Summary of the dossier: Nonapeptide and Pentapeptide Mixture

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Caregen submits this application for the approval of Nonapeptide and Pentapeptide mixture as a novel food. The application has been prepared in accordance with the requirements of Commission Implementing Regulation (EU) 2017/2469 of 20 December 2017 laying down administrative and scientific requirements for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods, the European Food Safety Authority (EFSA) Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283, and EFSA's Administrative guidance on the submission of applications for authorisation of a novel food pursuant to Article 10 of Regulation (EU) 2015/2283.

Nonapeptide and Pentapeptide mixture (Trade name: Deglusterol) is a powdered ingredient comprising a combination of 2 synthetic peptides Nonapeptide (Trade name: Deobetide) and Pentapeptide (Trade name: Adiporin) which are composed of the following amino acids: alanine, arginine, asparagine, glycine, leucine, lysine, methionine, serine, threonine, tryptophan. The peptides are independently produced and then mixed to form the final ingredient. The mixture is proposed to be used in food supplements for adults, excluding pregnant or lactating women, at 30 mg/day. Food supplement products containing Nonapeptide and Pentapeptide mixture will be labelled with a statement to the effect that they should be consumed by adults only, excluding pregnant or lactating women.

Analysis of several independent representative batches of the Nonapeptide and Pentapeptide mixture and of their component peptides, demonstrates that the manufacturing process produces a consistent product that complies with the established specifications and is free of chemical and microbiological contaminants. Analytical data demonstrate that residues of the processing aids are either undetectable or within levels that do not present a safety concern. Stability data demonstrate that the Nonapeptide and Pentapeptide mixture, alone and in the final product, is stable under accelerated conditions that are equivalent to 2 years at ambient conditions.

Nonapeptide and Pentapeptide are likely to be digested by peptidases in the intestinal lumen before being absorbed as amino acids, after which point they would be indiscernible from endogenous amino acids. An *in vitro* digestibility study showed that Nonapeptide and Pentapeptide were completely degraded in simulated intestinal fluid. Nonapeptide and Pentapeptide were not detected in any of the plasma samples collected from rats and dogs in the 90-day studies conducted with the Nonapeptide and Pentapeptide mixture, demonstrating that it is not systemically available following repeated administration. The allergenic risk of the Nonapeptide and Pentapeptide mixture is considered to be low due to the complete digestion of the protein under gastric and/or intestinal conditions.

A comprehensive battery of toxicology studies was conducted with batches of the Nonapeptide and Pentapeptide mixture that are representative of the ingredient intended to be commercially marketed, and in accordance with Good Laboratory Practice and appropriate internationally recognised test guidelines, where applicable. The Nonapeptide and Pentapeptide mixture was confirmed as non-genotoxic *in vitro* and *in vivo*. The 90-day repeat dose studies in rats and dogs demonstrated the safety of the Nonapeptide and Pentapeptide mixture at the highest doses tested. The results of the 90-day rat study provide a margin of safety of 595-fold from its intended use in food supplements. The safety of Nonapeptide and Pentapeptide mixture is corroborated by the results of a clinical human study wherein

consumption of 30 mg Nonapeptide and Pentapeptide mixture per day for 12 weeks was concluded to be safe.

Together, the weight of the available evidence on the Nonapeptide and Pentapeptide mixture supports the safe use of the ingredient under the proposed conditions of use.