Summary of the application: Calcidiol

Applicant: DSM Nutritional Products Ltd., Tour Nova 71 Boulevard National La Garenne Colombes, France

DSM submits a novel food application for Calcidiol, a new form of vitamin D for use as ingredient in food supplements targeting the general healthy population (including pregnant and lactating women) except children below the age of 3.

Calcidiol at the proposed use level of 10 µg/day is considered safe for the general population including pregnant and lactating women, elderly and children above 3.

Calcidiol is 25-hydroxycholecalciferol, and as a major metabolite of vitamin D3, human serum calcidiol is considered the best biomarker of vitamin D status. It is a vitamer of vitamin D3 (cholecalciferol), and is directly absorbed by the human body. Due to its biological activity which is 3 times higher than cholecalciferol, less Calcidiol is needed in order to reach the same blood level of 25-hydroxycholecalciferol as with vitamin D3. The proposed use level is 10 µg/person/day.

Calcidiol is formed from cholestatrienol by chemical synthesis and thus, follows the novel food submission requirements according to the class “chemical substances”. Extensive ADME information is provided including unpublished proprietary data. Studies in animals and humans show that oral calcidiol and cholecalciferol have similar ADME properties. Comparative ADME studies show that oral calcidiol is absorbed faster and also cleared and eliminated faster than oral cholecalciferol. Oral calcidiol results in wide tissue distribution with highest concentration in plasma and lower retention in tissues as compared to vitamin D3. Apart from the first step of 25-hydroxylation of vitamin D3, further metabolism is qualitatively the same for calcidiol and cholecalciferol, but metabolism is faster and more efficient with calcidiol. The relatively faster elimination and lower retention supports the safety of oral calcidiol supplementation. To support the safety of calcidiol as a novel food at an intended dose of 10 µg/day, several pre-clinical / toxicological studies were conducted thereby focusing on mutagenicity and genotoxicity as well as repeated dose toxicity aspects. Calcidiol showed no potential for mutagenicity in the Ames Test and the MLA Test. No indication of clastogenicity or aneugenicity was noted in the in vitro CA and in vivo MNT. No adverse effects were noted in a repeated dose toxicity study (OECD 408 compliant 90-day study), and the NOAEL was 180 µg calcidiol/kg bw/d, the highest dose level tested. Calcidiol has been studied in various human trials in healthy adults but also in sub-populations considered to be susceptible like infants, elderly or non-healthy subjects. Treatment in these clinical settings ranged from 5 to 120 µg/day and from single dose up to 4 years of treatment. No adverse or serious adverse events related to calcidiol were observed in these human trials.