
THE USE OF ALTERNATIVES TO TESTING ON ANIMALS FOR THE REACH REGULATION

Every three years, ECHA submits a report to the European Commission on the implementation and use of non-animal test methods and testing strategies used to generate information on intrinsic properties and for risk assessment. It is published in accordance with ECHA's obligations under Article 117(3) of the REACH Regulation. Under the REACH Regulation, (EC) No 1907/2006, testing on vertebrate animals (e.g. rats, other mammals or fish) can only be used as a last resort to fulfil information requirements for registration.

REACH foresees several ways to avoid unnecessary animal testing. Data sharing and joint submission of information are the main principles behind the registration process which significantly reduce the need for animal testing. In addition, the regulation foresees the possibility to justify waiving of tests or use of adaptations to fulfil the information requirements. This report provides an update on the use and implementation of non-animal testing methods and testing strategies used by companies to meet the information requirements. At the same time, the report provides an overview of ECHA's activities to promote the development and use of alternatives and discusses opportunities and challenges in moving away from animal testing for the risk assessment of chemicals in a regulatory context.

The data presented follows a similar format compared to previous editions, covering the availability of experimental data, the options used to comply with information requirements, and the period when the studies were conducted. The cut-off date for data analysis for the purpose of this report has been set to 31 July 2022, three years after the previous edition.

For the first time, this report provides a separate data analysis of newly registered substances since the previous edition, covering the period from 2019 to 2022, after the final REACH registration deadline in 2018.

The key findings from the data analysis are:

- Overall, adaptations continue to be used by registrants more than experimental studies to fulfil the information requirements; read-across is the most frequent adaptation followed by waivers, weight of evidence and QSAR.
- The majority (53%) of the available experimental studies in the REACH database is legacy data generated before the entry into force of REACH.
- *In vitro* test methods are increasingly used in registration dossiers, especially for skin corrosion/irritation and serious eye damage/eye irritation and skin sensitisation. The significant shift from *in vivo* to *in vitro* approaches, reported in the previous edition, continues between 2019 and 2022. About 50% of the studies conducted since 1990 for skin and eye irritation available in the REACH database, are performed *in vitro*; this percentage rises to about 90% for the most recent studies performed over the last three years.
- Experimental studies are more often used for the low tier testing needed to meet the information requirements for low tonnage substances, while adaptations are more commonly used for the higher tier testing requirements of substances registered at higher tonnage bands.
- There is more data generated through animal testing to investigate long term effects when comparing to three years ago. This is mainly due to the requests made under compliance checks for further testing when non-compliant adaptations were provided. For example, there is more experimental data available for pre-natal developmental toxicity and (sub)chronic repeated dose toxicity.
- When possible, new studies aiming to investigate potential for long term effects are increasingly performed in a combined fashion, to reduce testing on animals. For example, repeated dose toxicity tests are increasingly combined with toxicity to reproduction screening.
- Data analysis for the newly registered substances, over the past three years, shows that the majority, about 70% of these substances, are in the lowest tonnage band (REACH Annex VII) and overall the use of *in vitro* test methods is substantial.

Over the years ECHA has been active in using and promoting the use of alternative methods to animal testing within its mandate. We use alternative methods whenever possible for regulating substances and provide advice and guidance to registrants. ECHA has been active in international collaborations aiming to develop alternative methods such as the initiative on Accelerating the Pace of Chemical Risk Assessment (APCRA), the European Partnership for the Assessment of Risks from Chemicals (PARC) and at the Organisation for Economic Co-operation and Development (OECD) level. In addition, ECHA facilitates the research and development on New Approach Methodologies (NAMs) by making registration data readily available to the wider regulatory and scientific community.

In the OECD context, significant progress has been made with ECHA contributing through several expert and advisory groups to the development of OECD test guidelines, guidance documents as well as the development of case studies. ECHA has also co-led the work to develop a QSAR assessment framework (QAF) establishing criteria to validate QSAR results and has been a co-lead in the steering group to update the OECD guidance on grouping of chemicals. The development and regulatory acceptance of the QSAR toolbox has also progressed (with more than 30 000 users from industry, authorities, and academia), reaching the milestone of being included in the OECD guideline on Defined Approaches on skin sensitisation (OECD TG 497).

Looking forward, ECHA recognises that the topic of replacement of animal testing is highly relevant in the current policy context. We stepped up efforts to contribute to the scientific debate while continuing to implement the regulatory frameworks adopted by the legislator.

New Approach Methodologies currently represent a priority area for ECHA. We provide access to crucial data required for their development. To support this process, ECHA is rebuilding its public dissemination system with a focus to facilitate the re-use of data. The Agency is also expected to play a central role in the EU Common Data Platform which will provide further opportunities in this area. Furthermore, ECHA continues investing in developing the QSAR toolbox to integrate new information. For example, ECHA continues to integrate and use data from various sources such as the contributions from the pharmaceutical industry and from the US Food and Drug Administration (FDA). This will facilitate comparison of animal data and human data and contribute to the development of NAMs and reduction of animal testing.

We are also building internal capacity on NAMs by organising training for ECHA's scientists and Committees (Member State Committee (MSC), Committee for Risk Assessment (RAC)) to increase the level of knowledge on NAMs suitable for regulatory needs.

We have increased co-operation through platforms such as the European Partnership for Alternative Approaches to Animal Testing (EPAA) and APCRA to raise awareness of on-going work and exploit potential synergies. We believe that this will support developing a common understanding on what NAMs can achieve in the short and long term.

Finally, we are playing a more visible and active role in the scientific/regulatory community by steering flagship research projects dedicated to NAMs via PARC or Horizon Europe.

Moving forward, we recognise that a full replacement of animal testing will require advancement in scientific developments as well as policy changes. In this shift, two key questions will need to be addressed: how a new approach can cover the most relevant (adverse) effects and diseases of concern for society (for example, carcinogenicity, mutagenicity, reproductive toxicity, immunotoxicity, endocrine disruption, etc.) and how to ensure a similar or better level of protection for human health and the environment.

Such fundamental changes ultimately represent policy options. ECHA has the competence and is ready to support policy makers in developing suitable and robust approaches for regulating chemicals based on an increased use of NAMs and eventually, phasing out animal testing.