Background

In this guide

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1. A second draft statement on the safety of turmeric, considered by the Committee on Toxicity (COT) (TOX/2022/68; COT, 2022a), identified uncertainty regarding novel formulations of turmeric that might enhance the oral bioavailability of associated curcuminoids. In that draft statement, Members highlighted “that some of the… ‘novel’ supplement types such as micellar, nano, and micro formulations should be looked at in further detail, regarding their pharmacokinetics and therefore their impact on the active chemicals.”

2. A preliminary analysis that had been presented in the discussion paper on turmeric (TOX/2022/35; COT, 2022b) suggested that novel micro and nano formulations of curcumin represented approximately 10% of the curcumin market. The use of phospholipids to solubilise, coat and/or encapsulate curcumin for delivery in colloids (i.e., oil-in-water dispersions, see section “Lipid-based delivery systems” below, paragraphs 5 – 30), micelles, and liposomes was identified as the most prevalent amongst these. Figure 1 provides a schematic representation of these formulations. Many of these products claim that this increases the bioavailability of associated curcuminoids and leads to higher uptake by the consumer. Bioavailability refers to “the proportion of a substance which reaches the systemic circulation unchanged after a particular route of administration” and which is therefore available to biologically interact with target sites (TOX/2022/07; COT, 2023; Annex 5). Owing to its physicochemical properties, curcumin has inherently low oral bioavailability which has led to manufacturers’ attempts to produce more bioavailable formulations.

3. As a result of the issues raised in the discussion paper, it was decided that novel supplement formulations would form the basis of a general discussion paper. This current paper aims to define and review some of these novel formulations. It includes a discussion of the physicochemical parameters of several novel formulations, including coatings and/or lipid-based colloidal, micellar, liposomal, and lipid nanoparticles, as well as non-lipid-based delivery systems, and their associated physiological mechanisms. The paper also provides three case-studies assessing the impact of these delivery formulations on the oral bioavailability and pharmaco/toxicokinetic parameters of vitamin C, curcuminoids, and cannabidiol (CBD).