

Paradigm Shift in Progress

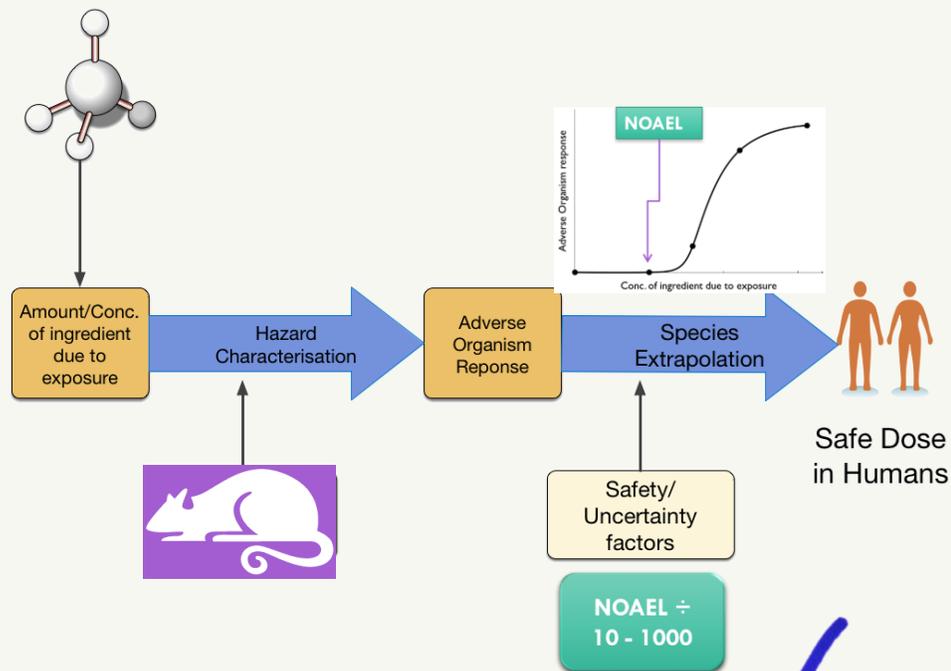
Is it time for a global NGRA Roadmap?

Dr Gavin Maxwell, gavin.maxwell@unilever.com

Safety, Environmental & Regulatory Sciences (SERS), Unilever

21st Oct 2025, ASCCT 2025

'Traditional' Risk Assessment



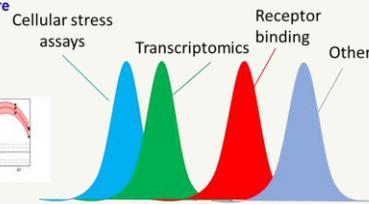
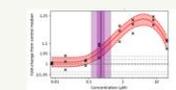
'Next Generation' Risk Assessment



Hazard identification and characterisation of ingredients



Point of departure derived from concentration-response data



Risk Assessment

Calculation of Bioactivity Exposure Ratio (BER)



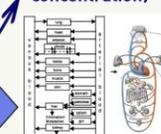
The BER/MoE is defined as the ratio of the PoD and the relevant exposure estimate

Consumer Exposure characterisation



Skin pen

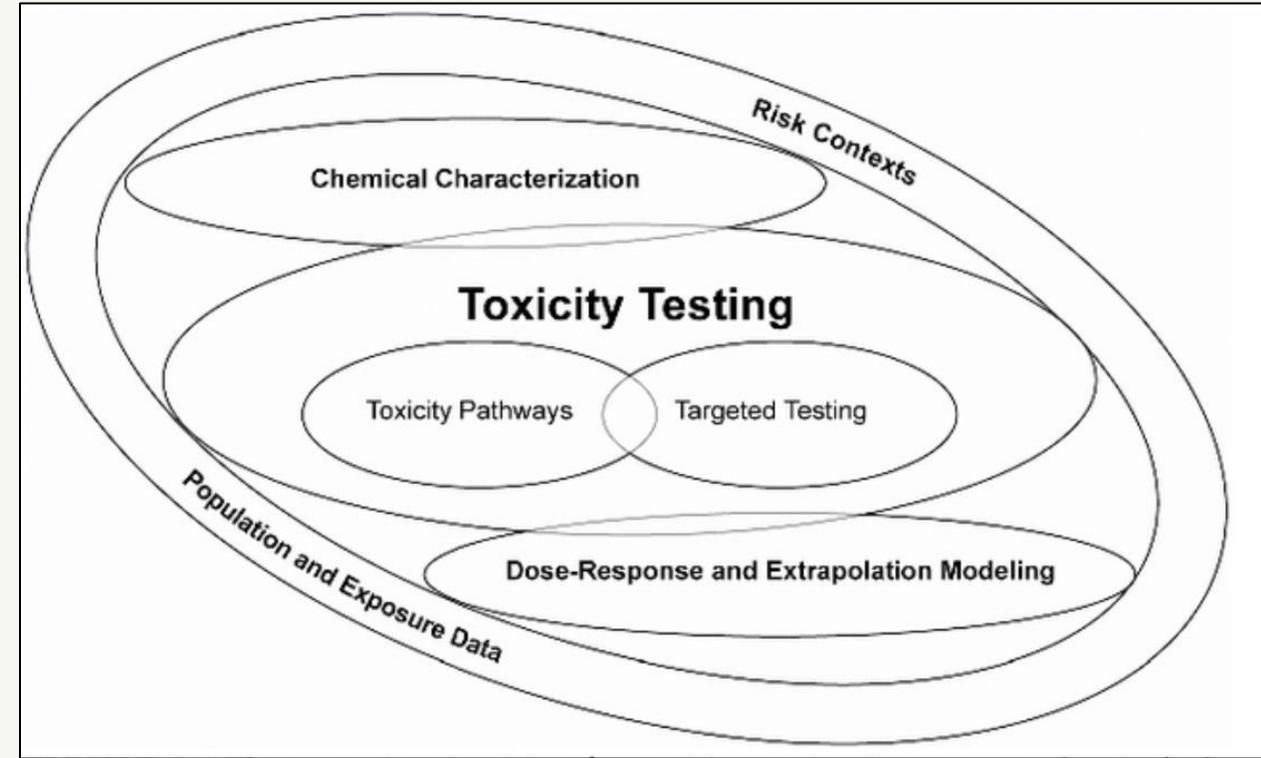
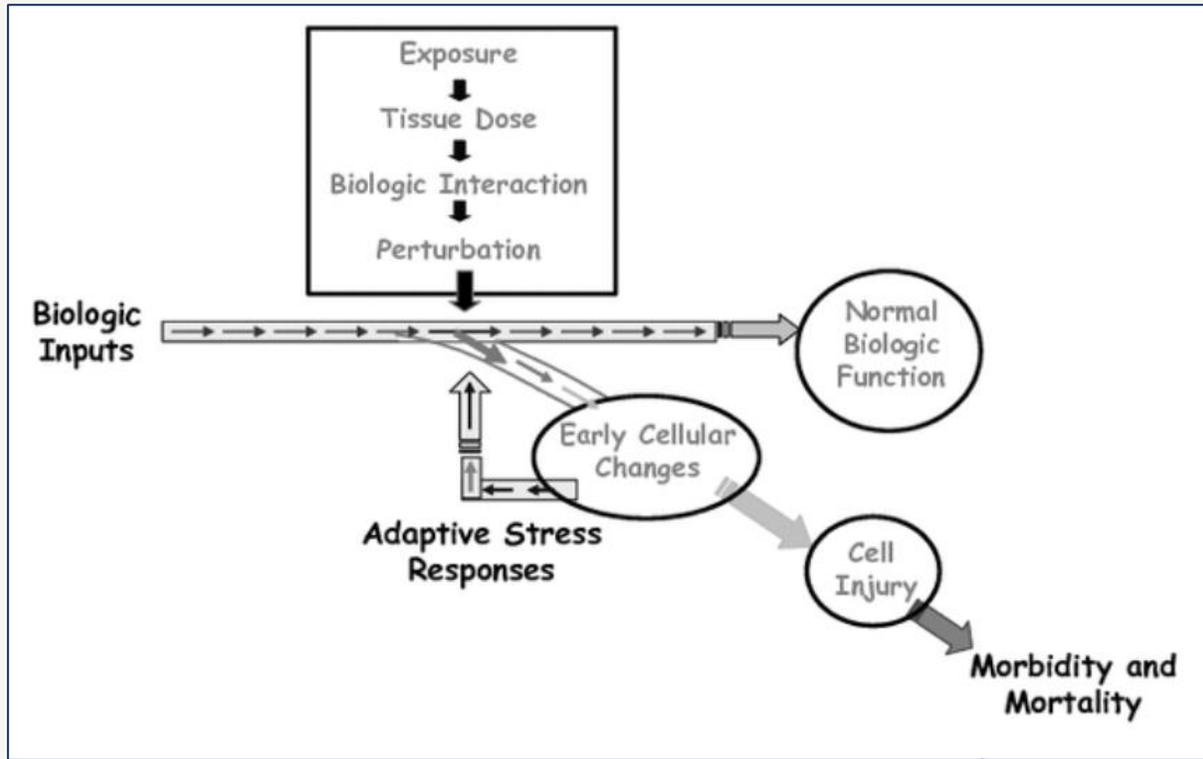
Exposure models (PBK, free/total concentration)



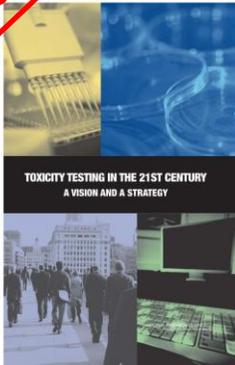
Exposure estimation: Plasma C_{max}



Next Generation Risk Assessment (NGRA) concepts

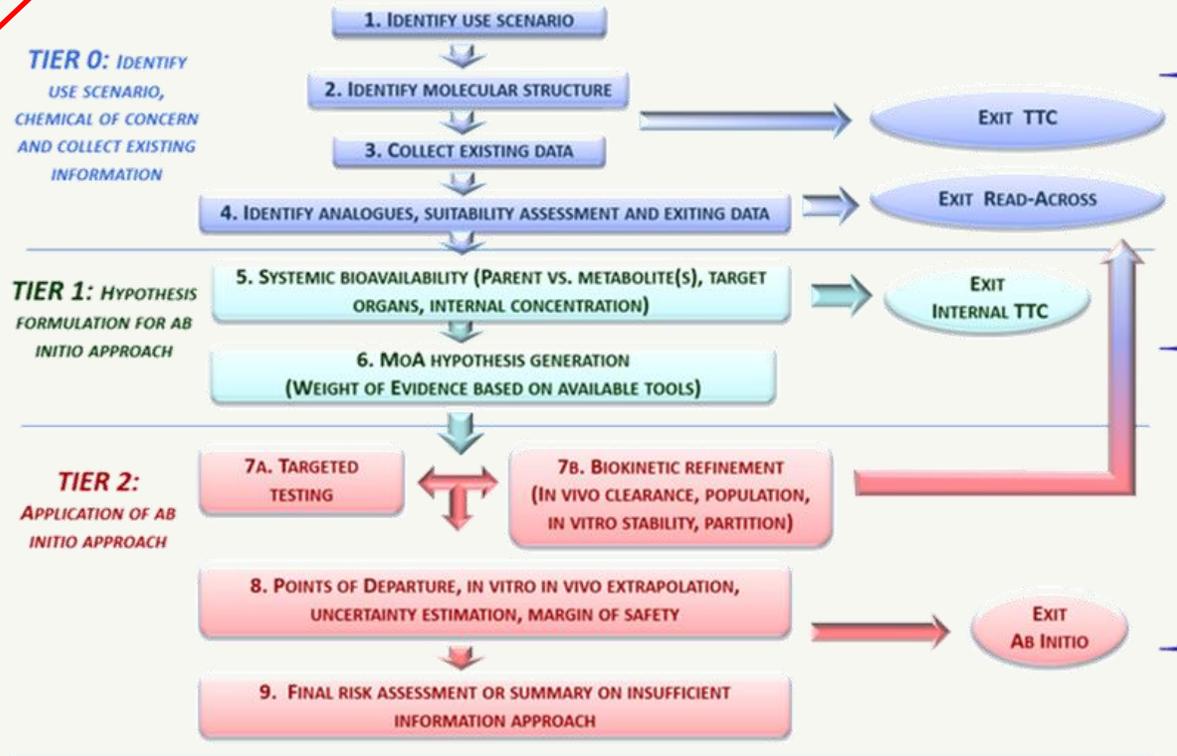


2007

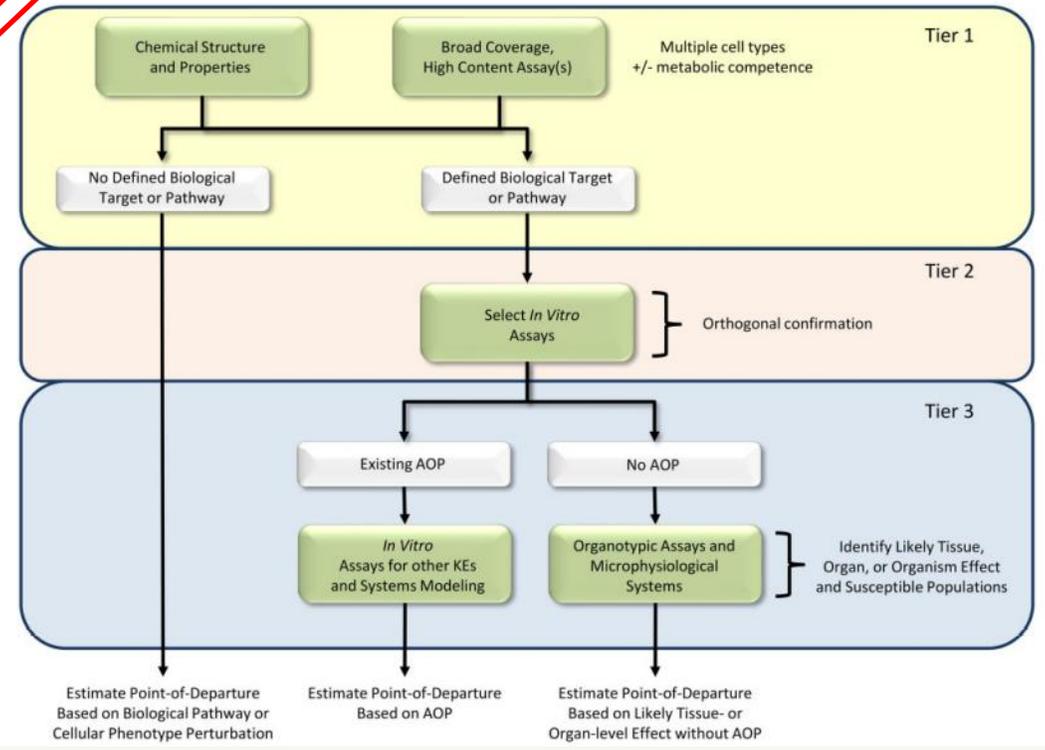


Next Generation Risk Assessment Conceptual Frameworks

2017



2019



Ab initio chemical safety assessment: A workflow based on exposure considerations and non-animal methods

The Next Generation Blueprint of Computational Toxicology at the U.S. Environmental Protection Agency



<https://doi.org/10.1016/j.comtox.2017.10.001>



<https://pubmed.ncbi.nlm.nih.gov/30835285/>

EU Scientific Committee on Consumer Safety (SCCS) created a 'safe space' to explore ab initio use of NGRA approaches for Cosmetics Safety



2023

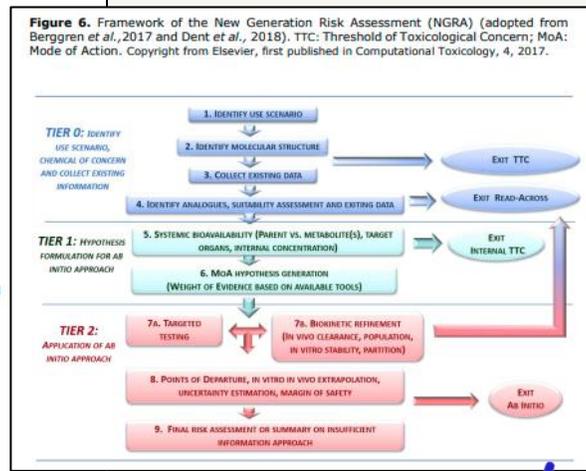
SCCS/1647/22
Corrigendum 2

Scientific Committee on Consumer Safety
SCCS

THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY EVALUATION
12TH REVISION

The SCCS adopted this guidance document by written procedure on 15 May 2023

The corrigendum 1 was adopted during plenary meeting on 26 October 2023, and the corrigendum 2 by written procedure on 21 December 2023



2025

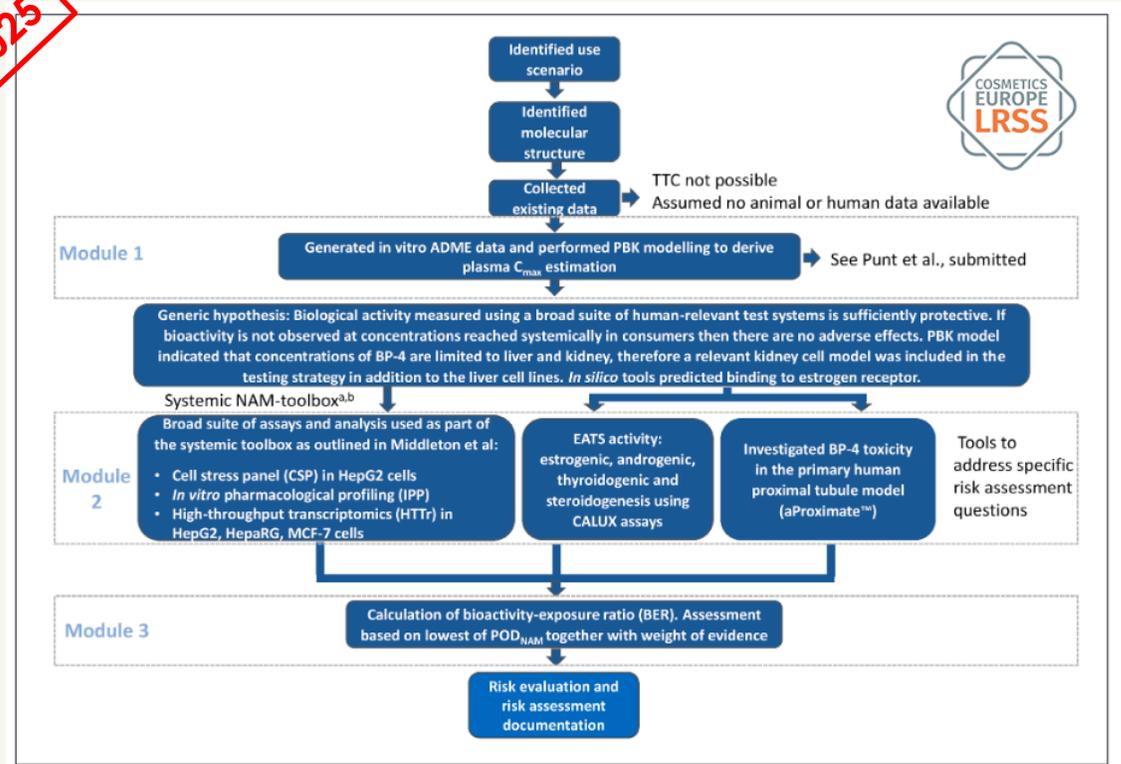


Fig. 1: NGRA case study workflow for 5% BP-4 in sunscreen body lotion
Adapted from Berggren et al. (2017) and Dent et al. (2021); ^a Middleton et al. (2022), ^b Cable et al. (2024).



SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation 12th revision

[SCCS 12th revision Notes of guidance](#)



Making safety decisions for a sunscreen active ingredient using next-generation risk assessment: Benzophenone-4 case study

<https://doi.org/10.14573/altex.2501201>

International Cooperation of Cosmetics Regulators (ICCR) & International Collaboration on Cosmetics Safety (ICCS) are standardising global best practice for NGRA for Cosmetics Safety



2018

2021

2025

Computational Toxicology 7 (2018) 20–26

Contents lists available at ScienceDirect

Computational Toxicology

journal homepage: www.elsevier.com/locate/comtox

Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients

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ARTICLE INFO

ABSTRACT

Consumer safety is a prerequisite for any cosmetic product. Worldwide, there is an ever-increasing desire to bring safe products to market without animal testing, which requires a new approach to consumer safety. Next Generation Risk Assessment (NGRA), defined as an exposure-led, hypothesis-driven risk assessment approach that integrates *in vivo*, *in vitro* and *in silico* approaches, provides such an opportunity. The coordinated nature of such NGRA means that the development of a prescriptive list of uses to assess safety is not possible, or appropriate. The International Cooperation on Cosmetics Regulation (ICCR) therefore tasked a group of scientists from regulatory authorities and the Cosmetic Industry to agree on and outline the principles for an exposure-led, hypothesis-driven risk assessment for cosmetic ingredients. This ICCR group determined NGRA to be human-relevant, exposure-led, hypothesis-driven and designed to prevent safety issues. It should be conducted using a tiered and iterative approach, following an appropriate selection of the available data, and using robust and relevant methods and strategies, and could be documented (engagement and eSICCR) about the logic of the approach and sources working on the risk assessment of cosmetics have a unique opportunity to lead progress in this approach, and cosmetic risk assessors are encouraged to consider these key principles relating such assessments.

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<https://doi.org/10.1016/j.comtox.2018.06.001>

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ARTICLE INFO

ABSTRACT

Next Generation Risk Assessment (NGRA) is an exposure-led, hypothesis-driven approach that has the potential to safety decision-making. However, significant effort is needed to develop and test the *in silico* based approach that underpins NGRA to enable confident application in a regulatory context. This ICCR group determined NGRA to be human-relevant, exposure-led, hypothesis-driven and designed to prevent safety issues. It should be conducted using a tiered and iterative approach, following an appropriate selection of the available data, and using robust and relevant methods and strategies, and could be documented (engagement and eSICCR) about the logic of the approach and sources working on the risk assessment of cosmetics have a unique opportunity to lead progress in this approach, and cosmetic risk assessors are encouraged to consider these key principles relating such assessments.

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<https://doi.org/10.1016/j.yrtph.2021.105026>

Paving the way for application of NGRA to safety decision-making for cosmetic ingredients

INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

Best Practice Guidance Document

Skin Sensitization Assessment: Using New Approach Methods for Substances in Cosmetics and Personal Care Products

[Skin Sensitization Best Practice Guidance](#)

Best Practice Guidance Document: Skin Sensitization: using NAMs for substances in Cosmetics

Ending animal testing of Cosmetic Products under China's Cosmetics Supervision and Administration Regulation (CSAR)

1989–2014: First stage of cosmetics regulations

- ✓ Pre-market registration
- ✓ Safety responsibility lies largely with the authorities
- ✓ Mandatory AT for finished products



NATIONAL MEDICAL PRODUCTS ADMINISTRATION
国家药品监督管理局



<https://english.nmpa.gov.cn/index.html>

2014-2021: Adopting of non-animal approaches

- ✓ Ingredient-based risk assessment via safety assessment report
- ✓ No mandate AT for domestic non-special use cosmetics

2021-2024: CSAR in place

- ✓ No mandate AT for majority of cosmetics (domestic and imported "common" cosmetics)
- ✓ AT is required for special cosmetics and a few types of common cosmetics

2024-2025: Full CSAR implementation

- ✓ Mix mandate AT and non-animal approaches (e.g., TTC, QSAR/Read-across; IATA)
- ✓ For new cosmetic ingredient registration using NAMS (i.e., novel non-animal approaches that have been validated with 10 chemicals)

Accelerating the Pace of Chemical Risk Assessment (APCRA) case studies demonstrate the feasibility of NGRA approaches



APCRA
ACCELERATING THE PACE OF
CHEMICAL RISK ASSESSMENT

Led by:



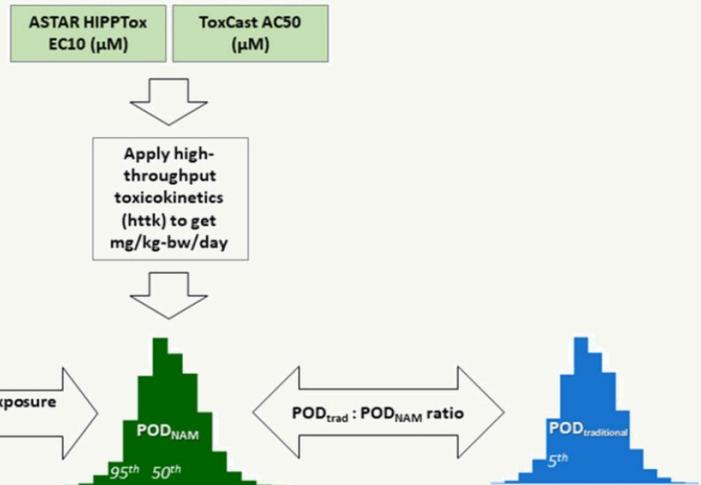
Health
Canada

Santé
Canada



<https://apcra.net/case-studies/>

2020



2025

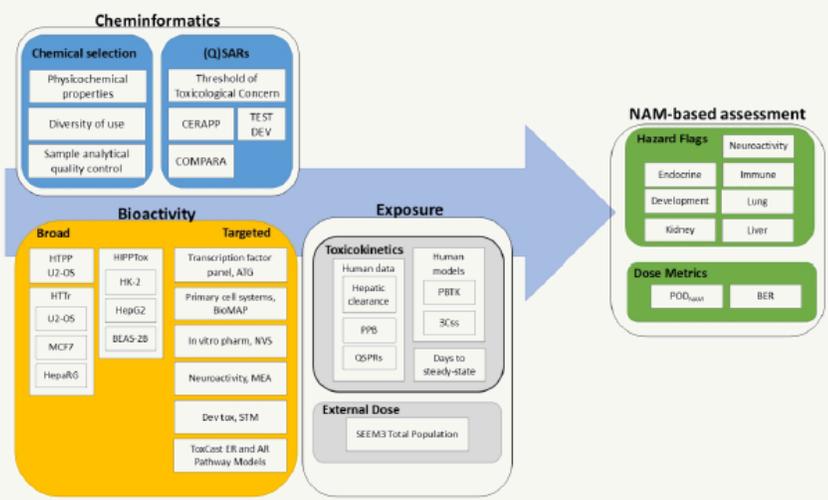


Figure 1. Overall workflow of the case study. This case study includes 448 substances with exposure predictions, *in vitro* assay data, HTTK information using the httk R package, and *in vivo* hazard information. The 50th and 95th percentile from the Monte Carlo simulation of interindividual toxicokinetic variability were used to estimate administered equivalent doses (AEDs), and the minimum of either the ToxCast or HIPPTox-based AEDs were selected as the $POD_{NAM, 50}$ or $POD_{NAM, 95}$. The POD_{NAM} estimates were compared with the fifth percentile from the distribution of the $POD_{traditional}$ values obtained from multiple sources to obtain the \log_{10} POD ratio. The \log_{10} bioactivity:exposure ratio (BER) was obtained by comparing the POD_{NAM} estimates to exposure predictions. All values used for computation were in \log_{10} -mg/kg-bw/day units.

Figure 1. NAM-based assessment (NBA) workflow. An overview of a NBA workflow that incorporates cheminformatics, broad and targeted bioactivity NAMs, via hazard flags, and exposure NAMs for internal and external exposures. The workflow culminates in a set of outputs for NBA, including hazard flags, $POD_{-}NAM$, and BER estimates.

Paul-Friedmann et al. 2020 APCRA

'retrospective' case study - To elucidate whether a "region of safety", i.e. a threshold below which no bioactivity or toxicity would be anticipated, can be identified using NAMs for a list of chemicals with existing human health evaluations.



Paul-Friedmann et al. 2025 APCRA

'prospective' case study - To demonstrate how NAM data and classical toxicological studies can be used to inform the hazard and safety profile of chemicals with limited or unclear toxicological data



Regulatory Agencies are signalling their readiness to transition their organisations to enable regulatory use of NAMs/NGRA



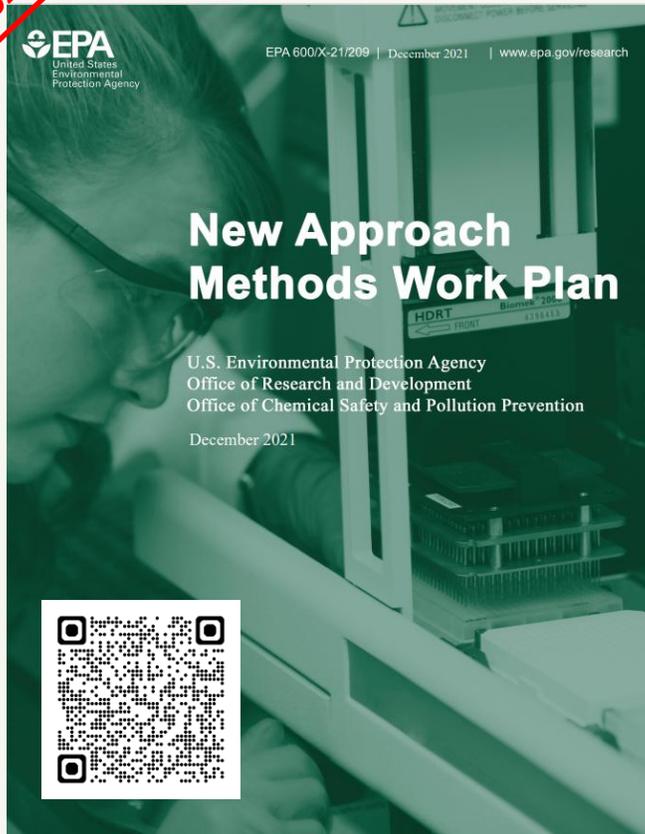
Environment and Climate Change Canada

Environnement et Changement climatique Canada



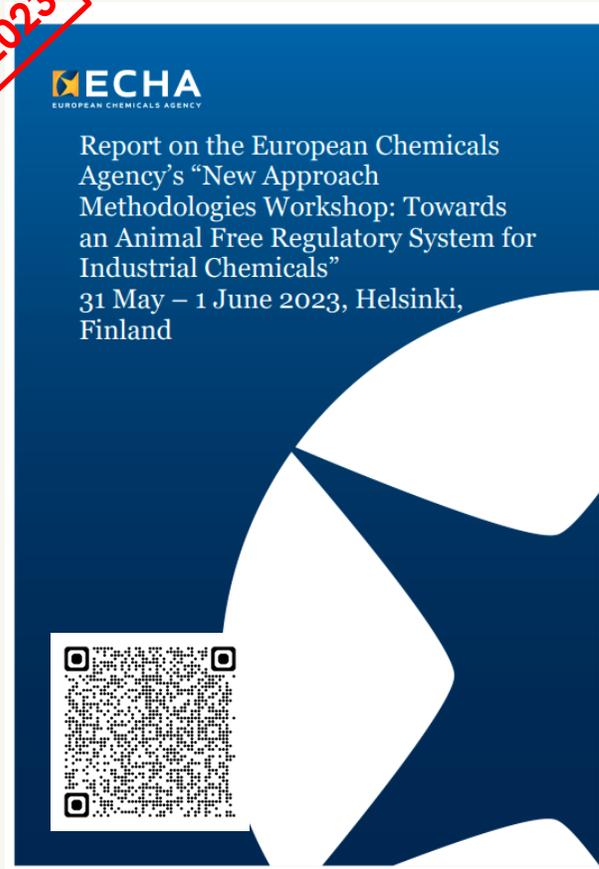
Health Canada / Santé Canada

2021



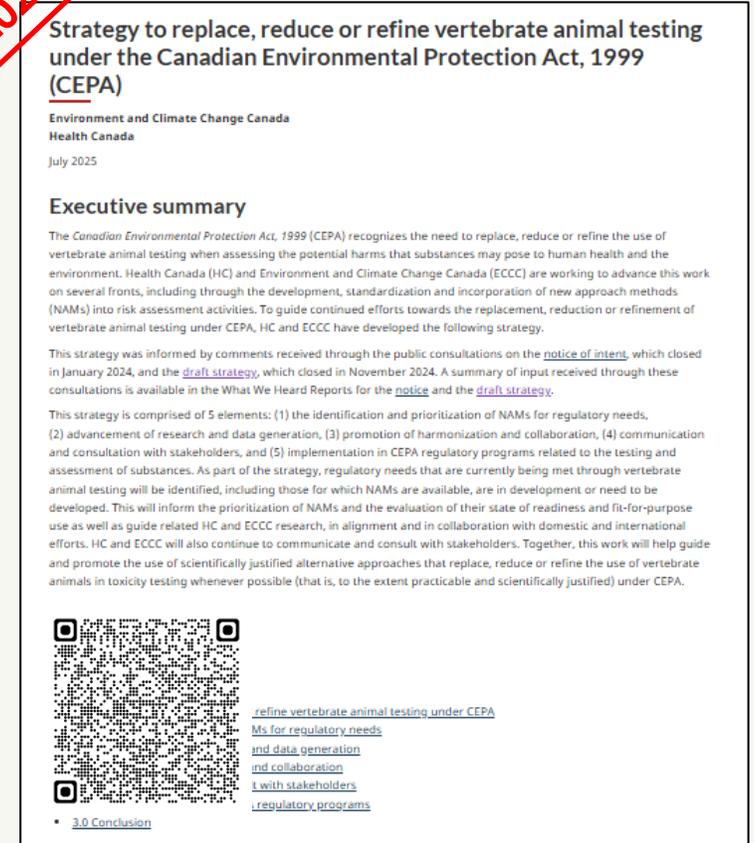
[New Approach Methods Work Plan \(epa.gov\)](https://www.epa.gov/research/new-approach-methods-work-plan)

2023



[towards-an-animal-free-regulatory-system-for-industrial-chemicals](https://echa.europa.eu/en/chemicals/new-approach-methodologies-workshop-towards-an-animal-free-regulatory-system-for-industrial-chemicals)

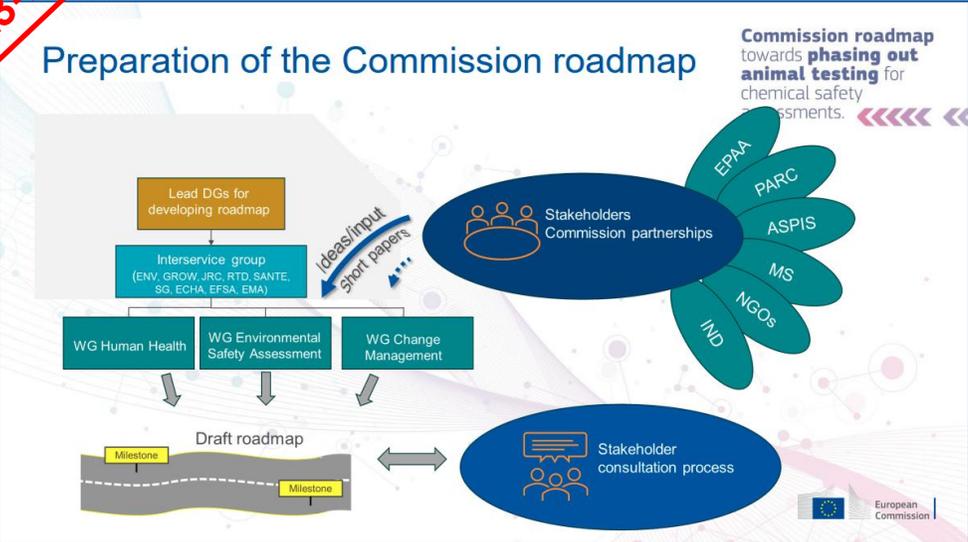
2025



[Strategy to replace, reduce or refine vertebrate animal testing under CEPA](https://www.ec.gc.ca/cepa/strategy-to-replace-reduce-or-refine-vertebrate-animal-testing-under-cepa)

Commission Roadmap to phase out Animal Testing for Chemical Safety will support a managed transition to NGRA in Europe *Unilever*

2023-26

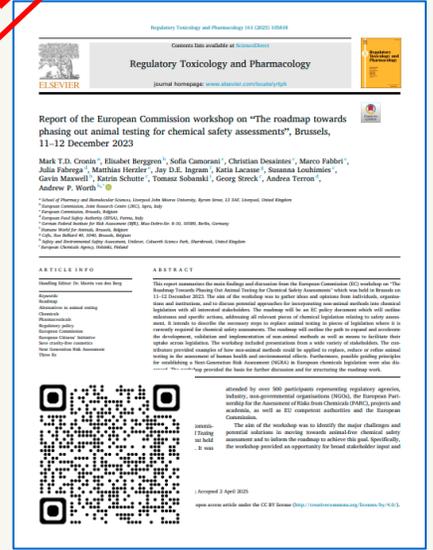


Commission Roadmap will be published in Q1 2026

Roadmap proposal developed by Human Health, Environmental Safety & Change Management working groups, 3 open workshops & consultations

Stakeholders (incl. EPAA, PARC, ASPIS) involved throughout helping to build trust & foster collaboration

2025



[Roadmap towards phasing out animal testing](#)

<https://doi.org/10.1016/j.yrtph.2025.105818>

European Partnership for Alternative Approaches to Animal Testing (EPAA) partnered with the Commission & other organisations to organise an **Animal-Free Chemical Safety Assessment conference** in March 2025



https://echa.europa.eu/documents/10162/127346428/AF-CSA_Conference+Report.pdf/d7994cf5-4b38-9a8a-9cbc-0c89da0dcad8?t=1749891499636

Commission Roadmap contains detailed cross-sector proposals for how to establish animal-free NGRA frameworks



2025

Short-term	Medium-term	Long-term
1. Establish cross-sector, animal-free Next Generation Risk Assessment (NGRA) frameworks		
Increase use of computational approaches		
Standardise ADME, PBK modelling & IVIVE		
Standardise PoD & tox signatures derivation from NAM data for complex regulatory endpoints		
Development of NGRA workflow for enabling systemic use of NAMs		
Establish NAM based frameworks for Carcinogenicity, DART, DNT, Endocrine Disruption, Genotoxicity & Systemic Toxicity		
	Nanomaterials / Nanoparticles Risk Assessment	
	Characterise protection levels/uncertainty & set acceptance criteria	
	Modernise CLP criteria	
2. Reduce number of animals & species tested, where justified		
2 nd species sub-chronic testing removal, 90-day dog study removal		
Develop tiered approaches to minimise use of animals & maximise use of NAMs		
Reduce long-term <i>in vivo</i> HH studies through smart <i>in vivo</i> studies		

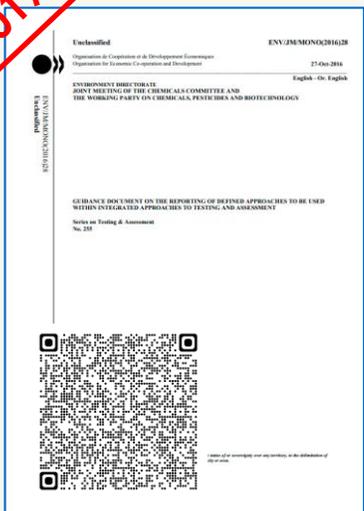


OECD Integrated Approaches to Testing & Assessment (IATA) & guidance *Unilever* are driving global standardisation of NGRA for chemical safety



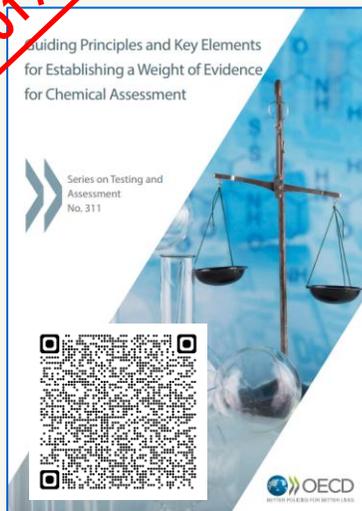
IATA combine multiple sources of information to conclude on the toxicity of chemicals and are developed to address a specific regulatory scenario or decision context.

2017



Guidance document on reporting of **Defined Approaches** for use in IATA

2019



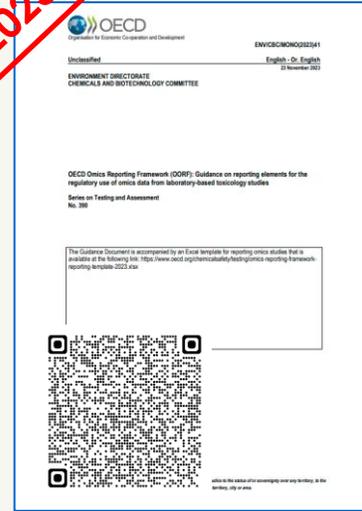
Guiding principles for establishing a **Weight of Evidence** for Chemical Assessment

2021



Guidance document on reporting of **Physiologically Based Kinetic (PBK) models**

2023



Omics Reporting Framework (OORF): Guidance on reporting elements for **omics data**

2023



(Q)SAR Assessment Framework: Guidance for **(Quantitative) Structure Activity Relationship models** and predictions



New leaders are emerging, signalling their willingness to drive & shape the global transition to NGRA: South Korea Unilever

✓ K-MOE



Key Roles in NAMs Application

- Policy Vision
- Infrastructure Building
- Human Resources

2030 Goal: 60% of Safety Data



K-MOE 2030 Vision:
60% chemical safety data with non-animal methods, advancing humane science and animal welfare



K-ECO NAMs Facility:
\$25M investment, building a non-animal testing center (Organoid, organ-on-a-chip, omics), completion 2026.

✓ K-MFDS



Key Roles in NAMs Application

- Technology Validation
- Standardization
- Development of NAMs



Managing Various NAMs:

- Validation and regulatory adoption of non-animal methods (phototoxicity, skin/eye tests, KeraSkin™ ISO)
- KeraSkin™-based medical device skin irritation test adopted as ISO 10993-23, Korea's first NAMs method to become an ISO international standard in 2025.

South Korea forms new organoid consortium for nonanimal testing



Launching 2025 K-Organoid Consortium:

- Consisted of 27 Korean companies, 18 institutions
- Standardize organoid-based NAMs, register OECD TGs.

✓ K-MAFRA



Key Roles in NAMs Application

- Leading National Policy Task
- Animal Welfare



Promoting Alternative Testing as a National Policy:
Enactment of the *Animal Welfare Basic Act* (2027) and legislation of the *Animal Alternative Testing Promotion Act*



Animal Welfare in MAFRA:
3rd National Animal Welfare Plan (2025–2029): advancing welfare through regulation, support centers, and protection measure



Acknowledgement: Prof. Jinhee Choi, Univ. Seoul

European Medicine Agency (EMA) has created 'safe spaces' & 'regulatory sandboxes' to support greater use of NAMs

The screenshot shows the EMA website header with the logo and navigation menu. The main content area features the title 'Regulatory acceptance of new approach methodologies (NAMs) to reduce animal use testing' with a 'Share' button. Below the title is a paragraph explaining that NAMs refer to novel methods compliant with the 3Rs principles (replacement, reduction, and refinement) for ethical animal use in medicine testing across the EU. At the bottom of the main content area are two buttons: 'Human' and 'Veterinary'.

Briefing meetings within EMA's Innovation Task Force (ITF)

EMA holds briefing meetings with new approach methodology (NAM) developers.

Scope

These meetings host informal discussions on NAM development and readiness for **regulatory acceptance**.

They take place within EMA's Innovation Task Force (ITF). This provides developers with a forum for early dialogue with EMA on **innovative medicines** and **novel methodologies**.

Experts from the **European medicines regulatory network** also participate in these discussions.

Applications are free of charge.

Outcome

EMA shares confidential meeting minutes with participating developers.

For more information on EMA's Innovation Task Force (ITF), see:

- [Supporting Innovation](#)

Scientific advice

EMA enables new approach methodology (NAM) developers to ask its [Scientific Advice Working Party](#) specific scientific and regulatory questions.

These questions can refer to the development and use of NAMs.

Scope

The scope is to consider including **NAM data** in a future **clinical trial** application or in **marketing authorisation application (MAA)** for a particular medicine.

Outcome

EMA's CHMP or CVMP issues a confidential final advice letter containing answers to the specific questions that developers raised.

For more information on requesting scientific advice from EMA, see:

- [Requesting scientific advice or protocol assistance from EMA](#)
- [Scientific advice for veterinary medicines](#)

Voluntary submission of data

Scope

Under the voluntary submission of data procedure, new approach methodology (NAM) developers can submit data obtained by using a NAM.

EMA does not use data generated with the NAM as part of its regulatory decision-making process, for instance within a MAA procedure. However, EMA evaluates these data independently.

This is for the purpose of NAM evaluation for possible future regulatory acceptance. It also aims to help EMA develop a better understanding of the potential added value of NAMs.

The voluntary submission of data procedure is also known as the safe harbour approach. This is because there is no 'penalty' in a regulatory sense for submitting the data (even if it does not concur with animal data).

Outcome

This procedure can allow the generation, compilation and review of data to help define and / or fine-tune a context of use for a NAM.

This also helps evaluate the readiness and limitations for **regulatory acceptance** of the NAM within a specific context of use.

In addition, it allows regulators to gain confidence in NAM data.

Moreover, this approach may help EMA draft qualification criteria for NAMs based on a context-of-use.

Qualification

New approach methodology (NAM) developers can apply for [CHMP](#) qualification.

Scope

They can do so if they have generated sufficient and robust **data**. This is needed to demonstrate the utility and regulatory relevance of a NAM for a specific context of use.

A **context of use** describes the circumstances under which the NAM is applied in the assessment of human or veterinary **medicines**.

A qualification team composed of EMA and experts from the [European medicines regulatory network](#) then assesses the data submitted to support the use of the NAM within medicine development.

For NAMs to be qualified in veterinary medicines development, the qualification procedure is carried out within the request for general [scientific advice](#) for veterinary medicines.

Outcome

EMA's CHMP can issue qualification advice on protocols and methods with the aim of moving towards a positive qualification opinion.

Based on CHMP's advice, EMA may propose a letter of support even when it cannot yet qualify a NAM.

This letter signals that EMA considers the preliminary data received to be promising. It can also raise awareness of the method proposed. Moreover, it can indicate EMA expectation to receive data that can further support a positive qualification opinion.

The CHMP can also issue a qualification opinion on the acceptability of a NAM within a specific context of use in drug development.

Before adopting a qualification opinion, the CHMP makes its evaluation open for public consultation by the scientific community.

To ensure public awareness, EMA publishes all qualification opinions.



European Federation of Pharmaceutical Industries & Associations (EFPIA): commitment to 3Rs & Commission Roadmap engagement

Unilever

2022

2024-25

PUTTING ANIMAL WELFARE PRINCIPLES AND 3RS INTO ACTION - European Pharmaceutical Industry Report - 2022 Update

EFPIA members support Phasing-In New Approach Methodologies

EFPIA members are committed to the science-based phase-in of methods to replace the use of animals for scientific purposes and the deletion of animal tests which are obsolete or redundant. EFPIA members aim to lead progress on this by engaging in a wide range of practical activities to help drive the development, uptake and promotion of non-animal technologies (NATs) and new approach methodologies (NAMs) so that these can be phased-in as soon as it is scientifically possible to do so.

The pharmaceutical industry members of EFPIA:

- Are fully committed to the principles of 3Rs;
- Continue to support the objectives of the Directive 2010/63/EU on the protection of animals used for scientific purposes which has enhanced animal welfare standards and mandated the application of replacement, reduction and refinement across the EU while ensuring Europe remains a world leader in biomedical research;
- Will continue to strive to go beyond what is legally required and work to develop and validate systems leading to improved 3Rs, animal welfare and high-quality science and technologies in every day practice and ultimately improve the lives of the people and animals that stand to benefit from the research. Training of staff will remain an essential element of good science and good welfare;
- Are committed to continue invest in collaborative research initiatives and projects to improve animal welfare and 3Rs, and support start-ups with expertise in new approaches as we transition from the Innovative Medicines Initiative (IMI – the largest health public private partnership) to the new Innovative Health Partnership (IHP);
- Will continue to work with regulators, the scientific community and civil society to improve implementation of the science and speed up regulatory acceptance of alternative methods in the EU and at a global level;
- Will strive to lead by example by disseminating beyond own department and own establishment to drive improvements in welfare and general quality of science;
- Will improve the systems in place working with academia, CROs, animal breeding and testing facilities to share good practices, new methodologies and lead by example by uptake of high 3Rs and animal welfare standards in the daily activities;
- Will be transparent in telling what we do and how we do it, to explain and justify where live animals are required and used and also inform on the work and commitment of companies to reduce the sectors reliance on animals;
- Will continue to identify, develop and implement their phase-in strategies and communicate on animal use through either dedicated webpages or CSR reports. Open communication and dialogue with the public are key to highlight our contribution to phasing-in replacement methods.

Basket 1

Animal experiments for which alternative technologies already exist or which are not scientifically necessary

➔ **Implementation plan with milestones**

Basket 2

Animal testing purposes for which there are concrete ideas and hypotheses for the development of alternative methods

➔ **Prioritization of R&D investments**

Basket 3

Animal testing, for which there is as yet no approach to replacing it with non-animal methods.

➔ **Evolution of Science Biggest Opportunity**

Investment Prio: Replacement (left) to **Investment Prio: Refinement** (right)

efpia 2nd EC Roadmap Workshop | 2



efpia
European Federation of Pharmaceutical Industries and Associations

Putting animal welfare principles and 3Rs into action

Pharmaceutical Industry Report 2022 Update



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European Federation of Pharmaceutical Industries and Associations

3 BASKETS FOR A ROADMAP TO PHASE OUT ANIMAL TESTING

Dr. Kerstin Kleinschmidt-Doerr, PhD, MBA
EFPIA Research Animal Welfare Group
Co-chair (CVO Merck)

US FDA Roadmap to Reducing Animal Testing in Preclinical Safety Studies & NIH prioritization of human-based research technologies

2025

FDA Roadmap to Reducing Animal Testing in Preclinical Safety Studies

Executive Summary

This roadmap outlines a strategic, stepwise approach for FDA to reduce animal testing in preclinical safety studies with scientifically validated new approach methodologies (NAMs), such as organ-on-a-chip systems, computational modeling, and advanced *in vitro* assays. By partnering with federal agencies like NIH and VA through ICCVAM, FDA can accelerate the validation and adoption of these human-relevant methods, improving predictive accuracy while reducing animal use. This transition will enhance public health by streamlining drug development and ensuring safer therapies reach patients faster, while positioning FDA as a global leader in modern regulatory science and innovation.

Background

There is growing scientific recognition that animals do not provide adequate models of human health and disease. Over 90% of drugs that appear safe and effective in animals do not go on to receive FDA approval in humans predominantly due to safety and/or efficacy issues (1). Animal-based data have been particularly poor predictors of drug success for multiple common diseases including cancer (2), Alzheimer's (3) and inflammatory diseases (4). Some medications which are generally recognized safe in humans, such as aspirin, may have never passed animal testing (5). Conversely, some compounds which have appeared safe in animal models have been lethal in human trials (5). These examples highlight basic physiologic differences between humans and other animal species.

Due to the limitations of animal testing as well as ethical concerns about animals testing, there has been increased focus within the scientific community on New Approach Methodologies (NAMs). NAMs encompass *in vitro* human-based systems, *in silico* modeling, and other innovative platforms that can collectively evaluate immunogenicity, toxicity, and pharmacodynamics in humans and provide an opportunity to improve the predictive relevance of preclinical drug testing while reducing or replacing animal use. NAMs also have enormous cost saving potential (6).

Recent legislative changes have signaled Congress is simultaneously open to regulatory innovation. In late 2022, Congress passed the FDA Modernization Act 2.0,² which explicitly authorized the use of non-animal alternatives (cell-based assays, computer models, etc.) to support an investigational new drug (IND) application and "remove[d] a requirement to use animal studies" for biosimilar biologics license application (BLA) (7). This landmark policy empowered FDA to accept NAMs in lieu of animal studies. Then in 2024, the Science Board to the FDA provided comprehensive recommendations on how the agency can spur adoption of scientifically validated NAMs.³

Public sentiment is also supportive of this transition with a recent survey finding that >85% of both Democratic and Republican-identifying adults felt that animal experiments should be phased out in favor of more modern methods.⁴ Together, scientific advances and policy drivers create an opportune moment for the FDA to chart a roadmap to reduce animal testing while improving drug development.

¹ https://www.fda.gov/oc/ohrt/documents/presentations/12145693_NAMs_Working_Group_Report.pdf

² H.R. 2660 - 117th Congress (2021-2022): FDA Modernization Act of 2021 | Congress.gov | Library of Congress

³ <https://www.fda.gov/media/182478/download?text=NAM%20Subcommittee%20Recommendations.all%20of%20FDA%20to%20use>

⁴ <https://opm.widen.net/s/qz7zth7bw/animal-testing-survey>

1 Roadmap to Reducing Animal Testing in Preclinical Safety Studies

- **FDA Roadmap outlines strategic, approach to reduce animal testing in preclinical safety studies using New Approach Methodologies (NAMs):**
 - organ-on-a-chip systems
 - computational modelling
 - advanced *in vitro* assays
- **FDA will accelerate the validation & adoption of NAMs by partnering with federal agencies like NIH & VA through ICCVAM**
- **The FDA roadmap seeks to:**
 - enhance public health
 - streamline drug development
 - ensuring safer therapies reach patients faster
 - position FDA as a global leader in modern regulatory science and innovation

2025

NIH to prioritize human-based research technologies

New initiative aims to reduce use of animals in NIH-funded research.

The National Institutes of Health (NIH) is adopting a new initiative to expand innovative, human-based science while reducing animal use in research. Developing and using cutting-edge alternative non-animal research models aligns with the U.S. Food and Drug Administration's (FDA) recent initiative to reduce testing in animals. While traditional animal models continue to be vital to advancing scientific knowledge, using new and emerging technologies can offer unique strengths that, when utilized correctly or in combination, can expand the toolbox for researchers to answer previously difficult or unanswerable biomedical research questions.

"For decades, our biomedical research system has relied heavily on animal models. With this initiative, NIH is ushering in a new era of innovation," said NIH Director Dr. Jay Bhattacharya. "By integrating advances in data science and technology with our growing understanding of human biology, we can fundamentally reimagine the way research is conducted - from clinical development to real-world application. This human-based approach will accelerate innovation, improve healthcare outcomes, and deliver life-changing treatments. It marks a critical leap forward for science, public trust, and patient care."

Some bodies of research have been inconclusive on the efficacy of translating the results of animal models to human diseases, such as Alzheimer's disease and cancer. These translational challenges to humans may be due to differences in anatomy, physiology, lifespan, and disease characteristics. While humans and animals may share genes, some studies have shown there could be functional differences between organ and body systems that may result in some translational limitations.

New and emerging technologies have begun to allow researchers to study health and disease using human information, making them an alternative avenue to yield replicable, translatable, and efficient results either alone or in combination with animal models. These technologies include:

- Organoids, tissue chips, and other *in vitro* systems that allow scientists to model human disease and capture human variability and patient-specific characteristics.
- Computational models that simulate complex biological human systems, disease pathways, and drug interactions.
- Real-world data that allow scientists to study health outcomes in humans at community and population levels.

To integrate innovative human-based science, the NIH intends to establish the Office of Research Innovation, Validation, and Application (ORIVA) within NIH's Office of the Director. The new office will coordinate NIH-wide efforts to develop, validate, and scale the use of non-animal approaches across the agency's biomedical research portfolio and serve as a hub for emergency coordination and regulatory transition for public health protection.

ORIVA will expand funding and training in non-animal approaches and awareness of their value in translational success. New funding opportunities will include evaluation criteria that assess methods based on their suitability for the research question, context of use, translatability, and human relevance. Infrastructure for non-animal approaches will also be expanded to make these methods more accessible to researchers.

In addition, grant review staff will participate in mitigation training to address any possible bias towards animal studies and integrate experts on alternative methods into study sections. NIH will also publicly report on research spending annually to measure progress toward reduction of funding for animal studies and an increase in funding for human-based approaches.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

"For decades, our biomedical research system has relied heavily on animal models. With this initiative, NIH is ushering in a new era of innovation," said NIH Director Dr. Jay Bhattacharya.

[FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs | FDA](#)

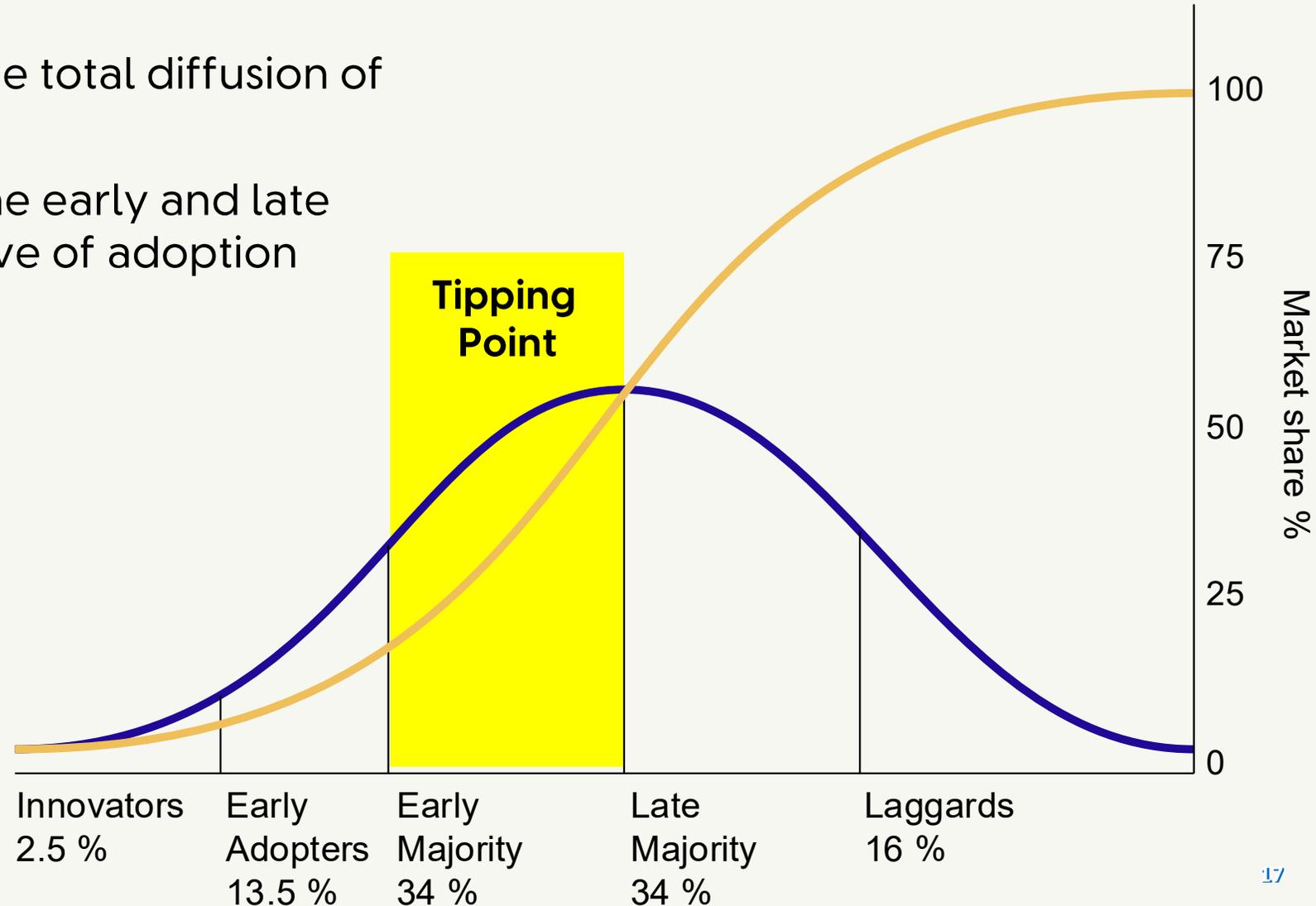
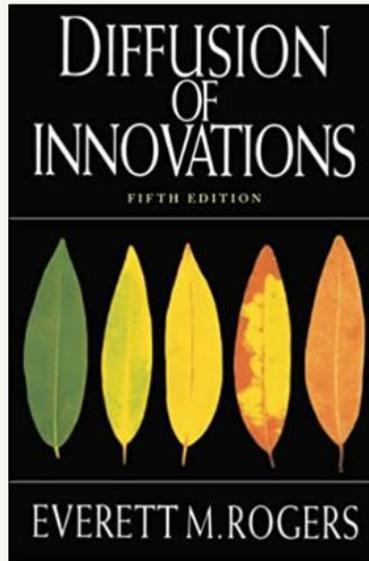
[NIH to prioritize human-based research technologies | National Institutes of Health \(NIH\)](#)



Have we reached a global tipping point in regulatory adoption of NGRA approaches?

Tipping Point

- critical mass, after which the total diffusion of an innovation is likely
- inflection point between the early and late majority in the sigmoid curve of adoption



[Diffusion of innovations - Wikipedia](#)

What statement do you agree with the most?
Please raise your hand to vote!

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1. **We have passed** the global tipping point for regulatory adoption of NGRA approaches
2. **We are passing** the global tipping point for regulatory adoption of NGRA approaches
3. **We have not yet passed** the tipping point for regulatory adoption of NGRA approaches



Is it time for a global NGRA roadmap?



Potential Global NGRA roadmap objectives:

- **Coordinate global transition** to actively manage the risks associated with the change
- **Accelerate knowledge exchange** to facilitate standardisation & AI automation of NGRA workflows
- **Rapidly scale education & training** to better enable upskilling of the global toxicology community
-

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