Summary of the dossier: Fermented soy germ powder

Applicants: Nutrition & Santé SAS (BP 106, Route de Castelnaudary 31250 Revel France), Otsuka Pharmaceutical Co. LTD (2-9, Kanda Tsukasamachi, Chiyoda-ku, Tokyo, Japan)

The novel food application requests for authorization of a fermented soy germ powder (brand name: SE5-OH®). SE5-OH® is a fermented soy germ powder which is derived from a fermentation of soy germ powder with *Lactococcus* 20-92 to metabolize isoflavone daidzein to *S*-equol. The specifications of SE5-OH® are detailed and are in compliance with European legislations, in particular: microbiological aspects, contaminants (including heavy metals) and pesticides.

The targeted group is the healthy adult population. The product is not recommended for pregnant and lactating women. The present submission seeks approval for intended use of SE5-OH® as an ingredient in the food supplement category (category 17).

Regarding the manufacturing process, soy germ powder goes through a fermentation with the selected equol-producing lactic acid bacteria *Lactococcus* 20-92 in an appropriate culture medium and is then dried to ultimately yield SE5-OH® powder. The manufacturing process is performed by Otsuka Pharmaceutical in accordance with HACCP (Hazard Analysis Critical Control Point) based principles, including quality control checks and in check processes. The final ingredient is safe and respects high quality standards in compliance with EU legislations. The suggested daily efficient oral intake for adults is 10 mg/day of *S*-equol corresponding to a maximum dosage of 2000mg of SE5-OH® in food supplements. The absorption, distribution, *metabolization* and excretion of SE5-OH® and its active ingredient *S*-equol have been deeply studied in several in vitro, in vivo and human studies. SE5-OH® constituents including *S*-equol are systemically available and the distribution, metabolism and excretion and other basic toxicokinetic parameters following a single dose have been determined. The half-life of SE5-OH® (*S*-equol) constituents is short, hence there is no limited or slow excretion or any other mechanism that may underlie possible bioaccumulation. For the genotoxic endpoint, SE5-OH® has been assessed in an Ames test, an in vivo micronucleus assay and in vitro chromosome aberration test. The three genotoxicity assays were accomplished under the Guidelines on Genotoxicity Tests of Pharmaceuticals (Notification No. 1604 of the Evaluation and Licensing Division, Ministry of Health and Welfare (MHW), Japan, November 1, 1999). All studies were accomplished under the good laboratory practice (GLP) Standards for Safety Studies on Drugs (Ordinance No. 21, March 26,1997), issued by MHW, Japan. With this battery of tests, SE5-OH® showed no mutagenic or genotoxic effect. All endpoints are clearly negative; therefore, it can be concluded that SE5-OH® is not a genotoxic hazard. A subchronic 91-day oral toxicity study and an acute oral toxicity study were performed using SE5-OH®. These studies were carried out under the revisions of Guideline for Single and Repeated Dose Toxicity Studies (Notification 88) issued by the Ministry of Health and Welfare in Japan, August 10, 1993. They were also carried out under the good laboratory practice (GLP) Standards for Safety Studies on Drugs (Ordinance No. 21, March 26,1997), issued by MHW, Japan.

The safety of the daily intake of 2000 mg SE5-OH®/day is based on these two studies and the clinical studies performed with SE5-OH® involving a large number of women and men. An in vitro allergenicity study with human sera showed that two low molecular weight proteins remained in SE5-OH® following processing from raw materials. ELISA testing showed that these allergens decreased by 1/10th and 1/100th.

Therefore, while processing reduces the risk, it does not eliminate it. SE5-OH® will thus be labelled in accordance with Regulation (EU) 1169/2011 Annex II. Overall, SE5-OH® is a fermented soy germ powder which is derived from a fermentation of soy germ powder with *Lactococcus* 20-92 to metabolize isoflavone daidzein to *S*-equol, intended to be used by adults excluding pregnant and lactating women as an ingredient in food supplements at a total maximum level of 2000 mg/day. Soy will be put in relief in the ingredient list for the allergic population.

SE5-OH® is safe for the consumption by the European population at the proposed conditions of use and no adverse nutritional effects are expected at the anticipated intake level.