HUMANE SOCIETY INTERNATIONAL

AFSA
ANIMAL-FREE SAFETY ASSESSMENT COLLABORATION

Upholding the principle of animal testing as a last resort under REACH

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ADVANCING

HUMAN-PREDICTIVE

APPROACHES IN TOXICOLOGY

& BIOMEDICAL RESEARCH

WORLDWIDE

About HSI

- HSI represents the largest force for animal protection globally, active on the ground in >60 countries across Europe, the Americas, Asia & Africa
- Our science team brings together experts in human & environmental toxicology, risk assessment, biomedicine, law and public policy, etc.
- Working with regulatory authorities, industry, policy-makers, academia and public interest stakeholders
- Accredited stakeholder of ECHA, EFSA, CARACAL, EURL-ECVAM, OECD Test Guidelines & AOP development programmes & other governmental advisory bodies on chemical safety (e.g. US EPA)

HUMANE SOCIETY INTERNATIONAL

AFSA COLLABORATION

The AFSA Collaboration works to accelerate global adoption of a modern, human-based approach to safety assessment that will better protect consumers and hasten the replacement of animal testing

WORKSTREAMS

COSMETICS

TOX21

CHEMICAL READ-ACROSS

VACCINES

Outline

1. Legal requirements to minimize and reduce animal testing
2. Adaptations to standard information requirements that reduce or avoid animal testing
3. Examples of guidance and projects
4. Acceptability of adaptations
5. Recommendations for future steps
6. What we would like to hear from the Forum

Legal requirements to minimize and reduce animal testing

Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes

Article 4 Principle of replacement, reduction and refinement

1. Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure.

Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

Article 1 Aim and scope

1. The purpose of this Regulation is to ensure a **high level of protection of human health and the environment**, including **the promotion of alternative methods for assessment of hazards of substances**, as well as the free circulation of substances on the internal market while enhancing competitiveness and innovation.

Article 13 General requirements for generation of information on intrinsic properties of substances

1. **Information on intrinsic properties of substances may be generated by means other than tests**, provided that the conditions set out in Annex XI are met. In particular for **human toxicity, information shall be generated whenever possible by means other than vertebrate animal tests, through the use of alternative methods, for example, in vitro methods or qualitative or quantitative structure-activity relationship models or from information from structurally related substances (grouping or read-across)**. Testing in accordance with Annex VIII, Sections 8.6 and 8.7, Annex IX and Annex X may be omitted where justified by information on exposure and implemented risk management measures as specified in Annex XI, section 3.

Article 25 Objectives and general rules

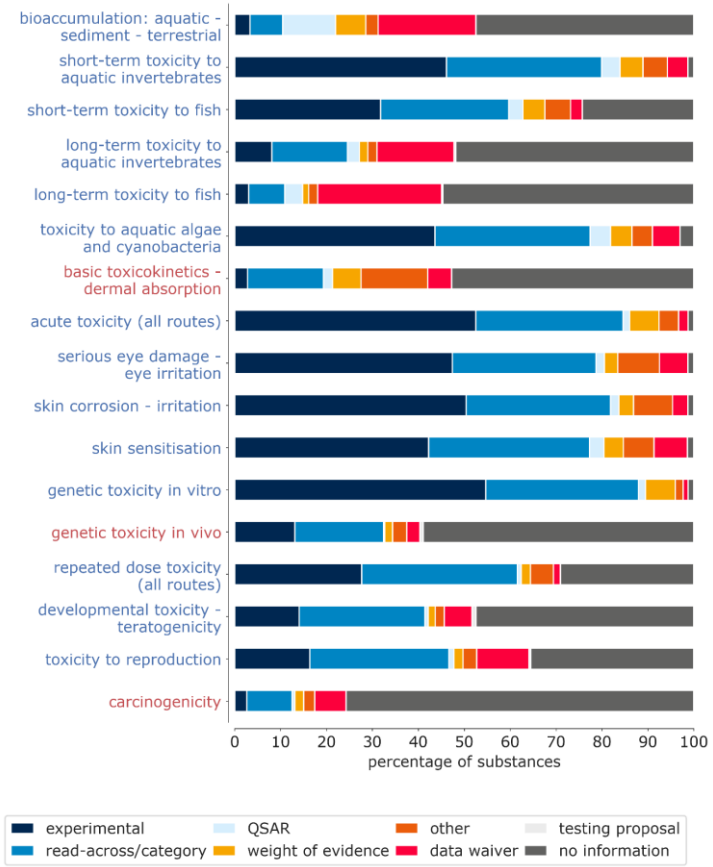
1. In order to **avoid animal testing, testing on vertebrate animals for the purposes of this Regulation shall be undertaken only as a last resort.** It is also necessary to take measures limiting duplication of other tests.

Adaptations to standard information requirements that reduce or avoid animal testing

Possible adaptations in REACH Annex XI(1) include:

- Use of existing data, including historical human data;
- Use of a weight-of-evidence approach;
- Information generated using quantitative structure activity relationships (QSARs);
- *In vitro* test methods; and
- Grouping of substances and read-across.

Adaptations to standard information requirements that reduce or avoid animal testing – Use



Frequency of the different options to fulfil the information requirements in 2019 (aggregated at IUCLID section level)

Option used	2019 average [%]	2016 average [%]
Experimental	27.1	27.6
Read-across/category	25.1	27.7
QSAR	2.6	3.0
Weight of evidence	3.7	3.7
Other	4.8	5.6
Data waiver	7.7	10.8
Testing proposal	0.2	0.3
No information	28.7	21.2

Options used to fulfil the information requirements on average, 2019 compared to 2016

Source: The use of alternatives to testing on animals for the REACH Regulation, Fourth report under Article 117(3) of the REACH Regulation, European Chemicals Agency, June 2020

Examples of guidance and projects

ECHA
EUROPEAN CHEMICALS AGENCY

Read-Across Assessment Framework (RAAF)

ECHA

Guidance on information requirements and chemical safety assessment

Chapter R.6: QSARs and grouping of chemicals

QSAR TOOLBOX

VEGA HUB

EUTOXRISK
Biological read-across

Cat-App

Unclassified **ENV/JM/MONO(2014)4**

Organisation de Coopération et de Développement Économiques
Organisation for Economic Co-operation and Development

14-Apr-2014

English - Or. English

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND
THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

GUIDANCE ON GROUPING OF CHEMICALS, SECOND EDITION

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OECD
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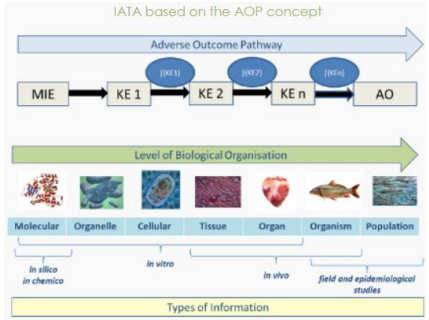
OECD Home › Chemical safety and biosafety › Assessment of chemicals › Integrated Approaches to Testing and Assessment (IATA)

Integrated Approaches to Testing and Assessment (IATA)

CASE STUDIES PROJECT

The Cooperative Chemicals Assessment Programme (CoCAP) was revised in 2014 to enhance the activity of the development and the application of IATA. This programme provides a forum for scientific exchange of approaches on how novel methods are applied to assess the hazard of chemicals, and establish common and best practices for the use of these methods for assessing different types of chemicals. The approaches described in the case studies are applicable in certain regulatory contexts outlined in the case studies. In other regulatory contexts, their fit for purpose would need to be determined.



Acceptability of adaptations

- Registrants are making use of adaptations under REACH ✓
- But are adaptations successfully meeting the requirements of REACH, i.e., effectively avoiding animal testing ?

Report on the statistics on the use of animals for scientific purposes in the Member States of the EU in 2015-2017 (EC 2020):

"*Between 2015 and 2017, the uses to satisfy legislative requirements for (…) industrial chemicals legislation uses (+17%) saw an increase*"

Acceptability of adaptations (cont'd)

Weight of Evidence (WoE)

"experience from evaluation also indicates that such adaptations provided by registrants are often found to be incompliant "

Reported quality deficiencies:

- No reliable sources of information
- WoE not documented sufficiently
- Each element of the standard requirement is not sufficiently covered

QSARs

"for aquatic toxicity, the QSAR approach as applied by the registrants worked well in the majority of cases (68 %) while for bioaccumulation, the majority (70 %) had issues"

Reported quality deficiencies:

- Applicability domain of the model
- Reliability of the prediction is often not sufficiently scrutinised

Read-across

"experience from evaluation indicates that such adaptations provided by registrants often fail to comply with the legal requirements"

Reported quality deficiencies:

- Poor documentation
- Insufficient substance identification
- Significant deficiencies in the quality of the source studies
- Lack of or low quality of supporting data,
- Lack of qualitative and quantitative data to support predictions based on toxicokinetics
- Shortcomings in the hypothesis and justification of the toxicological prediction

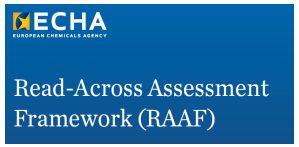
Source: The use of alternatives to testing on animals for the REACH Regulation, Fourth report under Article 117(3) of the REACH Regulation, European Chemicals Agency, June 2020

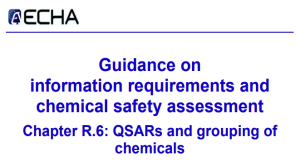
Acceptability of adaptations (cont'd)

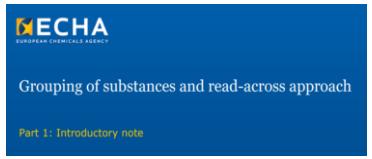
Despite the wealth of existing guidance, support tools & related work over many years, there are still many issues with the acceptability of alternatives → ***increase in animal testing***

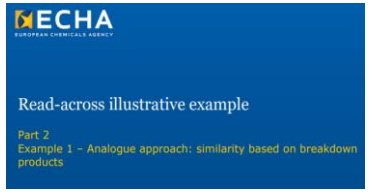
Example with Read-across

ECHA → **Acceptance** ← **Registrants**



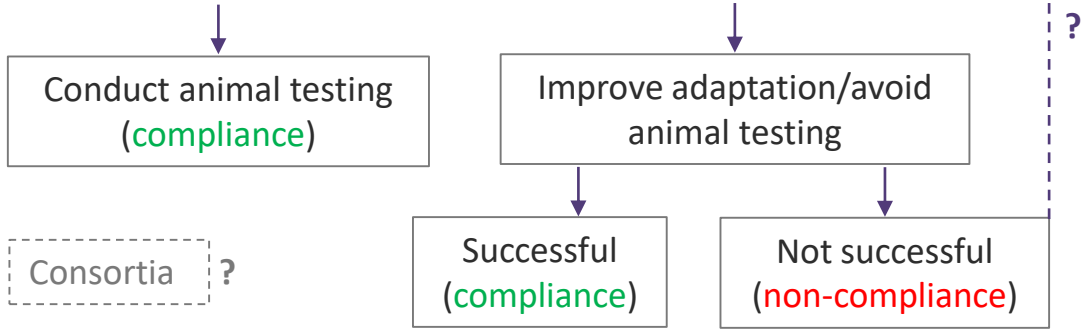






- Need to update/improve adaptations
  but how to determine exactly what needs improving (and how) until feedback is received? [even with RAAF]

- Feedback is received ⟷ Compliance Check
  i) short deadline (30 days) to clarify/improve [*impractical*]
  ii) decide next steps to fill data gap



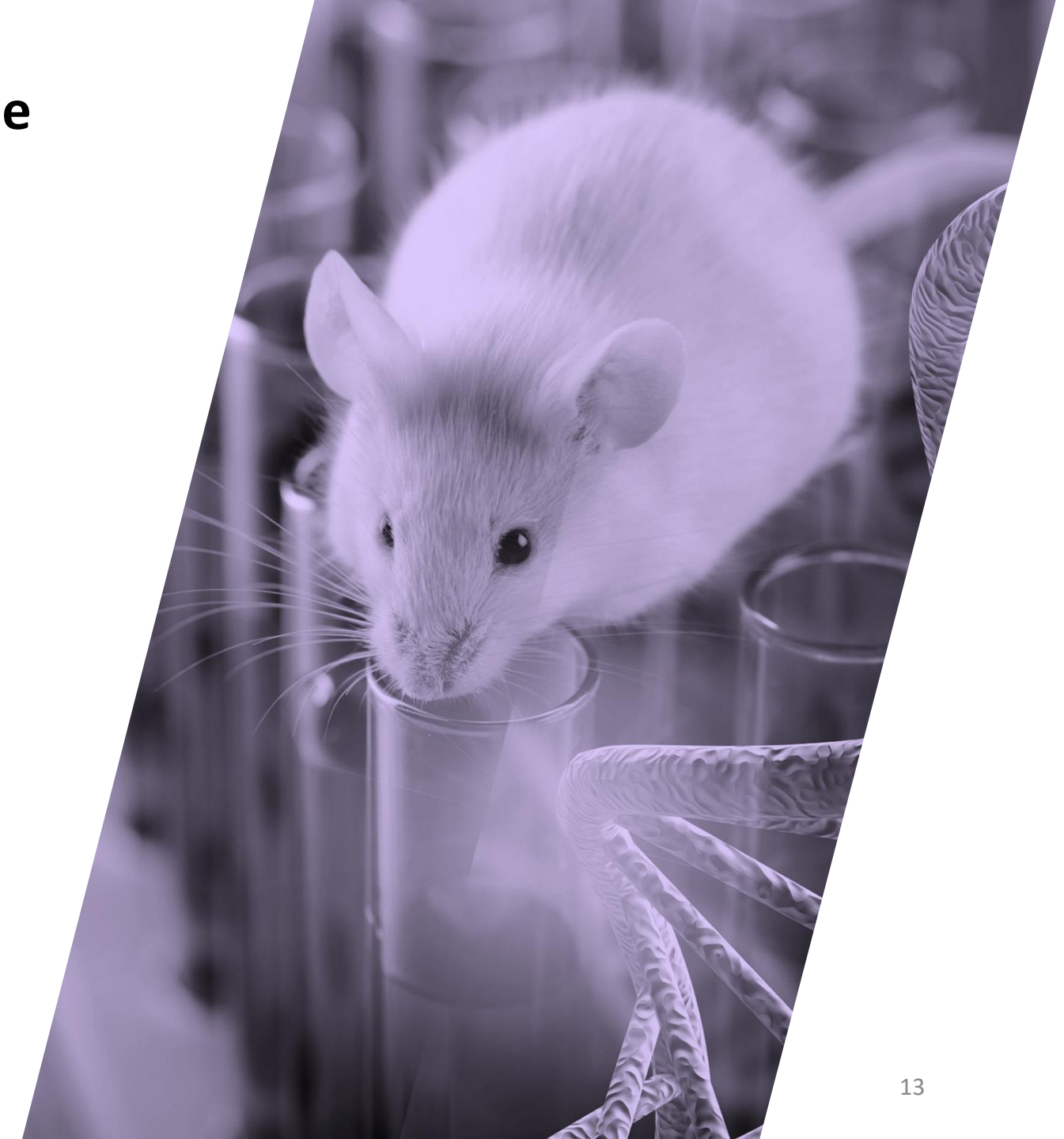
Recommendations for future steps

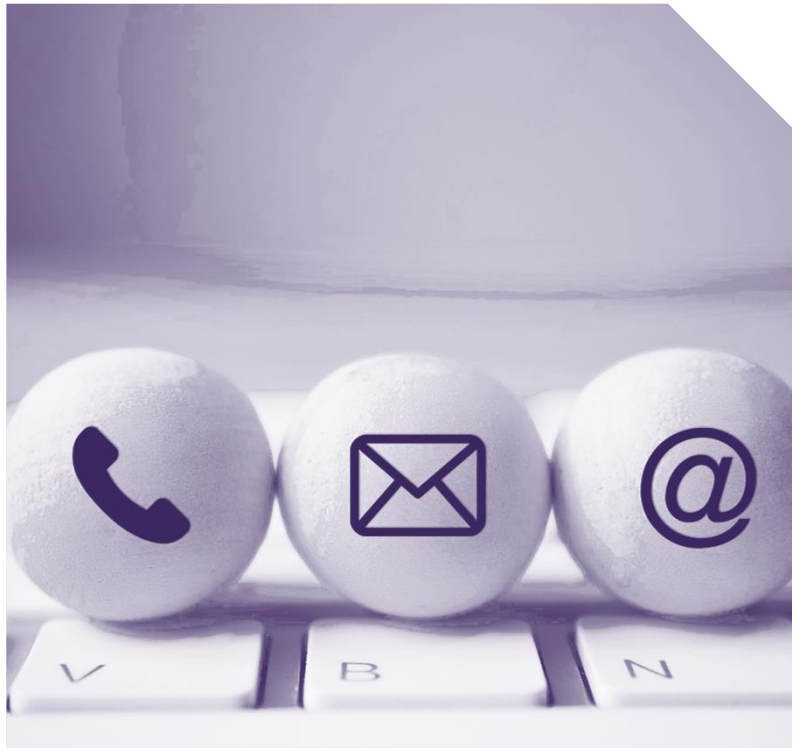
What can be done to improve the situation, and uphold the principle of animal testing as a last resort?

- Commitment from ECHA's leadership to fully replace animal testing in the long-term, and to decrease the upward trend in the short- to medium-term
- Implementation of a strategic plan that demonstrates a proactive commitment to the development and promotion of alternative methods
- Concrete steps to improve the issues identified by ECHA related to the acceptability of non-animal methods and adaptations, which could include the following actions:
  - Provide more positive examples of Read-across and other adaptations accepted to fulfil REACH requirements
  - Open a channel between ECHA and Registrants to discuss technical/scientific issues and suitability of testing strategies, to improve their chances of being accepted
  - Publish life-like examples on the application of RAAF
  - Flexibility on the application of RAAF
  - Define an acceptable, adequate level of uncertainty
  - Flexibility on timelines to improve adaptations
  - Work collaboratively with registrants, be open to feedback (ex. of users of the RAAF) to evolve and adjust the framework for assessment
  - Promote the use of NAMs to support Read-across, in particular for higher tier endpoints (rather than short-term animal studies to demonstrate similarity)
  - When a data gap is identified, consider first whether it would impact the risk management measures, as otherwise it might be omitted

What we would like to hear from the Forum

- Understand how the Forum enforces the principle of animal testing as a last resort
- What measures ECHA could take to promote the development and use of NAMs
- Forum’s views on what could increase regulatory acceptance/confidence in NAMs
- What steps can be taken to revert the trend of increasing animal testing





Thank you!

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