Paving the way for a UK Roadmap: Development, Validation and Regulatory Acceptance of New Approach Methodologies (NAMs) in Chemical Risk Assessment

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INTRODUCTION

Some of the current challenges faced by UK chemical risk assessors are: large number of (groups of) chemicals that require assessment, lack of toxicological data on these chemicals and the speed and cost of traditional testing methods. One of the major recent scientific advancements is the development of New Approach Methodologies (NAMs) including high throughput screening, omics and in silico computer modelling strategies (e.g. Artificial Intelligence (AI) and machine learning) for the evaluation of hazard and exposure. This also advocates the Replacement, Reduction and Refinement (3Rs) approach to animal testing.

The future of food safety assessment of chemicals depends on our adaptability whilst using the best scientific methodologies. The vision is to be able to predict risk more rapidly and efficiently.

NAMs are gaining traction as a systematic method to support informed decisions on chemical risk assessment.

For regulatory agencies to incorporate these new capabilities brings both challenges and opportunities. Moving from research to risk assessment to regulatory setting and beyond, there must be suitable validation and acceptance of these emerging technologies.

METHODOLOGY

The UK Food Standards Agency (FSA) and Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) have produced a scoping paper, organised 3 workshops, held in international, multidisciplinary settings and including participation from regulatory agencies, government bodies, academia and industry.

The scoping paper 'Environmental, health and safety alternative testing strategies: Development of methods for potency estimation' reviewed by the COT provided an overview of NAMs.

The 'Exploring Dose Response' workshop enabled expert discussions on the latest NAMs as well as method validation including case studies, how to improve the use of exposure metrics in risk assessment and explored an approach that is fit for purpose when applied to human health risk assessment in the context of future food safety assessment.

The physiologically-based pharmacokinetics 'PBPK for Regulators' workshop enabled expert discussions and presentations on the application of PBPK to human health risk assessment in a regulatory context as well as potential future research.

RESULTS

The FSA and COT have developed a UK roadmap towards acceptance and integration of these NAMs including predictive toxicology methods using computer modelling, into safety and risk assessments of chemicals for regulatory decision making, with a focus on food safety.

The overall objectives of the roadmap are to:

1) identify latest available NAMs for optimal risk assessment;
2) learn from other regulatory agencies and beyond;
3) validate through case studies;
4) build confidence in NAMs in the regulatory setting;
5) develop skills and training as well as
6) implement and integrate NAMs in the regulatory setting.

The Roadmap utilises the 7 steps to integration and acceptance:

1) listening and learning;
2) identify and review;
3) training;
4) research and development;
5) collaboration and dissemination;
6) review and recommend; and
7) regulatory integration and acceptance

The UK NAMs Roadmap is one element of work that the FSA is undertaking in the area of incorporating NAMs into the regulatory setting. Other strands include, the FSA postdoctoral fellow in computational toxicology and partly funding a PhD student in toxicology using artificial intelligence.

DISCUSSION

NAMs and Integrated Approaches to Testing and Assessment are rarely accepted by regulatory bodies, however it is clear that we are now at a pivotal point where integration of such (methods/techniques) will be fundamental in more efficient and rapid risk assessment. The key question is how these approaches can be facilitated in a regulatory setting using the

supporting technology available. The use of these methods through various case studies as a ‘proof of principle’ concept is becoming apparent.

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Innovative technologies will be fundamental in the future for human and environmental safety. These emerging technologies should be reviewed and evaluated prior to integration into the chemical testing method, as part of the risk assessment process. Using a validation process via an evidence driven approach to address the data gaps in the risk assessment process will facilitate the acceptance and validity of these NAMs as well as pave the way for alternative methods and testing strategies with confidence.