Toxicokinetics

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10. Calcidiol has the same identity as the primary metabolite of vitamin D3 which is 25-hydroxycholecalciferol, also known as calcifediol (ACNFP, 2024). In

humans both vitamin D2 and vitamin D3 are converted into this primary metabolite in the liver, and then converted to 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) in the kidneys and other tissues (Perez-Lopez et al., 2015).

11. Calcidiol is more hydrophilic and has a shorter half-life than vitamin D3. The half-life of calcidiol has been reported by Barger-Lux et al., (1998) to be 19 days in a study in healthy young men and was estimated to be 13.4 days in healthy males aged 18-23 years by Jones et al., (2012). Vicchio et al., (1993) estimated a half-life of calcidiol of 10 days using a liquid chromatography/thermospray mass spectrometry method (Brandi and Minisola et al., 2013).

12. In their safety assessment of calcidiol as a novel food for use in food supplements, the ACNFP had not considered whether the use of calcidiol (a metabolite of vitamin D3) would affect the downstream metabolism and homeostatic regulation of circulating vitamin D3 metabolite levels. However, based on data submitted by DSM Nutrition Ltd it was concluded that “the applicant did not give reason to believe that 25-hydroxycholecalciferol" (also known as calcidiol) “as a novel food would be metabolised differently from 25-hydroxycholecalciferol coming from other dietary sources or via this pathway, or that it would have wider impacts on feedback regulation, related pathways or vitamin D homeostasis.” Ultimately, the ACNFP stated that calcidiol has the same identity as the endogenous metabolites of vitamin D3 (i.e. 25-hydroxycholecalciferol, calcifediol) and there is no evidence to suggest that they would behave differently in the body.

13. However, the ACNFP did note that information from literature suggested potential changes in metabolism in pregnant and lactating women (ACNFP, 2024). As discussed in the Statement on the potential effects of excess vitamin D intake during preconception, pregnancy and lactation, “a number of studies have reported uniquely high levels of 1,25(OH)2D during pregnancy; the conversion of 25(OH)D to 1,25(OH)2D during the first trimester (12 weeks of pregnancy) results in a doubling of 1,25(OH)2D levels, and that levels continue to rise 2- to 3-fold until delivery”. Although, this increase in 1,25(OH)2D occurs without onset of hypercalciuria or hypercalcemia. Furthermore “the increase in 1,25(OH)2D observed during pregnancy is not continued throughout lactation and “Pregnant women with normal placental function but non-functional renal enzyme 1-α-hydroxylase fail to increase circulating 1,25(OH)2D3 during pregnancy” (COT, 2022).

14. The ACNFP commented that data from literature supplied by the applicant reported serum 1,25(OH)2D3 levels to be similar in pregnant and lactating women in response to vitamin D supplementation were similar in pregnant and lactating women and in non-pregnant or non-lactating women (Institute of medicine, 2011).