# COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

## PBPK for Regulators Workshop Report: First draft (Reserved)

1. The future of food safety assessment in the UK depends on the Food Standards Agency's (FSA) adaptability and flexibility in responding to, and adopting, the accelerating developments in science and technology. The Tox21 approach[1] is an example of one recent advancement in the development of alternative toxicity testing approaches and computer modelling strategies for the evaluation of hazard and exposure. A key aspect is the ability to link active concentrations *in vitro* to likely concentrations *in vivo*, for which physiologically based pharmacokinetic (PBPK) modelling can provide estimates of *in vivo* concentrations.

2. The UK FSA and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) held a "*PBPK for Regulators*" workshop (December 2020) in a multidisciplinary setting with delegates from regulatory agencies, government bodies, academia and industry. The workshop provided a platform to enable expert discussions on the application of PBPK to human health risk assessment in a regulatory context.

3. Presentations covered current applications of PBPK modelling: in the agrochemical industry for *in vitro* to *in vivo* extrapolation (IVIVE); pharmaceutical industry for drug absorption related issues (*e.g.* the effect of food on drug absorption) and drug-drug interaction studies, as well as dose extrapolations to special populations (*e.g.* those with a specific disease state, paediatric/geriatric age groups, and different ethnicities); environmental chemical risk assessment fields; an overview of the current regulatory guidance; and a PBPK model demonstration[2]. This enabled attendees to consider the wide potential and fit for purpose of application of PBPK modelling in these fields.

4. Attendees further considered the applicability of PBPK models in the context of future food safety assessment, for refining exposure assessments of chemicals with narrow margins of exposure and/or to fill data gaps from more traditional approaches (*i.e.* data from animal testing).

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[1] Toxicology in the 21st Century (Tox21) is a United States federal research collaboration, testing thousands of environmental chemicals using non-animal methods for potential health effects. Further information is available on the Tox21 website. See also the US Environmental Protection Agency's website for adopting new approach methodologies.

[2] The PBPK model was RVis, which has been developed by the UK Health and Safety Laboratory. Further information is available on the Cefic website.

5. The overall conclusions from the workshop proceedings were as follows:

- PBPK modelling tools are applicable in the explored areas of use, and there is some expertise available for their utilisation.
- PBPK modelling offers opportunities from which to address questions for compounds that are otherwise not solvable.
- Widespread acceptance amongst regulatory bodies appears to be limited by lack of available in-house expertise.
- Familiarisation using real world case studies would help in developing more experts in the field and increasing acceptance.
- In a regulatory context, establishing fitness for purpose for the use of PBPK models requires multi-partite discussion and harmonised guidance.
- Finally, PBPK modelling is part of the wider "new approach methodologies" for risk assessment.

**Questions on which the views of the Committee are sought**

6. Members are invited to consider the following questions regarding the first draft of the "*PBPK for Regulators*" workshop report. Note that the first draft has been summarised by the Secretariat and that presenters will be asked to check the accuracy of their summarised contributions prior to its finalisation.

i). Does the draft report (as presented in Annex A) accurately capture the "*PBPK for Regulators*" workshop and its outputs?

ii). Have each agenda session been adequately summarised?

iii). Do Members wish to include any other materials in the report?

iv). Can the report be published as a COT statement?

v). Do Members have any other comments?

**Secretariat**
**February 2021**

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This Annex is not yet publicly available as it contains pre-publication information.

**Secretariat**
**February 2021**