Risk characterisation

In this guide

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1. Introduction and Background - Effects of calcidiol supplementation during preconception, pregnancy and lactation
2. Toxicokinetics - effects of calcidiol supplementation during preconception, pregnancy and lactation
3. Toxicity - effects of calcidiol supplementation during preconception, pregnancy and lactation
4. Health based guidance values - effects of calcidiol supplementation during preconception, pregnancy and lactation
5. Exposure assessment - effects of calcidiol supplementation during preconception, pregnancy and lactation
6. Risk characterisation - of calcidiol supplementation during preconception, pregnancy and lactation
7. Conclusions and Questions - of calcidiol supplementation during preconception, pregnancy and lactation
8. List of Abbreviations and Technical terms - of calcidiol supplementation during preconception, pregnancy and lactation
9. References - of calcidiol supplementation during preconception, pregnancy and lactation
10. Search Terms - of calcidiol supplementation during preconception, pregnancy and lactation
11. Annex A - of calcidiol supplementation during preconception, pregnancy and lactation

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98. All calcidiol-containing supplements available on the market did not exceed the ACNFP TUL of 40 µg/day. All supplements currently available on the

market with the exception of “D.velop Tablets Adult” were at the level EFSA established as safe (i.e., up to 10 µg/day). The “D.velop Tablets Adult” exceeded the level EFSA established as safe (i.e., up to 10 µg/day) by 2-fold.

99. The highest estimated exposures of calcidiol from food sources only, was 1.1 µg/day, which is significantly below the ACNFP TUL of 40 µg/day and the level EFSA established as safe (i.e., up to 10 µg/day). For food and calcidiol supplements combined, maximum mean exposures of calcidiol exceeded the level EFSA established as safe (i.e., up to 10 µg/day) by 2-fold. The minimum 97.5 th percentile intake marginally exceeded the level EFSA established as safe (i.e., up to 10 µg/day), whereas the maximum 97.5th percentile intake exceeded the level EFSA established as safe (i.e., up to 10 µg/day by 2.1-fold. However, all mean and 97.5th percentile chronic intakes of calcidiol from food and supplements combined were below the ACNFP TUL of 40 µg/day. Individuals with a loss of function mutation in enzyme CYP24A1 are more likely to have higher circulating levels of calcidiol in their blood as this enzyme is responsible for the breakdown of calcidiol and 1,25(OH)2D (Jones et al., 2012) and are therefore more prone to the effects of excessive calcidiol exposure.

100. It should also be noted that supplements are likely to be the greatest contributor to calcidiol intake in women of childbearing age, whereas calcidiol intake from the food sources alone is low. Furthermore, not all women of child-bearing age consume supplements. Results from the most recent NDNS (years 9-11) report have shown that between 2016-2019 20% of female respondents aged 19-64 years consume vitamin D supplements (Bates et al, 2020).

101. The main uncertainties in this assessment were that the NDNS does not specifically include data for pregnant and lactating women, so women of child-bearing age (i.e. 16-49 years) were used as a proxy for these consumer groups, and there is little information on how their diets might differ.

102. Further uncertainties include the limited data available on calcidiol’s safety in pregnant women. **Most of the human studies and case reports discussed include post-menopausal women and individuals with vitamin D deficiency and are therefore not specific to populations of women of childbearing age. Although in their 2024 opinion EFSA acknowledged that bioavailability and safety data were lacking for pregnancy and lactating women but considered “the data available for adults were sufficient to cover these population groups”. (EFSA, 2024).**

103. Other uncertainties may include background exposure from UVB radiation. Although, exposure to UVB radiation is unlikely to result in adverse serum 25(OH) levels, even when consuming dietary intakes of calcidiol, due to an inbuilt mechanism in the skin. SACN, 2016 stated that “prolonged sunlight exposure does not lead to excess production of cutaneous vitamin D”. This is “because endogenously produced pre-vitamin D3 and vitamin D3 are photolyzed to inert compounds” (SACN, 2018), thus preventing conversion into its primary metabolite; 25(OH)D, (i.e. calcidiol) (ACNFP, 2024; Perez-Lopez et al., 2015). SACN also stated that “Vitamin D3 is produced endogenously from 7-dehydrocholesterol (7-DHC) in the skin of humans and animals by the action of sunlight containing UVB radiation (wavelength 280-315 nm) or by artificial UVB light”. The 7-DHC in the epidermis is converted to pre-vitamin D3, which reaches a maximum concentration in the skin within a few hours (Holick et al., 1980)” (SACN, 2018).