Summary of the dossier: D-glyceric acid, (may contain also L-enantiomer of glyceric acid (2,3-dihydroxy propanoic acid), trade name Panavital

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This application concerns the placing in the European Union market of the novel food D-glyceric acid (may contain also L-enantiomer of glyceric acid (2,3-dihydroxy propanoic acid), trade name Panavital produced by fermentation suing naturally occurring bacteria, followed by a number of purification steps involving centrifugation, electrodialysis, precipitation, and drying.

Panavital is to be used in a number of food applications (foods intended to facilitate the expenditure of muscular effort, coffee, tea and herbal infusions and drinks, milk based products (unflavoured pasteurised and/or unflavoured and/or flavoured heat treated fermented milk products), cereal bars, table top sweeteners, fruit and vegetable drinks, flavoured drinks, and food supplements).

The application has been compiled in line with the administrative and scientific requirements of Commission Implementing Regulation (EU) 2017/2469 laying down for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. It is also in line with 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.

Panavital (reg. trademark), consists of D-glyceric acid, may contain also L-enantiomer of glyceric acid (GA or 2,3-dihydroxy propanoic acid). It has a molecular weight / molar mass: 106,0773 g/mol. Glyceric acid and its salts are water soluble substances. As a small molecule, GA is very easily absorbed into the body. It can be administered as such but in practical applications it is more convenient to form water soluble salt formulation that can be dried to powder formulation, e.g. with calcium, zinc or magnesium. Commercial formulation is typically a dry powder, e.g. calcium salt of glyceric acid that contains small amounts of crystallized water.

The biologically active enantiomer, D-GA metabolizes into glycolysis in a one-step reaction catalysed by glycerate kinase enzymes. In certain conditions D-GA can also be reversely synthesised from glycolysis in trace concentrations. As a fully natural metabolite, D-glyceric acid can be a priori considered safe at low / physiological concentrations. D-GA enhances energy metabolism of the tissues locally and by doing so it possesses also positive systemic enhancements all over the body, e.g. in the intestines. It is mainly excreted from the body via glycolysis into pyruvate and further to mitochondrial energy metabolism that forms CO2 and water as its natural end products.

The applicant's assessment considers that GA does not pose a safety risk to human health is based on toxicity and normal feeding tests with animals ranging from rats, mice, broiler chickens to worms (*C.elegans*). Neutral to positive health effects in 5-week GA administration to broiler chickens have been verified in reported 5 scientifically controlled feeding tests. Analyses by professional avian pathologist show that in 6 commercial field trials the intestinal health status of the birds has been good throughout the rearing. Importantly, this observation differs from similar rearing tests without coccidiostats in which follow up infections have typically showed up at some point. Additionally, also so called footpad dermatitis scores and other health indicators from very wide slaughterhouse reports show that the addition of GA into feed provides health benefits. From the toxicity tests, it can

be concluded that even with clearly higher doses than the maximal tested dose with broiler chickens do not result in any observable toxicity effects.

The applicant has also conducted numerous *in vitro* studies with e.g. rat neurons and many primary cells with no toxicity observed. In a 3-week in vivo tolerance study with male and female rats the daily doses of D-GA calcium salt (mixed into feed) were 100 mg, 500 mg and 1000 mg / kg of body weight (BW). In this *in vivo* experiment, 45 rats (24 males and 21 females) were tested in Finnish National Institute of Health. In comparison, recommended daily dose for broiler chickens for fattening ranges from some 5 mg/kg of body weight (BW) on average to some 10 mg / kg of BW on average, i.e. the studied rats received continuously in maximum 200 times the doses for broiler chickens. Tolerance / safety results from this study indicate that there was “no toxicity observed” in any of the groups.

A 6 day lasting and extremely wide dose-range toxicity and tolerability study of glyceric acid with *C. elegans* worms has also been performed in worms (*C. elegans*) at Biomedicum, University of Helsinki. The study showed some general toxicity effects at only the highest tested dose. All other doses were well tolerated. In vitro tests have been conducted also with human tissues (donated primary cells) showing no toxicity.

In light of the results of the toxicity studies conducted, and the recommended doses for humans which are less than one percent of the non-toxic doses observed in rats, the applicant has concluded that glyceric acid is extremely well tolerated and safe at the recommended doses.