Bayesian vs frequentist approach

In this guide

23. Annex A - References

93. Historically, BMD software for DRMs used frequentist methodologies. However, advances in numerical mathematics and developments in BMD software have made possible the use of Bayesian methods for the same approach (Shao and Gift, 2014; Shao and Shapiro, 2018). The significance of this development is reflected in EFSA's most recent 2022 guidance which recommends a change from a frequentist to Bayesian approach as the preferred approach for estimating the BMD and calculating credible intervals (EFSA, 2022).

94. Both PROAST and BMDS allows the user to run either (or both) Bayesian or non-Bayesian analyses (EFSA, 2022; US EPA, 2022). Non-Bayesian approaches, often referred to as "frequentist" or "maximum-likelihood estimation (MLE)" are based on likelihood calculations. In this approach, parameters are fixed and unknown and estimation involves finding the best estimate based on the data provided. Models fit by these methods report MLE and associated statistical measures such as p-values and goodness-of-fit evaluations. This approach has been criticised, (e.g., in a recent paper by Ji et. al., (2022)) as it may not account for all the model uncertainty and consequently, it may result in over-confident inferences and predictions (Clyde, 2003; Ji et al., 2022).

95. In the Bayesian analyses, by contrast, parameters are treated as random variables with their own probability distributions. Distributions describing the a priori uncertainty in the parameter values (the so-called prior distributions) are updated using the data under consideration to yield a posteriori distributions (EFSA, 2022; US EPA, 2022). In both the frequentist and Bayesian approaches, the objective of model fitting is the same: to best describe the dose-response data by searching for those parameter values that lead to a curve that describes the data well, as defined by some statistical criterion of good fit.

96. One consequence of using traditional frequentist methods for estimating model parameters is that parameters may be estimated even when the data provide little information on the parameter. This can lead, in some instances, to parameter values that may be considered a biologically implausible. JECFA, in their 2020 guidance, give the example of the Hill model for continuous data. In cases where the data does not suggest a sigmoidal shape to the dose response relationship, the data provides no information on the steepness parameter. As discussed, this has led to the recommendation that parameter constraints be considered in some instances to mitigate this possibility (see section on "Constraining or not constraining the models"). In contrast, parameter constraints

are not necessary when using Bayesian methods in general. When using the Bayesian approach, the WHO guidance recommends that priors should be reasonably diffuse over values of the target parameter and to mitigate against possible biases, a sensitivity analysis of the effect of the priors should be clearly documented (FAO/WHO, 2020).

97. As with the frequentist approach, Bayesian model averaging (BMA) has been suggested to address concerns regarding model uncertainty. In BMA, the "plausibility" of the model is described by the posterior model probability, which is determined using the fundamental Bayesian principles - the Bayes theorem - and applied universally to all data analyses.

98. Terminology and interpretation of the resulting outputs are also different but serve a similar purpose. The 90% confidence interval and significance levels typically used to describe uncertainty in the frequentist approach, are replaced in the Bayesian approach with two-sided 90% credible interval. This corresponds to an interval that covers 90% of likely values of the BMD (the probability that the BMD is within the limits of the credible interval is 0.9). Similar to the non-Bayesian approach, the 5% BMDL and 95% BMDU are defined as the lower and upper bound of a 90% CI for the BMD respectively (EFSA, 2022).

99. EFSA 2022 also note that the Bayesian approach can mimic a learning process; the posterior distribution is updated based on prior belief and the data provided, resulting in posterior distributions that reflects the accumulation of knowledge over time. A full discussion of Bayesian modelling in the BMD approach and the theoretical basis is provided in recent technical guidance and expert scientific opinion documents (EFSA, 2022; FAO/WHO, 2020; US EPA, 2022).