Questions put forward for the discussion sessions- 2021

In this guide

22. The below were the questions put forward for the discussion sessions.

Limitations / Ensuring fitness for purpose

- What are (if there are any), the limitations of using PBPK modelling in an agrochemical/pharmacological setting?
- Can PBPK models fully replace animal testing, or are there some cases where animal studies may still be required?
- Are there any circumstances where we can use simpler *in silico* compartmental models versus PBPK?

Potential applications

- Can PBPK models be used to provide relevant substances to benchmark against known human biomonitoring data?
- Exploration into intracellular dosing.
- Could PBPK modelling be used to convert estimates of external exposure into an estimate of internal exposure at the site where toxicity occurs to refine estimates of risk?
- PBPK modelling provides a way to incorporate kinetics into consideration in animal-free, *in vitro* based safety/risk assessment and to relative *in vitro* toxicity assay findings to human safe exposure estimates.
- Can PBPK models lower the reliance on default uncertainty factors, and would it reduce this uncertainty?

Validation for regulatory application

- Are there any harmonised guidelines available for regulators?
- Have there been any cases where there has been a human PBPK model developed without human data? If so, how was the model validated (if at all)?
- What are some of the hurdles to PBPK modelling being used more widely by scientists, and accepted by regulators?

Duties as regulators

- What aspects of the model do regulators have to check before it can be used in risk assessment?
- Are regulators expected to use PBPK models (for example, to double-check calculations, to examine the source code) or can regulators just take simulation results at face value?
- How could PBPK modelling be used more extensively in food safety assessment?
- Is the integration of PBPK models into current human health assessment methodologies a risk worth embracing?