Safety assessment of food additives
Impact of the changes in EFSA scientific methodology for deriving a reference point

BACKGROUND

The **no observed adverse effect level (NOAEL)** is the greatest concentration or amount of a substance at which no detectable adverse effects occur in an exposed population.

The NOAEL has been used historically as the reference point (RP) for estimating the health-based guidance values (HBGVs) such as acceptable daily intakes (ADIs) for food additives in long-term animal in vivo studies. To derive an ADI a safety or uncertainty factor (commonly 100) is applied to the NOAEL in the most sensitive test species. The 100-fold safety factor is considered to be the product of both species and inter-individual differences in toxicokinetics and toxicodynamics.

The Benchmark Dose (BMD) is the minimum dose of a substance that produces a clear, low level health risk, usually in the range of a 1-10% change in a specific toxic effect such as cancer induction. The lower bound (BMDL) is needed as a potential RP, and the upper bound (BMDU) is needed for establishing the BMDU/BMDL per ratio reflecting the uncertainty in the BMD estimate.

In 2022, EFSA's Scientific Committee updated its guidance on the use of the benchmark dose (BMD) approach in EFSA's risk assessments as an alternative to the traditional No-Observed-Adverse-Effect-Level (NOAEL) approach[1].

EFSA has reconfirmed its recommendation to use the BMD approach instead of the traditionally used NOAEL approach to identify a Reference Point, since it makes a more extended use of dose–response data and allows for a quantification of the uncertainties in the dose–response data. EFSA considers that the BMD approach is a scientifically more advanced method compared to the NOAEL approach for deriving a RP.

In principle, the BMD approach is applicable to all chemicals for which a dose–response relationship exists for at least one endpoint, irrespective of their category (e.g.pesticide, **food additive**, contaminant) **or origin (chemically synthesised or from natural sources)**.

[1] EFSA 2009 guidance was already updated in 2017. The update in 2022 introduces among others Bayesian model averaging as well as a harmonised set of dose-response models for continuous and quantal responses. Applications and user manuals (BMD & Bayesan BMD) are available on the EFSA R4EU Platform.

Federation of European Specialty Food Ingredients Industries
Avenue de Tervuren 13 A – Box 7 – 1040 Brussels
Phone: + 32 2 736 53 54 – info@specialtyfoodingredients.eu – www.specialtyfoodingredients.eu