Public summary of the dossier: Novel food application to change the current specification of phytosterols/phytostanols

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The current authorised specification of 'phytosterols/phytostanols', as defined in the Commission Implementing Regulation (EU) 2017/2470 (Union list of novel foods), describes phytosterols/phytostanols as 'sterols and stanols that are extracted from plants and may be presented as free sterols and stanols or esterified with food grade fatty acids'. The authorized specification set limits for β-sitosterol (< 81 %), β-sitostanol (< 35 %), campesterol (< 40 %), campestanol (< 15 %), stigmasterol (< 30 %), brassicasterol (< 3.0 %), and other sterols (< 3.0 %). Phytosterols/phytostanols are authorized to be used in certain food categories presented in the Union list of novel foods with a maximum level of 3 g/day. Also, additional specific labelling requirements in accordance with Annex III.5 of Regulation (EU) No 1169/2011 are mandatory.

The present novel food application contains two phytosterols/phytostanols ingredients that are phytosterols and phytosterol esters derived from sunflower: i) ADVASTEROL 90 S F and ii) ADVASTEROL ESTER S. Sunflower phytosterols are obtained from sunflower seeds-derived sunflower oil, and sunflower phytosterol esters by esterification of sunflower phytosterols with food grade fatty acids from vegetable oil. The distribution of the phytosterol fractions in the sunflower-derived products including β-sitosterol, campesterol, stigmasterol, β-sitostanol, brassicasterol, and campestanol is in accordance with the authorized specification for phytosterols/phytostanols, while the fraction 'other sterols/stanols' is slightly higher: ≤ 7 % vs. < 3.0 %. This is due to the natural composition and proportion of sunflower-based phytosterols/phytostanols. Therefore, a specification change for the proportion of 'other sterols/stanols' from < 3.0 % to ≤ 7 % is applied in the present application to enable the use of sunflower-based phytosterols and phytosterol esters pure or in mixtures with sterols of different sources in a higher fraction.

This application does not propose any additional food categories or increased level of total phytosterols/phytostanols. The conditions under which the novel food ingredient may be used, and additional specific labelling requirements will remain in accordance with the Commission Implementing Regulation (EU) 2017/2470. Furthermore, the principles of the manufacturing process of ADVASTEROL 90 S F and ADVASTEROL ESTER S are similar to the authorized phytosterols and phytosterol esters.

The safety of different phytosterol mixtures derived from plants has been evaluated by the Scientific Committee for Foods (SCF) and the European Food Safety Authority (EFSA) Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) resulting in the novel food authorisations by the Commission. The most relevant toxicological and human clinical studies that were included in the previous authority safety assessments are reviewed and discussed in this Dossier considering the proportion of the 'other sterols' used in those studies vs. ADVASTEROL 90 S F and ADVASTEROL ESTER S. Also, additional data which were considered to support the safety assessment are presented.

In this Dossier, the applicant decided not to present any new subchronic toxicity or reproductive toxicity studies of phytosterols containing a slightly increased proportion of the 'other sterols'. The ability of the toxicity tests to detect or discriminate the possible health consequences of such a small concentration difference in the 'other sterols' fraction is likely to be insufficient as biological tests are subject to variability in the outcome originating from a variety of environmental and biological factors. Also, all duplicated animal studies should be avoided.

The available *in vitro* and *in vivo* studies indicated the lack of mutagenic or genotoxic activity of phytosterols and phytosterol esters, and do not propose safety concerns due to the slightly increased proportion of the 'other sterols'. With respect to the previous studies on subchronic and reproductive toxicity, although the used phytosterol mixtures contained lower proportions of the 'other sterols' compared with ADVASTEROL 90 S F and ADVASTEROL ESTER S, the studies were conducted with structurally related phytosterols. Of note, as the absorption of phytosterols from the intestine is low, according to the available data usually lower than 5 % in healthy individuals, the relevance of the differences in the phytosterol composition of ADVASTEROL 90 S F / AVASTEROL ESTER S vs. the phytosterol mixtures used in the previous toxicity studies is reduced. In the present application, the lowest reported No-Observed-Adverse-Effect-Level (NOAEL) value of the available subchronic and reproductive toxicity studies, and the anticipated intake of the 'other sterols' were utilised to calculate the Margin of Safety (MOS). The MOS calculations were performed to evaluate the safety of the specification change which results in slightly increased intake of the 'other sterols' from foods enriched with phytosterols. In adults, the MOS calculations resulted in values of 616-3850 at the mean and 280-1400 at the 95th percentile, while in toddlers the estimated mean and maximum intakes of the 'other sterols' resulted in the MOS values of 342 and 125, respectively. These MOS values comply with the requirement of MOS > 100 and demonstrate the safe exposure to the 'other sterols'.

In the previous authority safety evaluations, the included toxicity studies on vegetable-oil based phytosterol ester mixtures were mainly conducted using soybean-derived products. As presented in this Dossier, delta-7-stigmastenol and delta-7-avenasterol are the 'other sterols' that differ the most between the soybean and sunflower phytosterols. Therefore, an extensive literature search to identify additional toxicity studies on delta-7-stigmastenol and delta-7-avenasterol was conducted. Based on the literature review, only two studies for delta-7-stigmastenol on cytotoxicity were detected. Thus, the safety data on delta-7-stigmastenol and delta-7-avenasterol are very limited, but do not suggest safety concerns.

The main concern of phytosterol intake on nutritional safety has been the possible reduction in the absorption of fat-soluble vitamins. Phytosterols and phytostanols have been observed to reduce plasma carotenoid concentration, while in several human clinical trials conducted with plant sterol- or stanol-enriched products no other marked adverse health effects were detected. Of note, the mandatory statement of the use of the plant sterol enriched foods as part of a balanced and varied diet, including regular consumption of fruit and vegetables to help maintain carotenoid levels, in accordance Annex III, 5.1.6 of Regulation (EU) No 1169/2011 reduces the above-mentioned safety concern.

The particle size distribution of ADVASTEROL 90 S F and ADVASTEROL ESTER S samples were analysed in accordance with EFSA guidance. No particles at the nanoscale were detected in the samples at the detection limits defined by EFSA.

In conclusion, the available toxicological and human clinical studies with different sterol mixtures, and the particle size distribution study do not propose potential safety concerns due

to the small changes in the phytosterol fractions. Based on the scientific evidence available and the performed MOS calculations, the proposed specification change of phytosterols/phytostanols does not pose a safety risk to human health under the current conditions of use. The labelling of the end products will be done in accordance with the principles presented for the labelling of foods with added phytosterols or phytosterol esters in the Regulation (EU) No 1169/2011.