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Workshop Report

EU Roadmap for Phasing Out Animal Testing for Chemical Safety Assessments: Recommendations from a Multi-stakeholder Roundtable

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Abstract

The commitment to develop a roadmap for phasing out the use of animals for chemical safety assessments was part of the European Commission's response to the European Citizens' Initiative "Save Cruelty-Free Cosmetics – Commit to a Europe Without Animal Testing". The roadmap aims to outline milestones and specific actions to be implemented in the short to long-term to ultimately phase out animal testing for chemical safety assessments. To advance this goal and help define a structure of the roadmap, a multi-stakeholder roundtable workshop was organised by five animal protection non-governmental organisations in June 2024. The roundtable aimed to explore and define key elements and organisational structures for shaping the roadmap and identify pathways to facilitate the transition to a non-animal testing regulatory framework. Participants discussed a range of critical issues such as revising legislation and guidance, facilitating validation/qualification and regulatory acceptance, strengthening coordination, providing education and training in non-animal approaches, transparency and accessibility to data, establishing metrics to measure progress and securing funding. The importance of a multi-faceted approach integrating scientific, regulatory, policy, ethical, societal, and practical dimensions was emphasised, along with the critical role of transdisciplinary collaboration and combining diverse knowledge, ideas, and technologies to achieve optimal outcomes. This report summarises the main findings and discussion points and provides concrete recommendations. These are intended to facilitate the Commission's work to develop the roadmap and may serve as a valuable resource for similar initiatives worldwide.

Plain language summary

As part of its response to the European Citizens' Initiative "Save Cruelty-Free Cosmetics – Commit to a Europe Without Animal Testing", the European Commission committed to developing a roadmap to eliminate the use of animals for the safety testing of chemicals. Five animal protection non-governmental organisations organised a roundtable in June 2024 to support this effort, bringing together experts from different fields. The roundtable aimed

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to identify important elements and organisational structures for shaping the roadmap and explore practical steps to move to a regulatory system that does not rely on animal testing. Discussions covered revising current chemicals legislation, accelerating the acceptance of non-animal methods, creating EU databases to improve data sharing, strengthening cooperation and communication, building skills and expertise in non-animal methods, monitoring progress and increasing funding. This report summarises the main ideas and recommendations from the roundtable to help guide the Commission's work on the roadmap.

1 Introduction

In 2021, the European Citizens' Initiative (ECI) "Save Cruelty Free Cosmetics - Commit to a Europe without Animal Testing" was launched in response to significant concerns about an expected increase in animal testing due to new policies[1]. The ECI called for some critical legislative priorities, including the commitment to a roadmap to phase out all animal testing in the EU and modernise regulatory science. The ECI gathered over 1.2 million validated signatures from EU citizens. In July 2023, the European Commission released its response to the ECI, in which it committed to immediately launch work to develop a roadmap for phasing out the use of animals for chemical safety assessments (EC, 2023a). The roadmap intends to outline milestones and specific actions to be implemented in the short to longer term to phase out animal testing for chemical safety assessments. In doing so, the roadmap will analyse and describe the necessary steps to expand and accelerate the development, uptake and implementation of non-animal methods across legislation. The roadmap encompasses fifteen areas of legislation covering chemicals, pesticides, biocides, pharmaceuticals, and workplace safety, among others (EC, 2024a). The roadmap is due to be finalised early in 2026 and will be followed up by an implementation phase that sets the planned actions in motion (EC, 2024b).

Given the expected complexity of the Commission's roadmap and the involvement of a wide range of stakeholders and their diverse backgrounds, there is a significant risk of becoming mired in excessive detail at an early stage. To mitigate this risk, the roadmap needs a clear structure. Building on the 2023 workshops organised by the European Chemicals Agency (ECHA, 2023a) and the European Commission (EC, 2024a), an in-person multi-stakeholder roundtable was organised by five animal protection non-governmental organisations (NGOs) on 18 June 2024. The roundtable aimed to advance the dialogue between key stakeholders and help structure the roadmap for phasing out animal testing for chemical safety assessments in the EU.

Forty-one participants attended the in-person multi-stakeholder roundtable, providing a balanced representation of Commission services, EU agencies, EU Member States, academia, industry, non-profit research organisations and non-governmental organisations. The roundtable was divided into two sessions to: (1) explore and define key elements and organisational structures for shaping the roadmap and (2) identify pathways to facilitate the transition to a non-animal testing regulatory framework. Discussions took place both in break-out group sessions and in wider moderator-led plenaries. An initial summary report outlining only the key recommendations arising from the roundtable discussions was published in October 2024[2] to support the Commission's second workshop on the roadmap, held later that month. A timeline of the evolution of the roadmap - from its inception to its final delivery - is illustrated in Figure 1.

The outcomes of the discussions, as presented in this paper, are intended to facilitate the Commission's work to develop the roadmap and guide discussions with the broader stakeholder community.

2 Key elements and organisational structures for shaping the roadmap

In session one of the roundtable, participants were asked to identify key elements and organisational structures needed to develop and implement the roadmap. In this context, elements represent the highest-level groupings or a selection of interventions of a roadmap's initiatives, all contributing to a particular impact that cuts across goals and outcomes. The

Fig. 1: Timeline highlighting the evolution of the roadmap for phasing out the use of animals for chemical safety assessments, from the submission of signatures of the European Citizens' Initiative (ECI) "Save Cruelty Free Cosmetics – Commit to a Europe without Animal Testing" to the expected delivery by the European Commission (EC)

[1] https://citizens-initiative.europa.eu/initiatives/details/2021/000006_en (accessed 31 January 2025)
[2] https://zenodo.org/records/13889254 (accessed 31 January 2025)

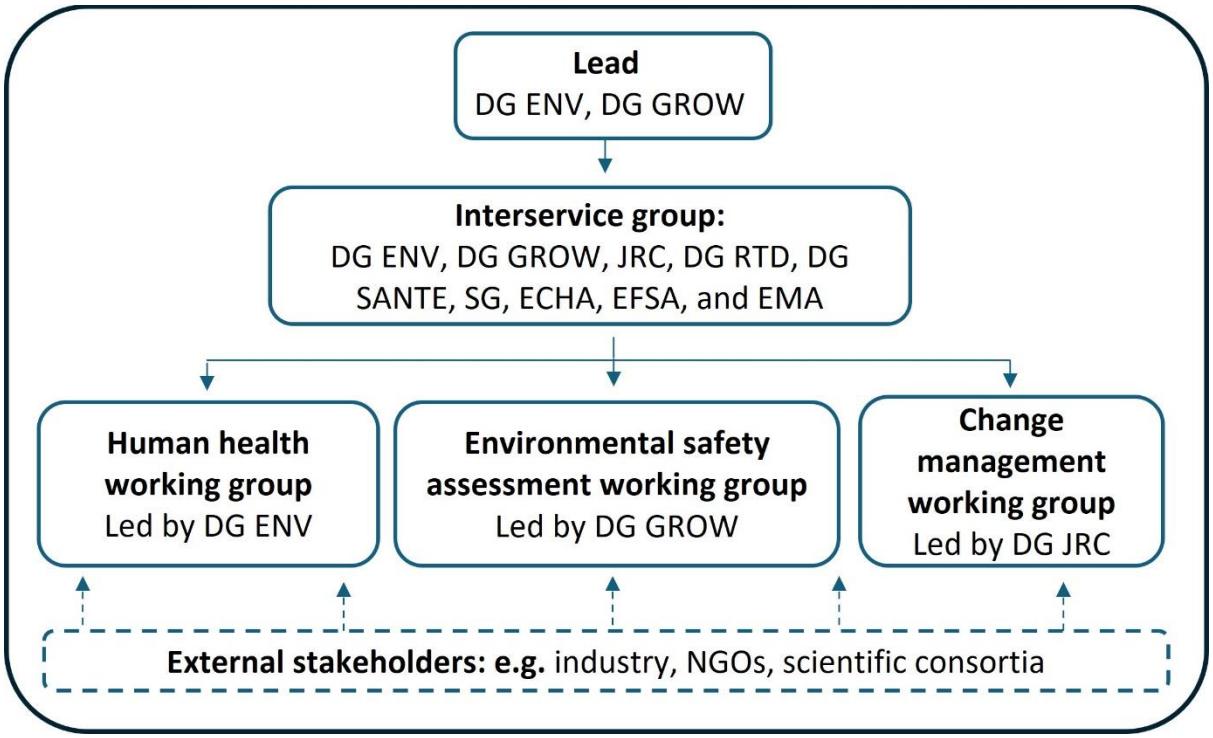

Fig. 2: Organisational structure proposed by the Commission, including the Directorate-General for Environment (DG ENV), the Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs (DG GROW), the Joint Research Centre (JRC), the Directorate-General for Research and Innovation (DG RTD), the Directorate-General for Health and Food Safety (DG SANTE), the Secretariat-General (SG), European Chemicals Agency (ECHA), European Food Safety Authority (EFSA), and the European Medicines Agency (EMA)

Commission's proposed actions for structuring the roadmap[3] and the core elements outlined in the Commission's Communication replying to the ECI (EC, 2023a) provided a helpful starting point for discussions. The dialogue concerning organisational structures and key elements for a roadmap was enriched by considering the Commission's proposed organisational structure (Fig. 2) and the concept of Next-Generation Risk Assessment (NGRA), an exposure-led, hypothesis-driven risk assessment approach that integrates *in silico*, *in chemico* and *in vitro* approaches (Dent et al., 2018; Carmichael et al., 2022). In particular, proposals from the Partnership for the Assessment of Risks from Chemicals (PARC) for implementing NGRA in the EU chemicals legislation were considered. PARC is a multinational European project that involves close to 200 institutions, from 24 EU Member States and 5 non-EU countries, including universities, public health organisations, research institutions, national health authorities, health care institutes, the European Chemicals Agency (ECHA), the European Food Safety Authority (EFSA) and the European Environment Agency (EEA) and aims to enable the transition to NGRA to protect human health and the environment (Herzler et al., 2025). Specifically, the PARC Task 2.2 "Knowledge management and uptake into policy" group has developed ten guiding principles as well as four tentative work streams (scientific development, regulatory acceptance, policy implementation and change management) to guide and structure future efforts in this area[4].

To expand the scope of the discussion, the concepts and roles of transformative governance and transformative change were introduced, emphasising their relevance in driving large-scale and long-term societal changes. Transformative governance can be defined as "the formal and informal (public and private) rules, rule-making systems and actor-networks at all levels of human society (from the local to global) that enable transformative change" (Visseren-Hamakers et al., 2021). In turn, transformative change can be described as "a fundamental, society-wide reorganisation across technological, economic and social factors and structures, including paradigms, goals and values" (Visseren-Hamakers and Kok, 2022). Given the complexity of interests, goals, and values associated with animal testing, transitioning to a non-animal testing regulatory framework requires transformative change. Indeed, the transition to non-animal methods faces challenges that extend beyond technical limitations, primarily encompassing significant social barriers[5]. Therefore, incorporating a change management component is essential to successfully transitioning from a current state to a desired future state by identifying and addressing scientific, regulatory, economic and societal challenges. Participants were presented with Figure 3, which illustrates a restructured model integrating the Commission, PARC, and change management approaches to facilitate discussions on organisational structures. The figure highlights the importance of avoiding siloed operations and fostering collaboration across

[3] https://single-market-economy.ec.europa.eu/document/download/597e75f7-fa32-4731-a42a-aed5b1ad26e6_en?filename=1.4.%20Georg%20Streck_Intro_workshop_roadmap.pdf (accessed 31 January 2025).
[4] https://www.parcopedia.eu/wp-content/uploads/2023/12/20231218_NGRAroute_principles_and_work_streams.zip (accessed 31 January 2025)
[5] https://precisiontox.org/wp-content/uploads/2024/02/D6.1-Report-on-Socio-Technical-Barriers-26Jan.pdf (accessed 31 January 2025)

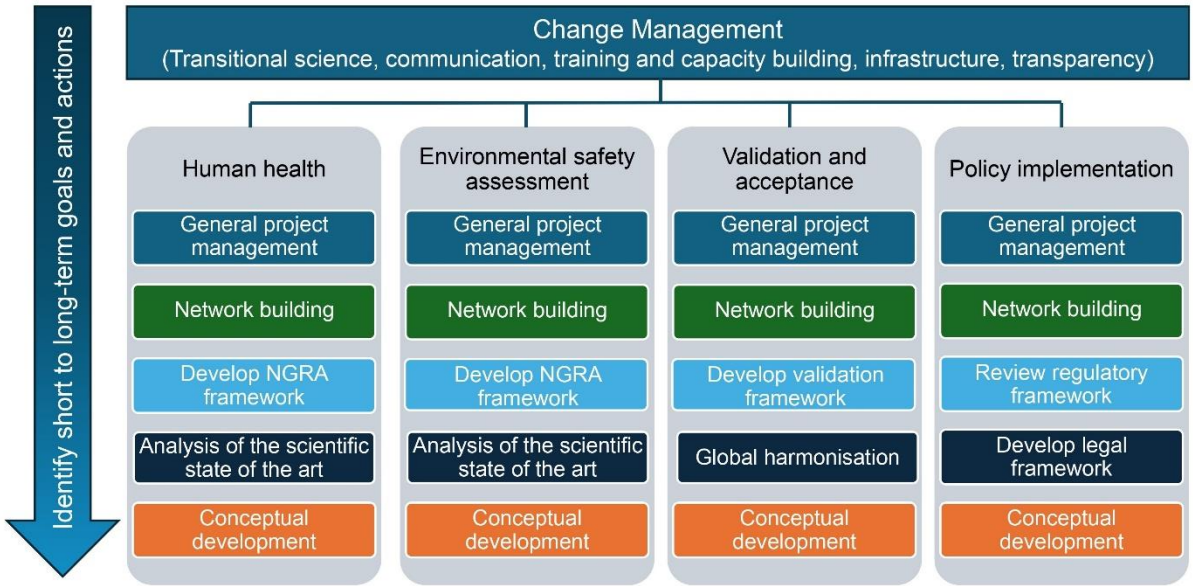

Fig. 3. Illustrative framework integrating the Commission, Partnership for the Assessment of Risks from Chemicals (PARC), and change management approaches highlighting the importance of avoiding siloed operations and fostering collaboration across working groups and positioning change management as an overarching element

working groups while emphasising the overarching role that change management can play in transitioning to a non-animal regulatory system.

The key elements identified during the discussions are outlined in the subsections below. These subsections compile participants' perspectives and do not reflect a consensus among them.

2.1 Revision of legislation and guidance

The EU legislation for chemical safety assessment continues to rely heavily on animal-based data to meet information requirements, even when legislation states that animal testing should be conducted only as a last resort (Fentem et al., 2021). While regulations generally allow the use of non-animal data, often as an adaptation of standard data requirements, they fall short of providing clear and sufficient detail to incentivise its use. Animal protection NGOs stressed that to keep pace with advances in non-animal approaches and to encourage, facilitate, and improve their use, current regulatory frameworks and guidance documents need to allow for faster uptake of these approaches. Similarly, given the dynamic, non-linear nature of change, legislation must be sufficiently able to respond to unforeseen opportunities, challenges and the newest scientific developments while ensuring a consistently high level of protection and legal certainty, i.e., that methods and approaches comply with the relevant legislation. Ensuring legal certainty would necessitate greater clarity on when a registrant has generated sufficient data on a substance and its properties, especially when results, regardless of the method used, are inconclusive or indicate non-toxicity. An overly prescriptive and static regulatory framework risks becoming obsolete as the landscape evolves. There is also a need to simplify and harmonise chemical legislation, including removing conflicting legislation and using clear, user-friendly language. For example, the 'one substance one assessment' (OSOA) approach, aimed at improving the efficiency, effectiveness, coherence and transparency of issuing safety assessments of chemicals across different pieces of EU legislation (EC, 2023b), could be strengthened to foster stringent data requirements across different regulations, minimise conflicting guidance and harmonise safety evaluations. Furthermore, when updating existing legislation, opportunities for facilitating international harmonisation should be kept in mind to aid the transition away from animal testing in chemical safety assessment.

While revising current legislation and guidance may take time, immediate action can be taken to maximise the use of existing non-animal approaches and minimise the use of animals within the current regulatory framework. For instance, animal tests should be removed from regulatory annexes promptly as non-animal approaches are validated and accepted, and redundant tests with no additional informative value should be removed from legislation. Incorporating tiered approaches and strategies into legislation is also essential to facilitate the use of non-animal approaches and enable efficient decision-making processes based on multiple lines of evidence. The need to consider new methods and approaches, the context of use within future regulatory practices, and their value in making regulatory decisions was also highlighted.

Moreover, several participants stressed that future chemicals legislation must place greater emphasis on exposure science and assessment, emphasising that toxicological safety has always been a matter of both hazard and exposure, rather than focusing solely on hazard information. Rather than attempting to replicate animal tests, non-animal approaches aim to provide more relevant and targeted information about a chemical to allow exposure-based safety assessments. According to some participants, the successful implementation and use of non-animal approaches for chemical safety assessments rely, among other factors, on transitioning to a more risk-based approach that prioritises context-specific exposure assessment. In addition, a better understanding of human and environmental exposure levels and the role of exposure data in different regulatory contexts is crucial for informed, evidence-based decision-making based on non-animal approaches. In this regard,

the OSOA approach can play a critical role in monitoring and harmonising the use of the same substances across various legal frameworks. This is key to a more comprehensive understanding of internal substance exposure.

It was further suggested that the roadmap should clarify key questions such as: i) whether non-animal approaches should be developed and applied to single or grouped toxicity endpoints; ii) whether a standardised list of these approaches should be established rather than relying on a case-by-case approach; and iii) whether chemical properties alone could predict the safety of specific levels of chemical exposure or if a supplementary battery of tests is required. For example, understanding the structure of a chemical may be sufficient to identify potential harm, regardless of species considerations.

2.2 Analysis of the status quo

Understanding where non-animal approaches to chemical safety assessment can be immediately applied and where gaps or limitations exist in their development and use is crucial for prioritising efforts and resources. To this end, a coordinated effort should be made to identify and document opportunities, gaps, barriers, and challenges across sectors. For example, discussions highlighted a significant gap in the availability of non-animal approaches to better protect the environment and biodiversity, address complex human health endpoints, and derive Point of Departure (PoD) values for setting safe levels. In the context of pharmaceutical medicinal products, the European Medicines Agency (EMA) has published two reflection papers on regulatory requirements and opportunities to implement the 3Rs (EMA, 2024a, 2025). Currently under revision, these papers provide an overview of the main animal tests required for the regulatory testing of medicinal products for human and veterinary use, information on opportunities for limiting animal testing that can already be implemented, where appropriate, as well as information on opportunities that may become available in the future.

Conducting a more general mapping exercise, complemented with systematic reviews, would be valuable to achieve a comprehensive overview of the current landscape, including a clear understanding of current standards and levels of protection for human health and the environment and insights into current information requirements and how these are being met. This overview would simplify identifying opportunities to use non-animal approaches, such as NGRA frameworks, and where research and development are needed according to the regulatory needs. Incorporating ongoing EU and international initiatives, as well as a comprehensive dataset of non-animal approaches and the information they provide, would enhance the mapping and help identify best practices and successful strategies from other Member States and countries. Additionally, leveraging artificial intelligence could significantly enhance the process by enabling real-time updates to the mapping as new data becomes available (Aldoseri et al., 2023; Kleinstreuer and Hartung, 2024).

2.3 Coordination

A robust and leading voice is essential to drive change and manage the complex transition to a non-animal regulatory system. Existing tools and resources will only provide the expected support with a clear and strategic direction. To this end, some participants suggested that a supervisory steering committee, independent from the European Commission, should be established to successfully guide and coordinate the implementation process. This committee would be crucial in defining roles and responsibilities, mapping activities, facilitating stakeholder communication, providing regular updates, actively promoting work, and monitoring progress. It would ensure that each area's needs and existing sectoral legislation are understood and considered.

2.4 Regulatory acceptance

Test method validation is a process based on a scientifically sound and independent evaluation that establishes the reliability and relevance of a particular test, approach, method, or process for a defined purpose (OECD, 2005). This involves the evaluation of various performance parameters to ensure that the method consistently and accurately performs its intended function. Conducted under standardised and controlled conditions, validation has generally been required to facilitate and accelerate international regulatory acceptance of test methods. However, validation is a time- and resource-demanding process that is not adequately funded in the current situation, contributing to the slow progress of important work in this area (Gourmelon et al., 2024; Jacobs et al., 2024). While the OECD Guidance Document 34 for validation (OECD, 2005) is being updated to align with rapid scientific progress, this effort alone will not accelerate the process. It is crucial to raise awareness of the readiness concept in the development and optimisation phase and ensure adequate funding for validation and subsequent steps to drive progress.

It is important to recognise that other international harmonisation systems exist beyond the OECD framework, such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). While these systems also have limitations, primarily the time required to develop guidance, they do not impose the same validation requirements. Additionally, the Biological Standardisation Programme of the European Directorate for the Quality of Medicines & HealthCare and the inclusion of a method in the European Pharmacopoeia also serve as validation mechanisms.

Alternative pathways to regulatory acceptance should be explored to help improve the uptake and implementation of non-animal methods. Such an exploration will require a deeper understanding of the requirements for regulatory acceptance, including a clear definition of the scientific and regulatory 'relevance' of a particular method or approach, the drivers for acceptance of non-animal approaches, and the incentives for regulators to accept non-animal approaches for regulatory decision-making.

The strategy should emphasise that non-animal approaches are not designed or intended to be a direct one-to-one replacement for animal testing, except for very specific or acute adverse health effects, and that a more holistic approach is needed. Additionally, it needs to be considered that even if a non-animal method is scientifically valid, it may not fully meet the regulatory requirements currently addressed by *in vivo* tests. As a result, its regulatory applicability may be limited. Complex toxicological assessments should use a battery approach consisting of diverse non-animal methods with varying

levels of complexity. Furthermore, any non-animal method should apply to all chemicals for which it is intended to replace the *in vivo* test. Therefore, post-validation and first learnings must clarify if the proposed context of use and domain of applicability cover sufficient broad chemical space. Moreover, expanding approaches to pre-validation and qualification criteria for research projects with regulatory applications are proposed to streamline the process and ensure alignment with regulatory expectations.

For medicines, validation is less relevant than qualification. The qualification of novel methodologies is "a voluntary, scientific pathway allowing developers of innovative drug development methods to request from European medicines regulators the qualification of these instruments within a predefined context of use" (EMA, 2024b). For medicines, the qualification of a method could be an acceptable alternative pathway to regulatory acceptance.

Bridging the gap between method development, validation, harmonisation, and regulatory acceptance will also require dedicated funding and the development of clear sustainability strategies, i.e., detailed plans for the project or product handover upon completion. Effective strategies include building partnerships with regulators and industry stakeholders and creating detailed implementation plans that extend beyond the project lifecycle. Consideration of the pathway from method development, validation, and harmonisation to regulatory acceptance will ensure accountability and support to maximise the value and impact of research results and facilitate their translation into practice.

It was also suggested that the concept of 'safe harbours' be explored to provide spaces where safety assessments based on non-animal approaches can be discussed early in the regulatory process. This could also positively influence regulatory acceptance and use of non-animal approaches by building confidence in their validity, particularly regarding the concept of the OSOA initiative. The EMA's Innovation Task Force[6] could serve as a model regarding a 'safe space' for discussion between method developers, substance manufacturers, and regulators to help build confidence in non-animal approaches. To facilitate interactions between method developers, substance manufacturers and regulators, it is crucial to identify the barriers to the widespread use of 'safe harbours' and make the necessary adjustments. This would require fostering mutual trust between registrants and regulators based on confidence and transparency in using non-animal methods in regulatory submissions.

2.5 Global acceptance and harmonisation

Global acceptance and harmonisation are vital issues to consider when developing a roadmap. Strategic alignment with international frameworks and initiatives prioritising non-animal approaches will help ensure successful implementation and impact of the roadmap. Equally important is the need to understand how to achieve mutual acceptance of data and consensus on how non-animal approaches can fulfil regulatory requirements at the EU level, with active engagement from EU regulators across Member States, as well as on a global scale. International coordination efforts should be strengthened to facilitate this, with the EU taking a leading role in advancing global collaboration and acceptance using the best available science.

Among the activities that could be initiated, it was suggested that regular engagement with international stakeholders be increased and global data sharing be facilitated to improve the collection and evaluation of existing non-animal approaches in coordination with the OECD. Furthermore, the priorities set out in the working groups established by the Commission to advance the work on the roadmap place the EU in a position to take a leading global role and would be synergistic with the EU test method development and validation strategy proposal[7].

2.6 Collaboration and communication

Achieving our common goals demands a unified approach. We must foster strong collaboration and build robust networks between stakeholders, sectors and disciplines within the EU and globally to succeed. Building an interconnected community would lead to increased knowledge and data sharing, valuable insights into different perspectives, and alignment of expectations and needs. An open and collaborative environment would also facilitate the streamlining of activities, effectively eliminating silos and ensuring that all efforts are harmonised as far as possible. Inclusive participation is fundamental to this process, enabling all stakeholders to contribute to the roadmap.

The promotion of 'cross-fertilisation' was identified as a critical action to strengthen cross-sectoral cooperation and adaptability to change. This concept refers to the transdisciplinary combination of knowledge, ideas and technologies to achieve optimal results. It emphasises the value of multiple perspectives, recognising that what constitutes success or ambition may vary in different contexts. Encouraging cross-fertilisation and multidisciplinary collaboration is not only mutually beneficial but also essential for building trust, a critical component of successfully transitioning to a new system. Through structured change management, potential areas of resistance can be identified in an early stage, allowing for the implementation of targeted strategies to minimise disruption. Additionally, this approach ensures that stakeholders are well-informed and equipped to navigate the transition effectively while simultaneously ensuring that the safety of human health and the environment will not be compromised.

For instance, to overcome traditional scientific silos, incorporating the expertise of social scientists would broaden perspectives and encourage innovative thinking in the field of chemical safety assessment. Organising 'transition science' courses to reflect on the fundamental changes needed in a society's culture, structures and practices to transition to a new system could also be a valuable step in this direction, fostering open communication and collaboration between all stakeholders to co-create solutions.

A clear interest was expressed in developing a comprehensive multi-stakeholder communication strategy. This strategy would foster dialogue and interaction between stakeholders, sectors, and working groups. Its main objective is to

[6] https://eic.ec.europa.eu/document/download/07d8682a-6a27-4148-a544-4e56c2adf53d_en?filename=2.%20F.Ehmann%20-%20ITF.pdf (accessed 14 February 2025)
[7] https://circabc.europa.eu/ui/group/a0b483a2-4c05-4058-addf-2a4de71b9a98/library/616824f8-fafb-4962-b14c-a37029049992/details (accessed 14 February 2025)

identify potential synergies while respecting sectoral differences and to eliminate redundancies while keeping everyone informed of developments in different areas. To this end, a multi-faceted approach to communication is suggested. This approach should use various communication tools and channels tailored to the specific audience, such as establishing regular in-person stakeholder meetings, creating dedicated cross-sectoral discussion forums, and using multiple visual and audio tools. Crucially, the source of information plays a pivotal role, and trusted voices within relevant communities can significantly increase stakeholder receptivity to messages. The work of the EMA provides a valuable example through initiatives like its 3Rs Working Party[8]. Similarly, the European Partnership for Alternative Approaches serves as an effective platform for fostering productive dialogue across industry and the European Commission and linking to other stakeholder groups. In addition, including the EU Reference Laboratory for alternatives to animal testing (EURL ECVAM) in stakeholder meetings can provide significant benefits, drawing on its in-house experience and expertise.

Inclusive collaboration within the Commission's working groups is essential in allowing all stakeholders, including regulators and sectors, to contribute their perspectives, needs, and expectations and ensure a comprehensive approach. For example, the pharmaceutical industry's work on an actionable roadmap based on a 'three-basket approach' for phasing out animal testing offers valuable insights to advance the transition to a non-animal testing regulatory framework (EC, 2024a). Regular interaction and open communication between working groups are imperative to prevent silos and ensure transparency and alignment. To facilitate this, a dedicated project manager or management team is recommended to oversee and streamline cross-sector efforts, supported by robust reporting mechanisms. Additionally, establishing expert pools or readily available contact lists is a valuable measure to provide timely support to the Commission on specific issues targeting human health and the environment.

The lack of clear definitions for terms such as 'new approach methodologies' (NAMs), 'safety', 'relevance', 'validation', and 'acceptance' is a significant barrier in cross-disciplinary discussions and studies. To this end, establishing a common understanding of specific terms is necessary to ensure all stakeholders have the same understanding to enable effective collaboration, define common goals, and identify challenges in transitioning to a new system. It was noted that open and honest communication about existing data and processes, the limitations of the current system, and the potential of non-animal approaches is critical to building trust and facilitating support for the transition to a new non-animal regulatory system.

2.7 Transparency and accessibility to knowledge and data

Increased transparency and accessibility of knowledge and data emerged as another key element. Discussions highlighted the need for a more transparent decision-making process, with particular emphasis on demonstrating that animal testing is genuinely used as a last resort and providing public access to regulatory decisions. In particular, greater efforts should be made to document which non-animal approaches have been considered and rejected (and the reasons for their rejection) before recourse to animal testing. This would serve as a valuable resource for developing non-animal approaches and explain why non-animal methods are currently rejected. Greater transparency in reporting the number of animals used for chemical testing is also requested, including detailed breakdowns by country and sector, as well as animal uses outside the EU to comply with EU legislation. Likewise, concerted efforts are needed to promote an open science culture to increase the sharing of knowledge, data and tools, as well as best practices in open collaboration with all stakeholders. Such efforts should include facilitating efficient data sharing of studies, regardless of their results.

Possible solutions include developing effective incentives to encourage companies to share data and be mindful of confidential business information and competition limitations. Suggestions include the creation of a centralised, user-friendly EU database to compile non-animal testing approaches and the development of a curated data repository specifically designed for artificial intelligence applications. Additionally, supporting scientists in sharing their non-animal innovations with EU agencies from an early stage can accelerate familiarity and uptake of these techniques once suitably advanced.

In line with the OSOA initiative proposed in the Chemicals Strategy for Sustainability, the Commission's proposal to establish a common data platform on chemicals (EC, 2023b) is considered a valuable tool to significantly improve the efficiency, effectiveness, coherence and transparency of issuing safety assessments of chemicals across different pieces of EU legislation. Such a platform can greatly improve access to chemical data by removing technical and administrative barriers to data reuse. Moreover, it can promote the principles of open data, increase transparency, foster stakeholder dialogue, and build confidence in using non-animal approaches. However, to ensure maximum transparency, there must be full access to data in a usable format to enhance wider stakeholder engagement, including academia and the public.

The incorporation of data from companies could dramatically improve this platform. Still, it is recognised that companies will require effective incentives to encourage data sharing and compliance with Findable, Accessible, Interoperable and Reusable (FAIR) principles (Wilkinson et al., 2016).

2.8 Education and training

Robust training programmes covering the spectrum of non-animal approaches, the functioning of legal frameworks, and regulatory requirements are essential to the widespread adoption and successful implementation of non-animal approaches. Such programmes can ensure that stakeholders are well equipped with the necessary expertise to use these approaches effectively, interpret the resulting data accurately, build confidence in them, and easily navigate the regulatory landscape. This process would require a meticulous assessment of each stakeholder group's specific education and training needs, including academia, regulators, industry (including contract research organisations and small and medium-sized enterprises (SMEs)) and even the trainers themselves, to ensure a targeted and impactful approach.

The critical need to prioritise education in non-animal approaches in undergraduate and postgraduate programmes was also emphasised. Integrating these approaches can equip future researchers with the tools and knowledge to effectively

[8] https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/3rs-working-party. Accessed 6 March 2025

use and interpret data from non-animal methods, fostering a future generation proficient in these advanced techniques. This is particularly important in countries where resource constraints currently impede the integration of such approaches into science curricula. Similarly, integrating courses on non-animal approaches into secondary school curricula presents a valuable opportunity to equip students early with the expertise needed to meet the growing demand for specialists in non-animal technologies and advancing human-relevant science (Holloway et al., 2021). By adapting curricula to reflect the emerging non-animal paradigm in science, the next generation of students can play a pivotal role in driving the full replacement of animal testing.

To support these efforts, leveraging the expertise and approaches developed by relevant stakeholders is crucial. For instance, the Animal-Free Safety Assessment (AFSA) Collaboration Master Class[9] offers a detailed e-learning program designed to build stakeholder confidence and proficiency in non-animal safety assessment methods, particularly in cosmetics, by emphasising next-generation risk assessment techniques. Similarly, the EPIC webinar series[10], co-organised by the U.S. Environmental Protection Agency (EPA), PETA Science Consortium International, the Institute for In Vitro Sciences, and the California Department of Pesticide Regulation, promotes collaboration by sharing best practices, innovative tools, and regulatory advancements in non-animal approaches. An additional example is the NAM Use for Regulatory Application (NURA) Learning Portal[11] developed by the Physicians Committee for Responsible Medicine, which provides tailored educational resources to support regulatory applications of these methods. Another example is the Education and Training Platform for Laboratory Animal Science (ETPLAS) learning modules[12], particularly modules 52 (Searching for (existing) non-animal alternatives) and 60 (Developing in vitro methods and approaches for scientific and regulatory use) and the e-learning course on "Systematic Reviews of Animal Studies." These initiatives highlight the significant resources available to advance training programs and promote the global adoption of non-animal approaches.

2.9 Measure progress

The establishment by the Commission of a robust and transparent monitoring and evaluation framework, with clearly defined tools, indicators, and a functional reporting system, would provide invaluable insights into the progress and impact of implemented actions and allow for the strategic allocation of efforts and resources to priority areas. It also allows for the necessary adjustments to ensure that actions remain aligned with established objectives. Using data on the uptake of non-animal methods and *in vivo* approaches as guides (ECHA, 2023b; EC, 2023c), specific targets and milestones could be set for each stakeholder group. Such a framework, with regular checkpoints and time-bound deliverables for each sector stakeholder group, would objectively measure success and foster a culture of accountability; the metrics on animal use in research and development activities collected by the U.S. Environmental Protection Agency could serve as a useful model in this respect[13]. Additional suggested success criteria include business impact, innovation outcomes, sector competitiveness, and socio-economic indicators. The transition away from animal testing should not only drive scientific progress but also carefully monitor potential disruptions to interconnected systems, ensuring that impacts on SMEs and industry competitiveness are adequately considered and supported. Moreover, introducing a certification or standard to incentivise and publicly recognise field leaders could motivate others to follow suit.

2.10 Funding

Securing stable and sufficient funding streams is vital for transitioning to a new non-animal regulatory system. With a sound financial base, this transition will be significantly improved. In particular, there is a need for estimating the costs of change and increasing financial resources to (i) support, modernise and accelerate the development, validation and implementation of non-animal approaches across different sectors; (ii) build new or expand existing EU infrastructures specifically dedicated to non-animal testing and the implementation of non-animal approaches into the risk assessment process; (iii) foster communication and collaboration among stakeholders; (iv) facilitate data sharing; and (v) provide the necessary education and training. To help estimate these costs, agreeing on clearly defined research and development objectives and criteria for measuring success is essential. Without clear objectives and agreed success criteria, increased funding may lead to multiple duplications of efforts. This fragmentation could be counterproductive, requiring additional resources to harmonise multiple, uncoordinated outcomes.

Increased financial support for (underfunded) 3Rs Centres and for referenced laboratories under the European Union Network of Laboratories for the Validation of Alternative Methods (EU-NETVAL), whose mission is to provide support for EURL ECVAM validation studies to assess the reliability and relevance of non-animal methods, was also proposed, particularly for countries with limited capacity to validate and implement non-animal approaches.

3 Identify pathways to facilitate the transition to a non-animal testing regulatory framework

Based on discussions from the first session of the roundtable, the second session focused on five key workflows to advance the transition to a non-animal testing regulatory framework: scientific development, validation process, policy development, regulatory implementation and change management. Participants were asked to reflect on their experiences, including the

[9] https://www.afsacollaboration.org/masterclass/. Accessed 6 March 2025.
[10] https://www.thepsci.eu/epicwebinars/. Accessed 6 March 2025.
[11] https://nuratraining.talentlms.com/plus/. Accessed 6 March 2025.
[12] https://learn.etplas.eu/. Accessed 6 March 2025.
[13] https://www.epa.gov/system/files/documents/2021-11/nams-work-plan_11_15_21_508-tagged.pdf (accessed 31 January 2025)

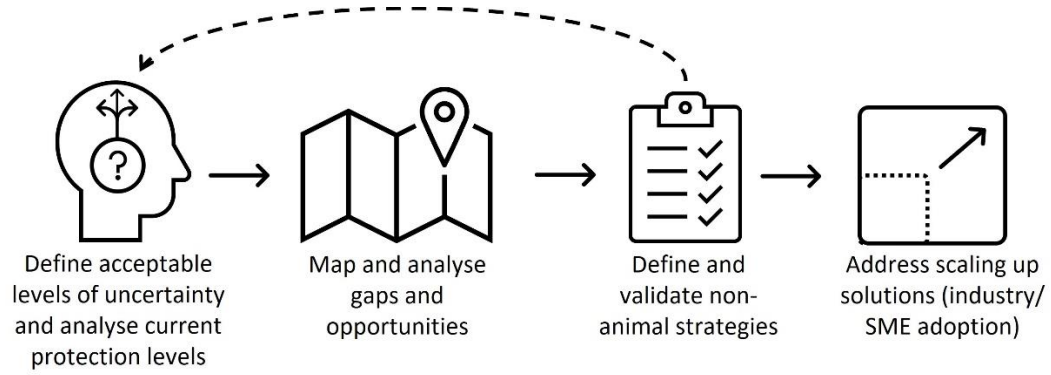

Fig. 4: Scientific development workflow to facilitate the transition to a non-animal testing regulatory framework

challenges of moving to new systems, how they might be overcome, and the resources and mechanisms required to meet the defined goals.

3.1 Scientific development

The roadmap should include actions aimed at channelling the winding path of scientific discovery into a structured, step-by-step process (Fig. 4). As noted in session one of the roundtable discussions, a key element to support the transition toward a non-animal framework for chemical safety assessment is to analyse the status quo. Such a process would consist of a first stage where acceptable uncertainty levels and the current protection levels are defined across different regulations. A scoping exercise or dedicated workshop could facilitate a deeper exploration of these issues. The second stage would analyse gaps and opportunities in developing and using non-animal approaches for regulatory decision-making. In stage three, non-animal strategies could be defined and validated. This process contributes to and feeds back into stage one. The final stage would address the scaling up of solutions. This phase includes actions to increase capacity building, education, and training for structural programs. Additionally, this process will require the assessment of the testing capacities of contract research organisations and creating a centralised non-animal data set under the EU Common Data Platform.

Similar to the approach used in business cases, the proposed scientific development workflow must outline strategic priorities with defined timelines and demonstrate clear economic benefits. These elements can be instrumental in enhancing stakeholder buy-in, particularly from industry.

Regulatory approval of methods and legal certainty in the decision-making process are inherently linked; as such, the lack of regulatory approval for non-animal approaches and unclear regulatory expectations regarding their equivalency to animal tests can significantly hinder their acceptance and broader development and implementation within the industry. Likewise, industry and regulators must work together to ensure that decisions based on sound scientific evidence (using biologically relevant approaches) are understood, even when they may lead to adjustments in the use of certain substances. Cost considerations and applying rules and criteria originally based on *in vivo* studies can also be a significant barrier to adopting new non-animal methods, particularly for SMEs. While larger companies with established testing budgets may find the additional cost of implementing new methods manageable, SMEs with limited testing infrastructure may need more financial support to implement such change. However, a domino effect is likely; as larger companies embrace non-animal approaches, cost reductions, knowledge sharing, and supply chain pressures will likely encourage SMEs to follow suit. This approach could be strategic to planning pathways, with large companies paving the way, ultimately benefiting the industry area.

3.2 Validation process

An achievable intermediate goal for ultimately phasing out animal testing for chemical safety assessments is exploring and developing a strategy to improve the current validation process. Validation procedures need additional funding and streamlining to keep pace with rapid scientific progress. Improvement to the validation process would require establishing a clear evidence-based framework that is adaptable to different needs, depending on the sector and the context of use of the non-animal approach. Such a framework should define the steps, procedures and criteria for non-animal approaches to be deemed ‘relevant’ for regulatory acceptance and ‘ready’ for practical implementation. In the wider context of a roadmap, it will also be necessary to consider critical issues such as mutual acceptance of data, funding for validation, assessment of the context of use and scientific needs, and prioritisation of development or adaptation of test methods to meet regulatory research needs. The validation framework should validate new methods with the best data available, ideally and where possible, using biologically relevant data as a reference. For example, decisions on human safety would come from various sources, including cells and tissues of human origin or studies based on epidemiological data.

Developing an updated or alternative validation system for regulatory acceptance of non-animal approaches will require substantial funding and capacity building, including expanding expert networks dedicated to coordinating and facilitating validation studies. Streamlining regulatory acceptance will also need a clear delineation of stakeholder roles, including a possible redefinition of the role and tasks of EURL ECVAM in the validation and approval of non-animal approaches. Recognising the limited capacity of EURL ECVAM to coordinate all validation studies, establishing small validation units within individual regulatory agencies could be a practical solution to speed up the process. This approach also allows for tailor-made validations to meet each agency’s needs. However, safeguards must be implemented to prevent methods from being validated exclusively for a single agency. Regulatory agencies should be mandated to coordinate actions to advance validation

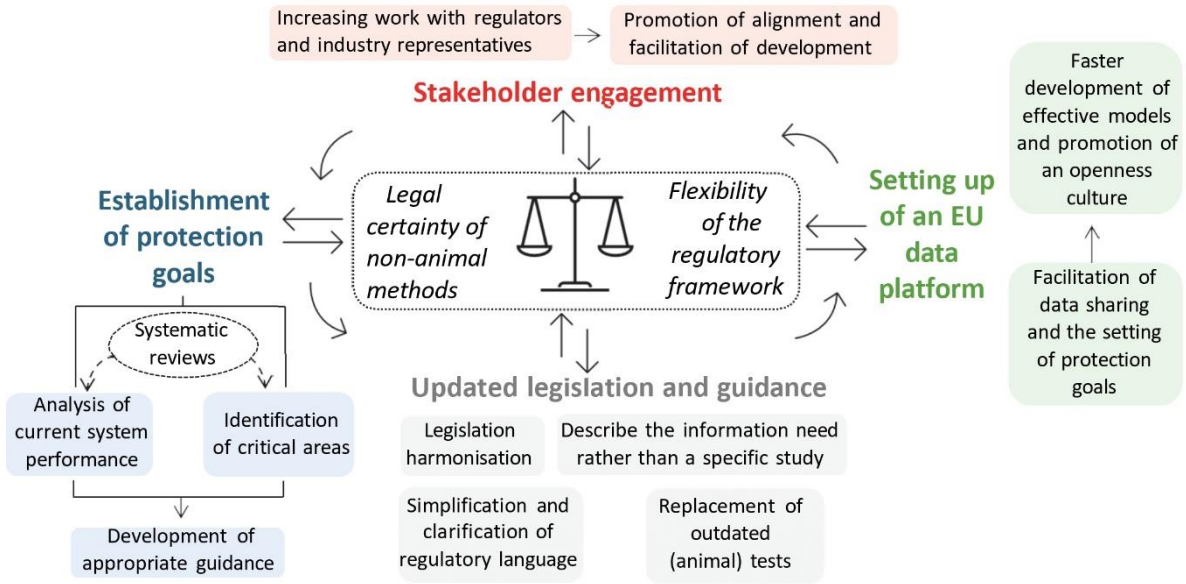

Fig. 5: Policy development workflow to facilitate the transition to a non-animal testing regulatory framework

efforts, such as prioritising guideline developments to meet EU regulatory needs, with adequate accompanying resources and in the context of international acceptance (e.g., OECD test guidelines).

It is important to note that the context of use-based qualification of novel methodologies, particularly for medicinal purposes, was not discussed and remains an area for further consideration.

3.3 Policy development

A critical intermediate goal in policy development is to achieve legal certainty for using non-animal approaches while maintaining a balance with flexibility within the regulatory framework. However, this also presents a significant challenge. A 'one-size-fits-all' approach or an attempt to replicate regulatory decisions may not be optimal for all non-animal approaches or all sectoral needs, particularly where protection goals, context of use or qualification criteria significantly differ. As such, this challenge poses the broader question of whether non-animal methods need to fit into the current regulatory framework or whether fundamental changes to the regulatory framework are required. Ultimately, it is recognised that achieving a regulatory framework without animal tests will require fundamental changes and that work underpinning those changes must commence in the short term. Several goals and key activities were identified to enable such changes (Fig. 5).

One roadmap priority goal will be clearly defining protection goals for each sector. To achieve this goal, the roadmap must incorporate intermediate goals such as developing a comprehensive understanding of how well the existing protection goals are being met and identifying areas where current protection is lacking or inadequate. Identifying data gaps in protection will require systematic reviews that consider sectoral requirements for safety and harm-benefit assessments, the context of use and acceptable levels of uncertainty. However, defining protection goals will help establish appropriate guidance for demonstrating proof of concept when developing non-animal approaches.

In achieving the balance between legal certainty and flexible regulatory frameworks, stakeholder engagement, including regulators, is also essential to ensure that all perspectives are considered. Effective engagement is required to promote alignment and facilitate the development of solutions that address all relevant needs and overcome existing barriers. Such engagement includes liaising with regulators and industry representatives from early developmental stages, recognising that larger companies may already have developed protection goals internally.

Developing a common EU data platform would also facilitate data sharing and setting protection goals. This platform must allow for the sharing of 'negative' results (i.e., those that fail to support the initial hypothesis with sufficient statistical evidence or contradict existing knowledge) and the recording of inconclusive studies, together with the identified reasons, to avoid replication of experiments and focus on more promising avenues. Such data sharing will lead to faster development of effective models and promote a culture of openness between science and regulators, helping regulators build confidence in using non-animal approaches.

Legislation and guidance need to be up to date to maintain a balance between legal certainty and flexible regulatory frameworks. Updates should include replacing tests on animals with accepted non-animal methods, whether they already exist or as they become available, simplifying and clarifying regulatory language, using method-agnostic language in legislation (i.e., avoiding language that suggests a preference for animal testing) and harmonising legislation.

3.4 Regulatory implementation

Three main intermediate goals were identified to enhance regulatory implementation: (i) the revision of existing regulations to explicitly allow the increased use of non-animal approaches for safety assessment; (ii) the establishment of well-defined criteria for regulatory acceptance of non-animal testing data and metrics for regulatory uptake; and (iii) the creation of 'safe spaces' for freely exchanging ideas, methodologies, and data. These spaces would allow room for creativity, experimentation,

and sharing of innovative proposals, as well as shared learning from successful and unsuccessful approaches. They could also encourage open and unfiltered dialogue between stakeholders, including, for example, scientific discussions with regulators on non-animal approaches.

To achieve the intermediate goals set out above, a set of core activities should be undertaken, including the following activities:

- Developing broadly applicable systems whereby non-animal data of varying types can be evaluated to demonstrate that a suitable level of protection has been achieved;
- Setting up working groups to propose clear, sector-specific regulatory acceptance criteria;
- Implementing legal requirements and operational guidelines for the 'safe spaces';
- Ensuring transparency by providing access to regulatory decisions to understand what has been done and what has and has not been accepted.

There is also a clear need to build greater confidence among stakeholders, including regulators, in using non-animal approaches and applying regulatory actions based on these approaches. For example, if existing regulations or guidance were more explicit about the use of non-animal approaches, regulators would be better equipped to interpret and implement them, potentially reducing the tendency toward conservative decision-making. Another way of incentivising regulators to adopt these approaches is to demonstrate how they can significantly speed up the safety assessment process while ensuring equal or better protection. Involving regulators in the early stages of developing non-animal approaches is essential to building early confidence in these approaches. In this way, developers will gain experience in regulatory science, and regulators will gain an understanding of the scientific basis of non-animal methods, thereby fostering greater confidence in their reliability and incentivising faster acceptance once the methods are ready for validation. In addition, case studies can serve as valuable tools for promoting understanding, disseminating knowledge and identifying the strengths and limitations of non-animal approaches. Increased support for developing more robust case studies was identified as a critical priority to effectively demonstrate practical applications, build confidence in using non-animal approaches in regulatory decision-making, and capitalise on the lessons learned from such case studies.

3.5 Change management

Change management will play a critical role in successfully transitioning from a current state to a desired future state by identifying and addressing scientific, regulatory, economic and societal challenges. Building support and including all parties required for change management is important. Achievable goals that are key to this process are the establishment of a coherent and aligned strategy to ensure a common approach, cross-sectoral harmonisation, and the implementation of milestones and indicators to measure progress. Achieving these goals will require the execution of a defined set of activities. These include establishing a governance framework, assigning working group owners, identifying synergies to co-create, identifying clear transition indicators to track progress, estimating the costs of change, and securing sustainable funding mechanisms to ensure long-term success.

Another essential activity is establishing an overarching direction to set clear milestones. Possible options include reducing animal testing by a certain percentage within a given timeframe, prioritising the replacement of the most severe tests and 'less relevant' tests, eliminating second-species testing and redundant tests, or focusing on the replacement of specific endpoints. However, further discussion is needed on what kind of milestones will be most effective and how to align them with other relevant working groups. Furthermore, discussions highlighted that phasing out the use of vertebrates could present an opportunity to consider phasing out invertebrates as a subsequent step.

Stakeholder engagement is an equally important component of change management. Effective engagement will require communication with academia, industry, animal welfare and environmental NGOs, and regulators to inform all parties of advances in non-animal testing approaches. It will also ensure that all stakeholders understand the need to move to a new system, build confidence in the change, facilitate smooth institutional adaptation to the new framework, and provide a sustainable transition economy over time. Clear communication channels between regulators and non-animal method developers will also be essential to bridge existing gaps. Building public confidence in a new system of chemical safety assessment will require communication efforts focusing on raising awareness of the safety and efficacy of non-animal methods while fostering an understanding of the rationale behind phasing out animal testing. Establishing effective communication requires the development of a comprehensive 'change toolbox' that includes elements such as communication strategies, training programmes, information exchange platforms and relevant case studies. Additionally, a capacity-building strategy with clear milestones should be developed.

4 Outlook and conclusions

A comprehensive roadmap with clear directions and unambiguous policies is essential to provide a structured framework for ultimately phasing out animal testing for chemical safety assessments. By aligning efforts within a common framework, the roadmap can act as a catalyst for establishing faster and more efficient testing and evidence-based decision-making systems while ensuring that human and environmental safety is not compromised, and that regulatory frameworks and practices keep pace with the rapid pace of scientific advances. A well-defined roadmap offers clarity and predictability, which are crucial for guiding future directions, integrating progress across sectors, and empowering stakeholders to make informed decisions about resource allocation and strategic priorities. Additionally, it can be instrumental in highlighting advances and initiatives, thereby avoiding duplication of efforts and addressing existing gaps.

Developing a comprehensive roadmap will require a multi-faceted approach integrating scientific, regulatory, policy, ethical, societal and practical considerations. A robust change management framework is, therefore, essential to orchestrate

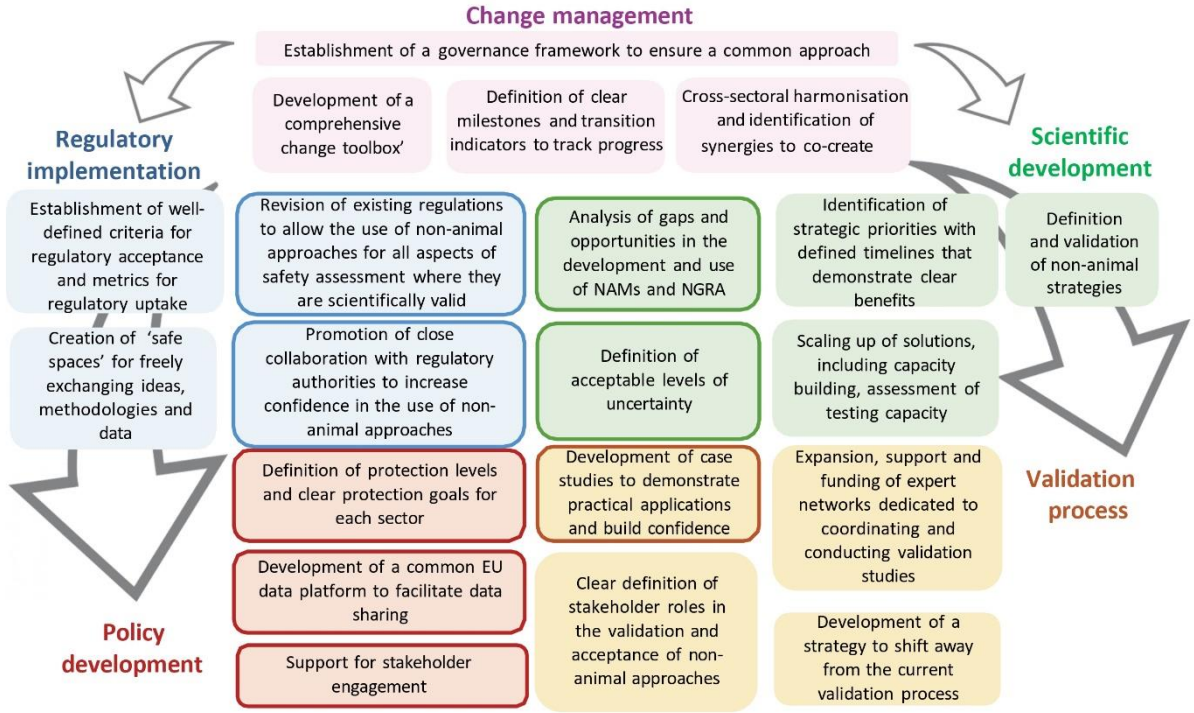

Fig. 6: Recommendations are divided into five workflows to facilitate the transition to a non-animal testing regulatory framework
The change management workflow should act as an overarching component providing guidance and coordination to other workflows. Boxes with a thick line represent recommendations pertinent to most or all workflows. Abbreviations: NAMs, new approach methodologies; NGRA, next-generation risk assessment

this multi-faceted endeavour. Rather than operating in isolation, the change management framework should act as an overarching component, providing guidance and coordination to other workflows (Fig. 6). Such a working model is exemplified throughout the discussions with the emergence of several recurring themes that span multiple workflows, including the need for a comprehensive assessment of existing systems and protection levels, the revision of legislation, and enhanced stakeholder engagement and collaboration.

Conducting a thorough evaluation of current systems requires a better understanding of how safety is defined, the level of protection provided by the current system for human health and the environment and how to achieve at least equivalent protection from an alternative system. This mapping exercise may also necessitate re-evaluating the desired level of protection. Protection goals effectively require acknowledging the underlying uncertainties. Therefore, the acceptable thresholds of uncertainty for a particular purpose (e.g., endpoints or regulatory requirements) for non-animal approaches need to be clearly defined as part of the assessment. This should be based on identifying the sources and evaluating the current level of uncertainty arising from using animal models as a benchmark.

Revising existing regulations is essential to explicitly allow the use of non-animal approaches for all aspects of safety assessment where they are scientifically valid. Importantly, the roadmap should not be a rigid, single path but a flexible network of diverse approaches, adaptable to evolving needs and scientific progress. To achieve maximum impact, the roadmap must be future-proof and applicable to all sectors and relevant regulations. Future-proofing the roadmap will require establishing flexible plans to address the diverse regulatory landscapes. It also necessitates a clear understanding of the desired future regulatory system and its rationale.

Our shared goals will be impossible without robust stakeholder engagement and collaboration. Coordinated efforts among stakeholders, sectors, and disciplines within the EU and globally are crucial to foster the exchange of information, deepen understanding of diverse perspectives, and align priorities more effectively. Establishing a well-connected community can break down barriers, streamline processes, increase transparency and build confidence in using non-animal approaches.

These recurring themes highlight the multi-faceted approach required to effectively develop the roadmap and need to be addressed simultaneously, rather than in silos, to achieve meaningful progress and ensure a successful transition to a new non-animal regulatory system (Fig. 6).

To accelerate the transition to a non-animal regulatory system, it is essential to simultaneously pursue the various actions and elements identified by the Commission, whether short-, medium-, or long-term. A synergistic combination of top-down and bottom-up strategies can optimise this process (Fig. 7). A top-down approach can establish clear policy directions with defined goals and criteria. At the same time, a bottom-up perspective can ensure practical implementation by addressing specific challenges and devising pragmatic solutions. Lessons from successful transitions in other sectors can provide valuable insights and help mitigate potential obstacles. The cosmetics industry is a compelling case study of how initial concerns about regulatory changes can evolve into a driving force for innovation and investment in non-animal science. By demonstrating that non-animal approaches can effectively assess the safety of chemical ingredients used in cosmetics and other consumer products, the cosmetics sector has not only met regulatory requirements but also guaranteed the protection of human health

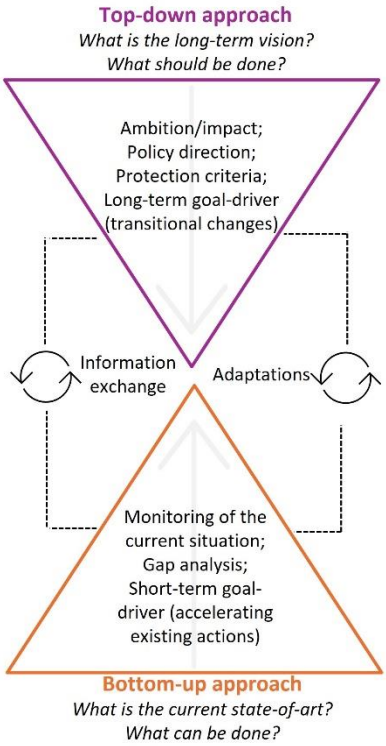

Fig. 7: Top-down and bottom-up strategies to accelerate the transition to a non-animal regulatory system

and the environment (Fentem, 2023). The cosmetics case study shows that a forward-looking approach can bring significant benefits with strategic support and the right incentives, even when faced with initial challenges.

In conclusion, developing a comprehensive roadmap for phasing out animal testing in chemical safety assessment represents a pivotal step towards a more ethical, scientifically advanced, and efficient regulatory framework. The multi-stakeholder roundtable aimed to help define a structure of the roadmap by identifying key elements, organisational structures, and pathways to accelerate the transition to a non-animal testing regulatory framework. Key discussion findings and recommendations are outlined below (Tab. 1). These can facilitate the Commission's work in developing the roadmap most efficiently and guide discussions with the broader stakeholder community. This report can also provide a sound basis and valuable resource for developing comparable roadmaps or policy frameworks aimed at phasing out animal testing in chemical safety assessments worldwide.

Tab. 1: Key recommendations for the development and/or implementation of the roadmap as identified during the roundtable

Key issues discussed during the roundtable	Key recommendations for the development and/or implementation of the roadmap
Coordination *To drive change and orchestrate the complex transition to a non-animal regulatory system*	• Establish a supervisory steering committee, independent from the European Commission, to oversee and guide the development of the roadmap with established indicators, tools and checkpoints. • Implement a robust change management framework, which should act as an overarching component providing guidance and coordination to other working groups. • Designate a dedicated project manager or management team to oversee and streamline cross-sector efforts, supported by robust reporting mechanisms. • Establish expert pools or readily available contact lists to provide timely support to the Commission on specific issues.
Collaboration and communication *To build an interconnected community and unified approach among all stakeholders for phasing out animal testing for chemical safety assessments*	• Develop a comprehensive and open multi-stakeholder communication strategy. • Foster strong collaboration and build robust networks. • Ensure regular interaction between working groups. • Encourage the sharing of knowledge, ideas, and technologies between different fields to strengthen cooperation and adaptability (cross-fertilisation). • Ensure open communication about existing data and processes, the limitations of the current system, and the potential of non-animal approaches. • Establish a common language that defines specific terms (such as

		'safety', 'relevance', 'validation', and 'acceptance') to enable mutual understanding and effective collaboration. ● Organise 'transition science' masterclasses between all stakeholders to co-create solutions.
	**Analysis of the status quo** *To identify and document opportunities, gaps, barriers, and challenges across sectors*	● Conduct a mapping exercise, complemented with systematic reviews where appropriate, to provide a comprehensive overview of the current landscape, including: - A clear understanding of current standards and levels of protection for human health and the environment. - Insights into current information requirements and use of data from animal and non-animal methods for chemical safety assessments. - An analysis of research, development, and regulatory needs. - An analysis of opportunities to use existing and upcoming non-animal approaches. - The determination of non-animal-based Next-Generation Risk Assessment frameworks and workflows to replace current animal tests for complex endpoints. - The identification of best practices and successful strategies from EU Member States and other (non-EU) countries.
	**Revision of legislation and guidance** *To keep pace with advances in non-animal approaches and incentivise their use*	● Based on the analysis of the status quo, identify necessary changes to the legislation and adapt regulatory frameworks, chemicals legislation and guidance documents accordingly. ● Strengthen the 'one substance, one assessment' approach to foster stringent data requirements across different regulations and minimise conflicting guidance. ● Simplify and harmonise the regulation of chemicals across regulatory sectors, including removing conflicting legislation and using clear, user-friendly language. ● Pending revision of the legislation, maximise the use of existing non-animal approaches and minimise the use of animals within the current regulatory framework.
	**Regulatory acceptance** *To facilitate and accelerate international regulatory acceptance of test methods*	● Explore (and implement, where already applicable) alternative pathways to regulatory acceptance without necessarily going through the traditional validation process while ensuring relevance and reliability. ● Establish pre-validation/qualification criteria and implementation plans for research projects with regulatory applications to streamline the process and ensure alignment with regulatory expectations. ● Establish a common database for data submission across regulatory sectors and regulatory fora to enhance stakeholder dialogue. ● Expand the concept of 'safe harbours' outside of time-sensitive regulatory processes to positively influence the regulatory acceptance and use of non-animal approaches.
	**Global acceptance and harmonisation** *To ensure the successful implementation of the roadmap and maximise impact*	● Align the roadmap with global initiatives and existing international frameworks that prioritise using non-animal approaches. ● Strengthen international coordination efforts to achieve mutual acceptance of data.
	**Education and training** *To reduce knowledge barriers, build confidence in the use of non-animal approaches and ensure their widespread adoption*	● Assess relevant stakeholders' specific education and training needs, such as regulators, industry, research institutes, and academia, to ensure a targeted and impactful approach. ● Identify measures to prioritise non-animal approaches in undergraduate and postgraduate programmes to equip future researchers with the necessary tools and knowledge to effectively use and interpret data from non-animal approaches.
	**Transparency and accessibility to knowledge and data** *To promote an open science culture and increase the sharing of knowledge, data, tools, and best practices in open collaboration with all stakeholders*	● Establish a more transparent regulatory decision-making process, with particular emphasis on demonstrating that animal testing is genuinely used as a last resort, and provide public access to regulatory decisions. ● Increase transparency in reporting the number of animals used for chemical safety assessments (including detailed breakdowns by country and sector, and the number of animals used outside the EU to comply with EU legislation). ● Develop effective incentives to encourage companies to share data and facilitate efficient data sharing of studies, regardless of their results, mindful of confidential business information and competition limitations.

		• Create a centralised, user-friendly EU database for compiling non-animal testing approaches and develop a curated data repository, in line with Findable, Accessible, Interoperable and Reusable principles, specifically designed for artificial intelligence applications. • Encourage scientists to share their non-animal innovations with EU agencies early to accelerate familiarity and uptake of these techniques.
	**Progress metrics** *To provide invaluable insights into the progress and impact of actions and allocate efforts and resources strategically*	• Establish a robust and transparent monitoring and evaluation framework with clearly defined tools and indicators and a functional reporting system. • Define regular checkpoints and time-bound deliverables, specific targets, and milestones for each sector stakeholder group to measure success and foster a culture of accountability. • Develop a certification or standard to incentivise and publicly recognise leaders in the field, as well as early adopters and contributors.
	**Funding** *To ensure a sound financial base to transition to a new non-animal regulatory system*	• Estimate the costs of change and secure stable and sufficient funding, in particular to: - Modernise and accelerate the development, validation and implementation of non-animal approaches across different sectors. - Provide the necessary education and training. - Build new or expand existing EU infrastructures to focus on non-animal testing and implementing non-animal approaches into the risk assessment process. - Better support (underfunded) 3Rs Centres and the European Union Network of Laboratories for the Validation of Alternative Methods laboratories. - Establish a data sharing system and devise a platform to foster stakeholder communication and collaboration.

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Conflict of interest

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