

Summary of the dossier: Zinc L-carnosine

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The application is submitted pursuant to Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, for the authorisation of zinc L-carnosine, a chelated complex compound consisting of Novel Food L-carnosine and zinc, as a Novel Food for use in food supplements.

Zinc L-carnosine is being proposed as a source of zinc at a dose of no more than 34 mg zinc per day (150 mg of zinc L-carnosine). This product has been available outside of Europe for a significant length of time, for the treatment of gastric ulcers (Japan [1994] and South Korea [2009]) and as a zinc supplement (US [2002], Canada [2014] and Australia [2015]).

Human pharmacokinetics, animal toxicity and human clinical trials information on zinc L-carnosine were provided in this submission dossier. Zinc L-carnosine is composed of zinc and L-carnosine, both substances found in the body, and dissociates into these separate components after ingestion. Zinc and L-carnosine are both absorbed and utilized by the body in a range of physiological processes. Although the absorption of zinc is known to vary greatly based on physiological needs as well as dietary factors, zinc from zinc L-carnosine has low absorption and is primarily eliminated in feces. L-carnosine is metabolized further to L-histidine which is primarily used in the production of proteins.

The activity of zinc L-carnosine in gastric support has been attributed to its slow dissociation and persistent presence in the gut with no systemic effects. Hence, the toxicity of zinc L-carnosine was found to be low. Serious adverse effects are only seen at high doses when the zinc contents exceed European Food Safety Authority's reported No Observed Adverse Effect Level (NOEL) of 50 mg zinc per day, and in niche populations of individuals with reduced liver functions, which is a general warning applicable for all substances metabolized by the liver, and in niche populations of copper deficient individuals, which is also a general warning applicable for all zinc supplements.

The use of zinc L-carnosine is supported by many clinical trials with the three largest trials having 4,879 volunteers, 691 volunteers and 202 volunteers. From the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) and clinical trials, the suggested and recommended use level is 150 mg zinc L-carnosine (34 mg zinc) per day in adults, and 100 mg zinc L-carnosine (23 mg zinc) per day in the elderly population. For the avoidance of doubts, children, pregnant woman, nursing women, individuals with reduced liver functions and copper-deficient individuals should only take zinc L-carnosine under direct supervision by a health professional. The aforementioned ADMET and clinical trial information were obtained from zinc L-carnosine that was manufactured under current Good Manufacturing Practices (cGMP) for active pharmaceutical ingredients.

These ADMET and clinical information are not applicable for any zinc L-carnosine substance that is manufactured under lower quality management. Hence, it is recommended that zinc L-carnosine as a Novel Food a) conforms to the Japanese Pharmacopoeia's monograph, b) is routinely compliant to the specifications, meaning that batch-to-batch quality is consistent over time, c) is qualified by a zinc L-carnosine reference standard qualified by the Japanese governmental organization, Pharmaceutical and Medical Devices Agency, d) is packaged in containment systems conforming to EU/EC regulations, e) has a shelf-life supported by accelerated stability study during transport and Zone II

long term stability study during storage, f) has at least one lot per year be placed on long term stability to monitor for changes. In sum, in consideration that zinc L-carnosine has been available outside of Europe for a significant long time since 1994, that there is sufficient ADMET and human data to prove its safety, and that its manufacture is managed under high quality standards, zinc L-carnosine should be approved as a Novel Food.