



Outcomes from BOS2

Leon Aarons

Key points

Modelling and simulation is driven by and informs the underlying science. Therefore a requirement for the acceptance of modelling and simulation is consistency and evidence of the underlying science. This is equally true for approaches that don't use modelling, although we would contend that there is no such thing as a truly model independent approach.

There is a perception that scientific evidence is being restricted by the nature of the studies required by regulatory authorities. For example, in a dose ranging study which only involves pairwise comparisons, it may not be possible to elucidate the nature of the dose-response relationship.

Modelling potentially can lead to greater precision in the detection of the signal from the background noise in clinical trials. This in turn leads to more efficient trials with a consequent saving in patients and costs. Of course this is only true when the model is a true representation of the system. Bias is one issue which has dissuaded some people from using a modelling approach.

Key points

Plausibility of the evidence is a major factor in acceptance of the modelling approach. In this sense it is important to distinguish between the system, that is the biology, and the drug. The biology includes demographic factors such as weight and physiological factors such as renal function, whereas the drug properties include physical chemical factors and pharmacological information, such as receptor affinity.

In general most people are happy with using a model for interpolation rather than extrapolation. However confidence in extrapolation can be increased by the use of external data and prior information. Similarly extrapolation is likely to be more acceptable for drugs which have a wide therapeutic window.

There is a feeling that the EMA lacks a sufficient number of assessors with modelling expertise. In part this may be due the fact that the assessors are not seeing a lot of modelling exercises, possibly due to the second point raised above. Nevertheless there is a perceived need for additional training for assessors.