europe. (2012) Viral Inactivation Related to Steam Sterilisation of Biological Products. Report available at https://www.vitacyte.com/wp-content/uploads/2025/01/IFAH-Europe-Sept-2012-Virbac-Laboratories.pdf

2 Sofer, G, Lister, D, Boose JA. (2003). Virus Inactivation in the 1990s – and into the 21st Century Part 6, Inactivation Methods Grouped by Virus. BioPharm International. 16(4)S-37-42

3 Wells, G.A.H.; et al. Portrait of experimental BSE in Pigs. In: Hornlimann, B.; Riesner, D.; Kretzschmar, H., eds. Prions in humans and animals. New York/Berlin: Walter de Gruyter; 2007: 275-278.

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