EUROPEAN COMMISSION
JOINT RESEARCH CENTRE
Health, Consumers and Reference Materials
Chemical Safety and Alternative Methods Unit
EU Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM)

Summary record

Workshop of the International Cooperation on Alternative Test Methods (ICATM) on the "The Future of Alternative Methods for Regulatory Testing and their Contribution to Public Health"

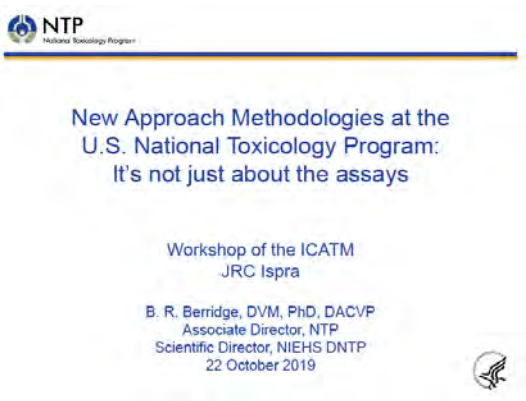
Joint Research Centre, Ispra, Italy, 22 October 2019

The JRC's EU Reference Laboratory for alternatives to animal testing (EURL ECVAM) hosted a workshop on "The Future of Alternative Methods for Regulatory Testing and their Contribution to Public Health" on 22 October 2019. It was held in conjunction with meetings of ECVAM's regulatory advisory network (PARERE) and its stakeholder forum (ESTAF). The aim of the workshop was to celebrate the 10th anniversary of ICATM[1], to raise ICATM's visibility and to discuss the future outlook of alternatives in the different jurisdictions of the ICATM partners.

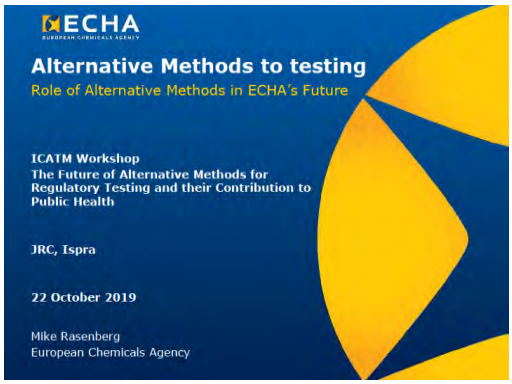
Invited participants from validation bodies, European agencies, national regulatory authorities and stakeholder organisations reflected on past achievements and looked to the future (see agenda in annex 1).

The former Director of the JRC's Directorate on Health, Consumers and Reference Materials, Prof. Elke Anklam, opened the workshop in the morning of 22 October. She described the roles, mission of the JRC and its place within the European Commission, and provided some background on ICATM and its purpose. This was followed by plenary lectures on "New Approach Methodologies at the US National Toxicology Program: It's not just about the assays" by Dr Brian Berridge from the US National Institute of Environmental Health Sciences and on "Facing the Challenges of Full Replacement in Regulatory Toxicology" by Prof. Maurice Whelan from the JRC's EURL ECVAM (the reader is invited to double-click on the pictures to open the presentations).

[1] On 27 April 2009, representatives from Health Canada, the European Commission, the National Institute of Health Sciences in Japan and the National Institute of Environmental Health Sciences in the United States signed the memorandum of cooperation establishing the International Cooperation on Alternative Test Methods. In 2011, the National Institute of Environmental Health Sciences in South Korea formally joined the cooperation. Since then, other governmental institutions from Brazil, Singapore and China have been participating in ICATM initiatives on an *ad hoc* basis.



Representatives from the EU agencies EFSA and ECHA then provided the agencies' perspective on the role of alternative methods in their work.



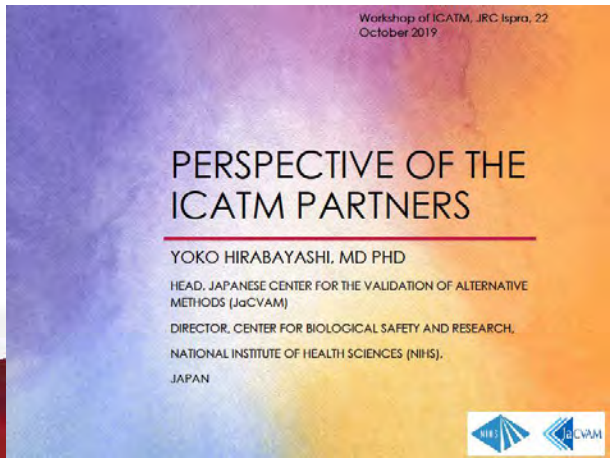
The perspective of the EU Scientific Committees on Consumer Safety (SCCS) and on Health, Environmental and Emerging Risks (SCHEER) were presented as well.

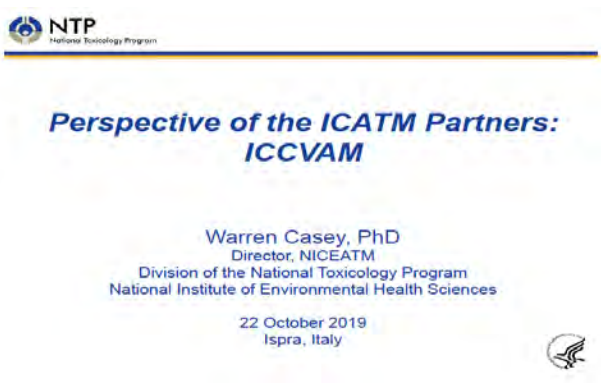
Prof. Vera Rogiers illustrated how alternative methods are currently being used in the framework of the SCCS' Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation, whereas Dr Renate Kraetke presented some examples from the work of SCHEER.

In the afternoon, the ICATM partners from Canada, Japan, South Korea, United States and EU presented the perspective from their respective jurisdictions.

They all addressed the following three questions in their presentation:

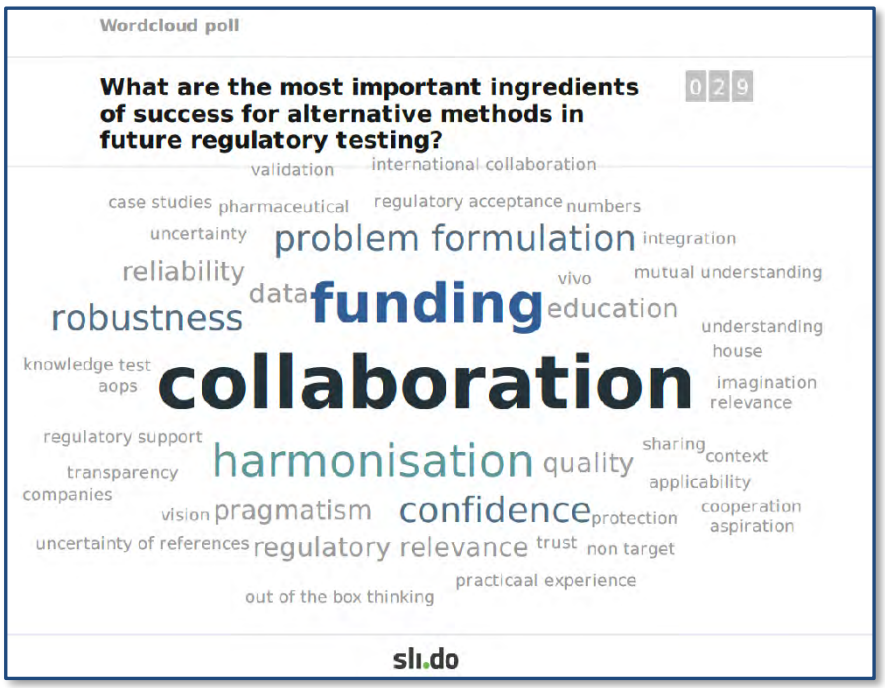
- Retrospective analysis: what has been achieved and learned?
- State of play: where do we stand now?
- Future outlook: where do we want to go/priorities in the different jurisdictions.





The ICATM partners' presentations were then followed up by a moderated discussion on the future outlook on alternative methods in regulatory testing where the participants were asked to discuss the following questions:

- What do you see as ingredient for success?
- What are the challenges encountered?
- What would be an added value for ICATM?



The three major ingredients for success for alternative methods in future regulatory testing according to the participants at the ICATM workshop were collaboration, funding and harmonisation.

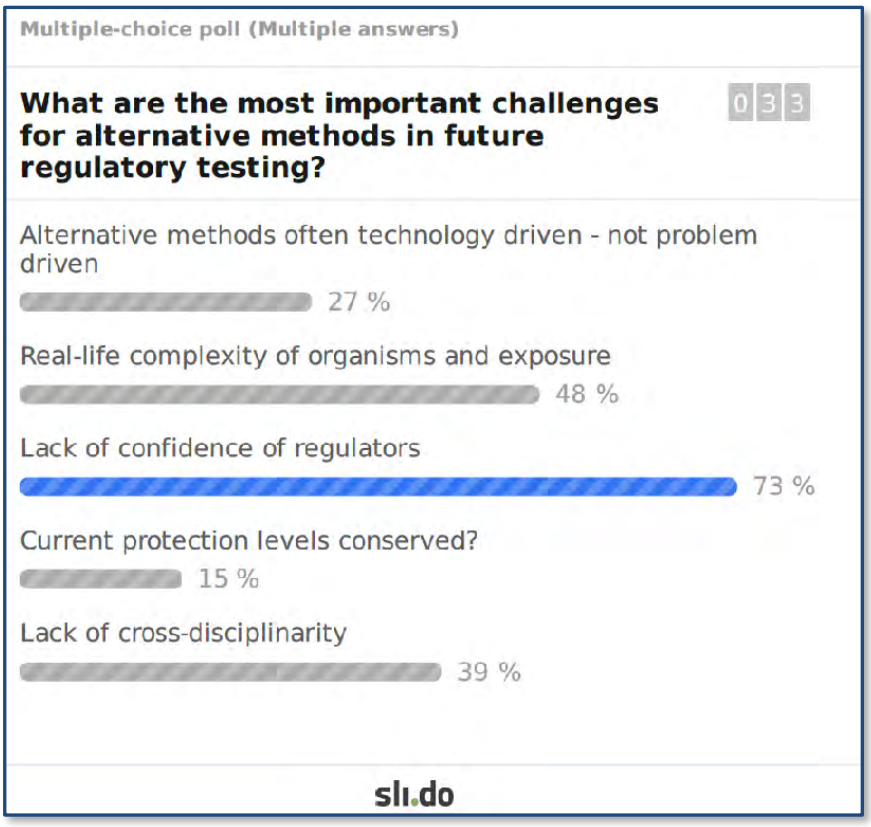
The participants were asked how to achieve better collaboration, and many of the replies referred to the need for facilitating communication, in particular between different stakeholder groups. Several participants suggested to use networks such as ICATM, PARERE and ESTAF, but also NETVAL and EPAA, to assist in creating better communication between different interest groups. This would also facilitate

joint decisions on how to progress. Joint decisions could be achieved by setting common goals and roadmaps, and, as such, also avoid duplication of efforts and initiatives. Several participants mentioned the benefit of working out case studies together, in particular by considering the regulatory needs, and of course, then exchange such experiences. Besides case studies, also best practices on how to carry out testing and assessments based on alternatives to animal tests, should be shared and elaborated in common. In addition, political pressure was thought to be helpful to stimulate faster progress.

In relation to how to achieve more funding, the participants expressed ideas such as not necessarily more, but better planned spending was necessary, e.g. under Horizon Europe and by Member State authorities; articulate social, economic and scientific benefits of using alternative testing; create new public-private partnerships; and apply fees for animal tests when used in regulatory authorisation procedures.

The third ingredient for success was harmonisation. Here there were mentioning of shared objectives, align global regulatory requirements and standardisation. The standardisation should be made across sectors and the right balance between flexibility and prescriptiveness was thought to be essential. It was also stated by several participants that at the current point in time it might be better to achieve acceptance of standards rather than acceptance of individual methods. A priority was to harmonise the test requirements under different pieces of legislation as well as under the law in different countries. The mutual acceptance of data, was essential to speed up assessment and not repeat studies already done. The OECD was recognised as a key player in the context of standardisation, but also ICATM could have an important role to play.

The facilitators had identified five challenges related to the future of alternative methods in regulatory testing that several lecturers had mentioned during their presentation at the workshop. The participants voted on the preferred options.



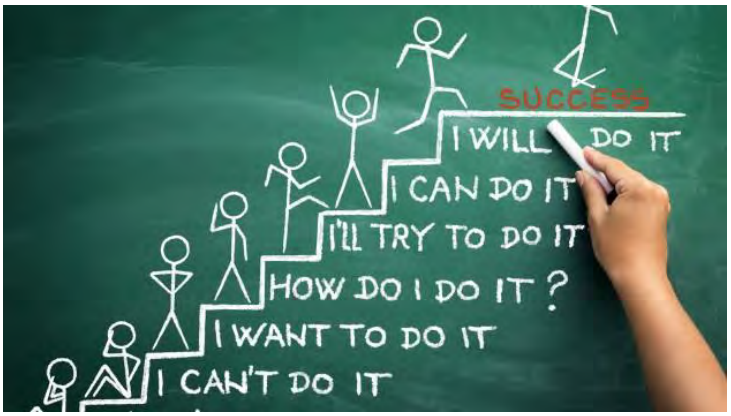
The resulting three main challenges according to the workshop participants were a lack of confidence of regulators, a real-life complexity of organisms and exposure and a lack of cross-disciplinarity.

What to do about the lack of confidence of regulators? The workshop participants suggested training, more interaction between regulators and scientists, illustrative and convincing case studies and deepening the understanding of uncertainties in current animal methods. It was also stated that it was time to demonstrate the regulatory need to move away from tick box thinking and not directly replace animal endpoints, and to stimulate a discussion on how to make a new more efficient regulatory framework.

The discussion on real-life complexity of organisms and exposure, started off with the reflection that we already ignore the complexity in exposure when we rely on animal data, and that the alternative methods can be applicable also to mixtures and combined exposure. It was mentioned that it is more important to protect than to predict the animal data, and to understand protection goals prior to building up testing strategies. It is important to understand which mechanisms are leading to adversity but also focus on more generic/unspecific effects frequently occurring in particular together with systemic toxicity. There is a need for closer collaborations between the *in silico*, *in vitro* and *in vivo* communities, and a more efficient development of AOPs, IATAs and DAs.

To address the lack of cross-disciplinarity, the participants suggested to focus on team science and involve clinicians to a larger extent. Interdisciplinary groups could be created to work on specific problems or case studies. It would be useful to include training and complete programs at university level to encourage scientists

to be cross-disciplinary. There should be more EU integrated projects focusing on the fact that there is "one health" to bring together different disciplines for an added value. It was also stressed that the terminology and abbreviations should be explained in any discipline or context used to be inclusive of different expertise.



The ICATM workshop participants finalised the discussion by suggesting how ICATM could contribute to reinforce the ingredients for success and meet the challenges in a future of alternative methods for regulatory testing (the results are captured in Figure 1).

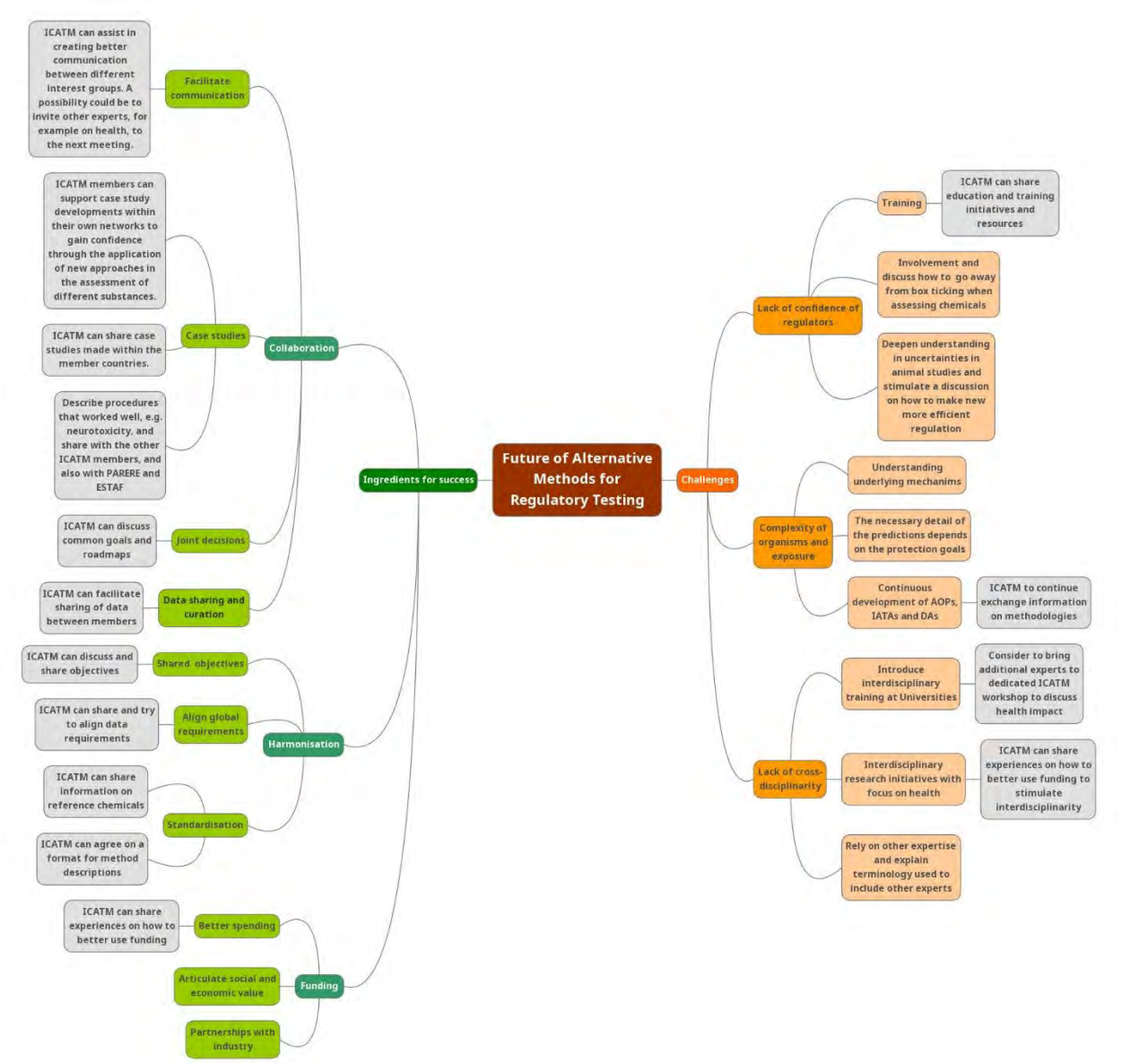


Figure 1. Overview of the discussions on how ICATM could contribute to reinforce the ingredients for success and meet the challenges in a future of alternative methods for regulatory testing.

With regard to the ingredients for success, the participants suggested e.g. that ICATM could facilitate communication between different interest groups, support case study developments within their own networks to gain confidence through the application of new approaches and share case studies undertaken within the respective Member Countries; discuss common goals and roadmaps; facilitate data sharing and data curation among Member Countries; share information on reference chemicals; share information on data requirements; support the

harmonisation of data requirements; as well as share experiences on how to more efficiently use funds.

With regard to the challenges that had been discussed, the participants suggested to share education and training initiatives and resources on new methodologies; continue to exchange information on new methodologies; continue to organise dedicated ICATM workshops with additional experts and share experiences on how to better use funding to stimulate cross-disciplinarity.

Annex 1. Agenda of the ICATM workshop "The Future of Alternative Methods for Regulatory Testing and their Contribution to Public Health".