Global transition to Animal-Free Regulatory Science

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Global Cosmetics Regulation 2025, 18th Nov 2025, Virtual

Next Generation Risk Assessment (NGRA) Paradigm Shift

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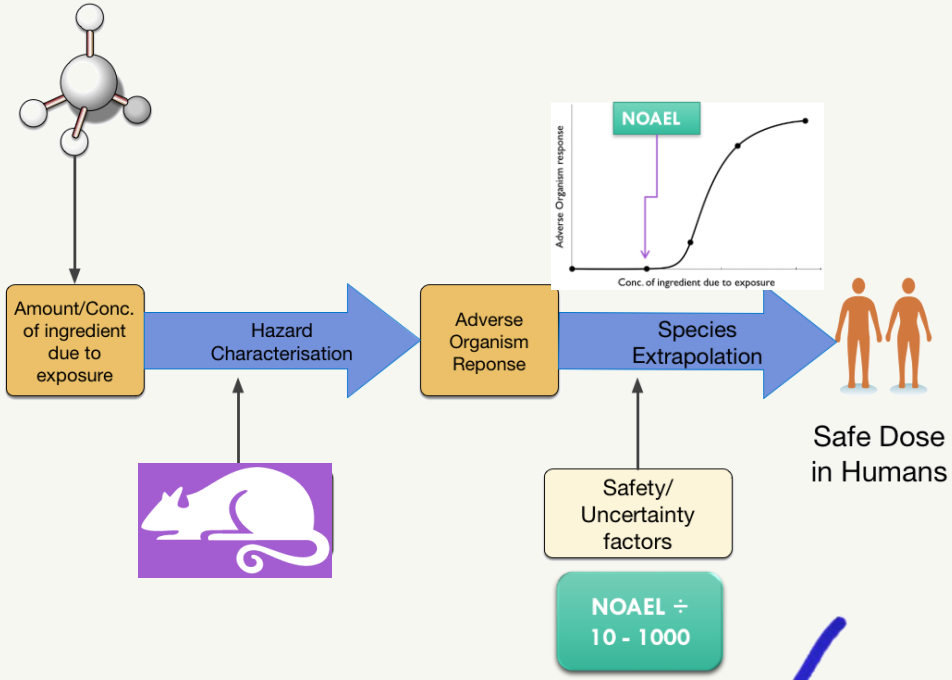
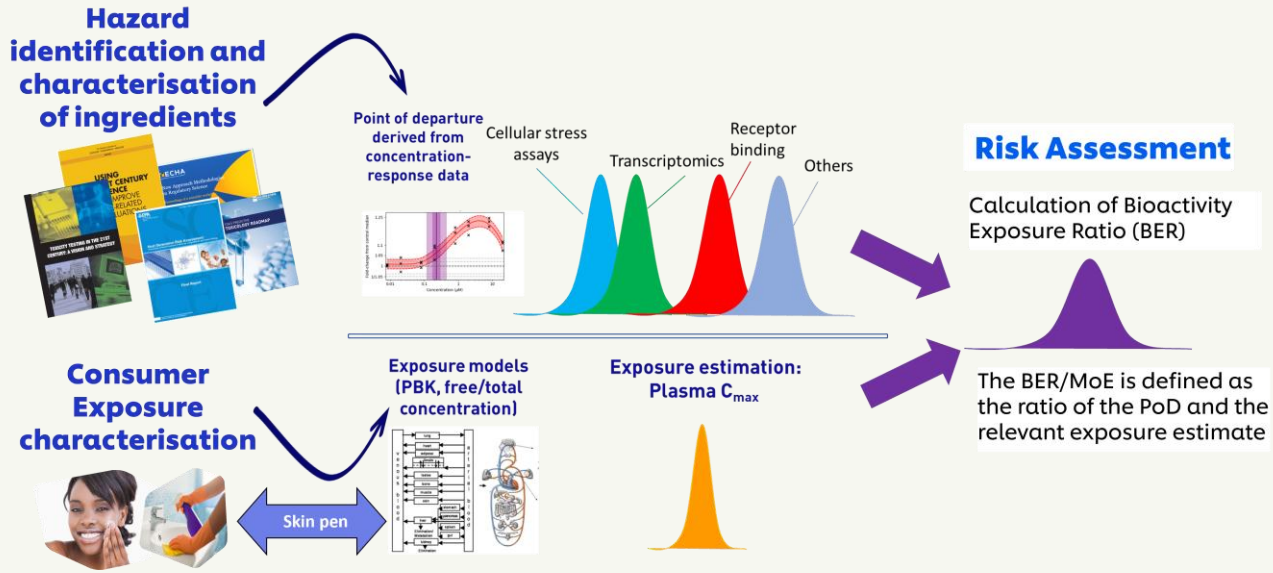
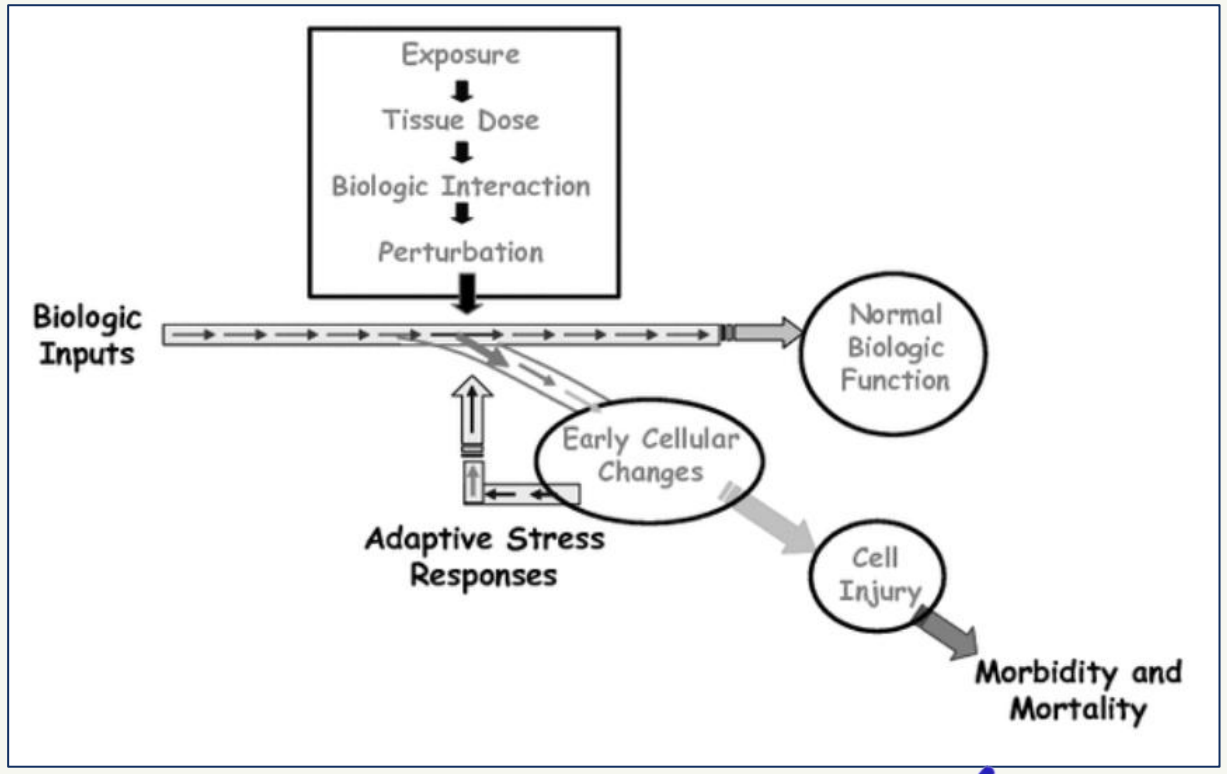
'Traditional' Risk Assessment

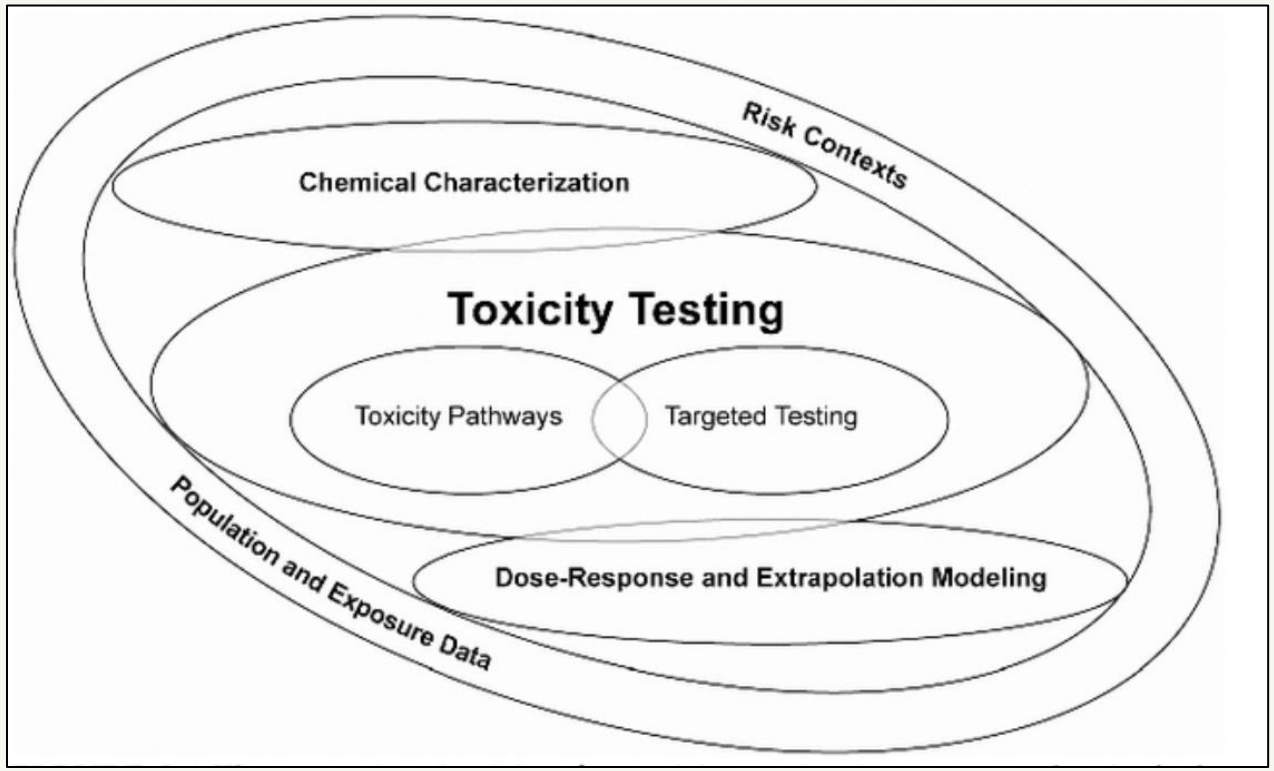


'Next Generation' Risk Assessment

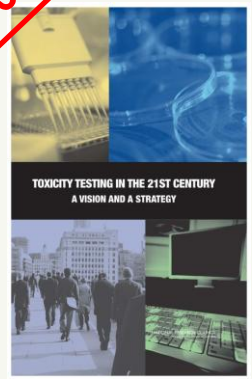


Next Generation Risk Assessment (NGRA) concepts





2007



[Toxicity Testing in the 21st Century: A Vision and a Strategy | The National Academies Press]

Next Generation Risk Assessment Conceptual Frameworks

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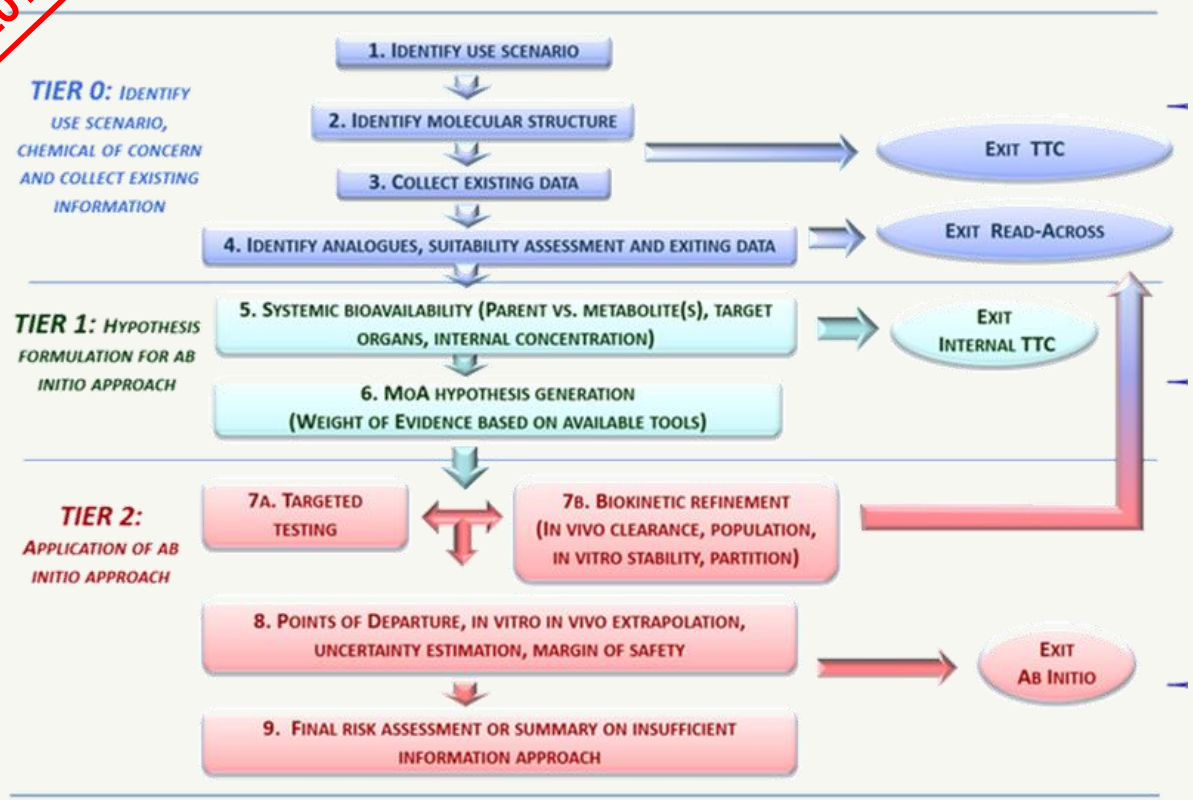
2017

SEURAT-1

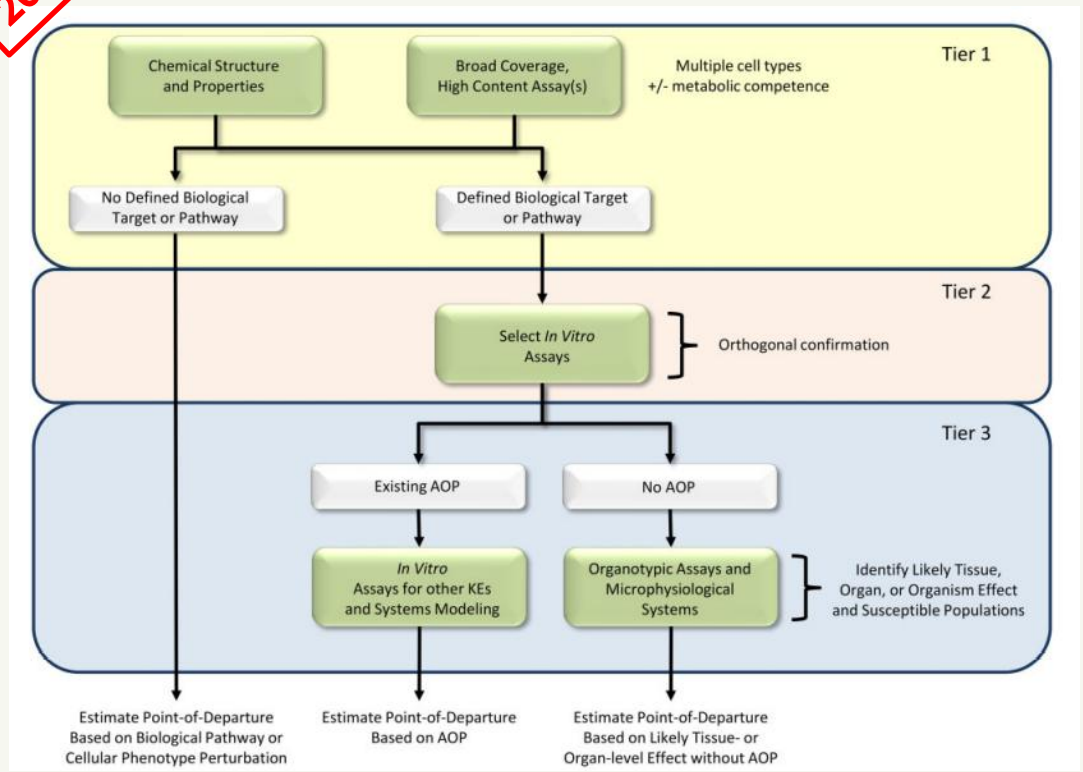


Ab initio chemical safety assessment: A workflow based on exposure considerations and non-animal methods

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

2019

EPA United States Environmental Protection Agency



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

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

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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

Scientific Committees

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

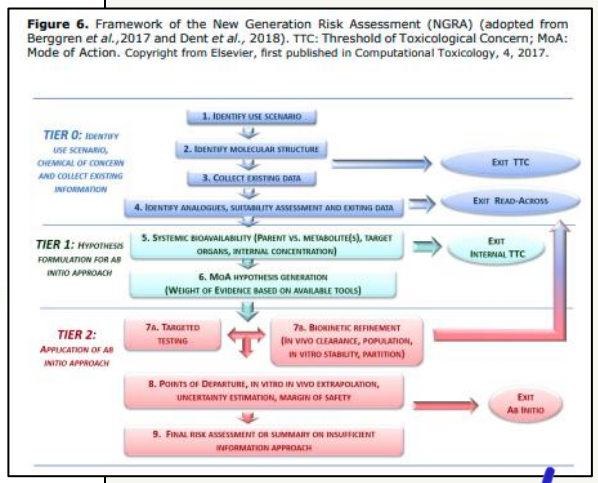

Figure 6. Framework of the New Generation Risk Assessment (NGRA) (adopted from Berggren *et al.*, 2017 and Dent *et al.*, 2018). TTC: Threshold of Toxicological Concern; MoA: Mode of Action. Copyright from Elsevier, first published in Computational Toxicology, 4, 2017.

2025

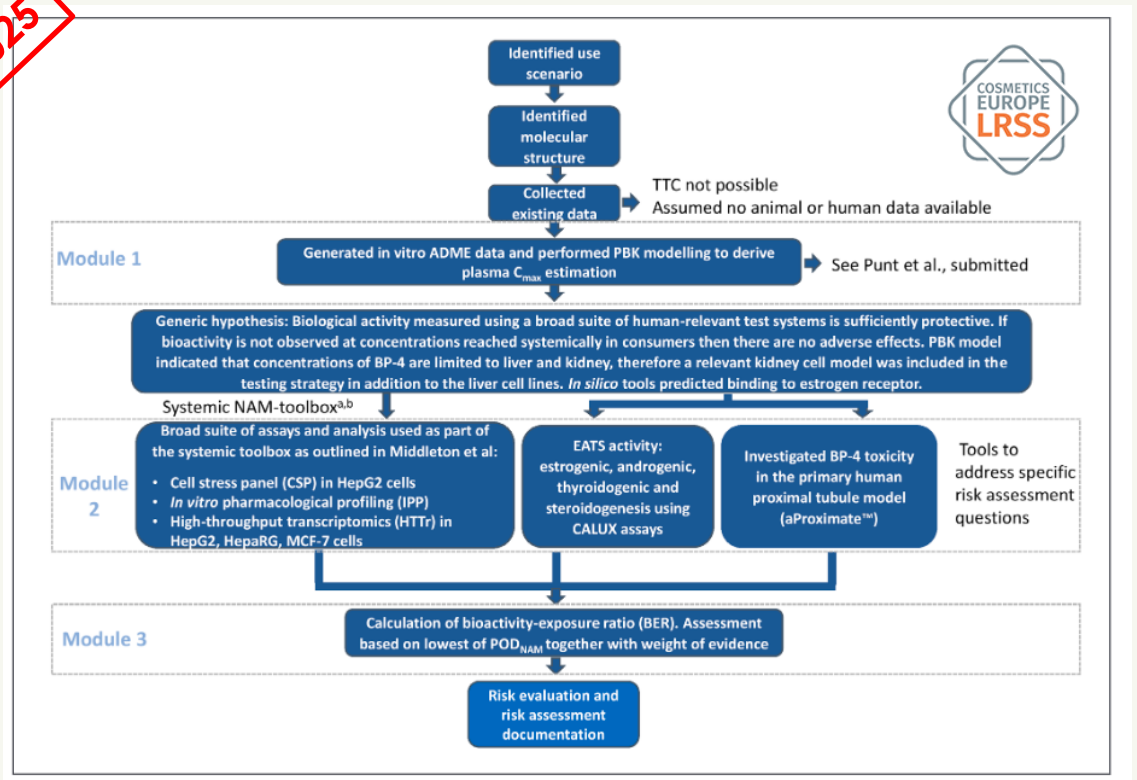

Fig. 1: NGRA case study workflow for 5% BP-4 in sunscreen body lotion
Adapted from Berggren et al. (2017) and Dent et al. (2021); [a] Middleton et al. (2022), [b] Cable et al. (2024).

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

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ICCR International Cooperation on Cosmetics Regulation

2018

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

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

ICCR International Cooperation on Cosmetics Regulation

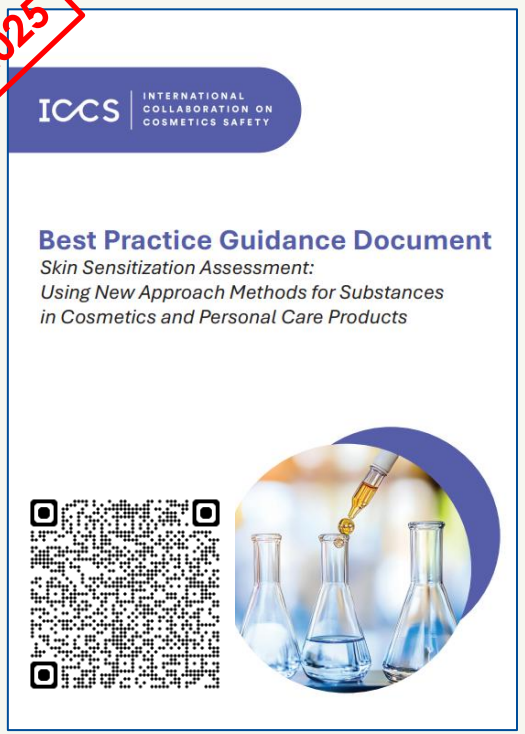
2021

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

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

ICCS INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

2025



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)

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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

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APCRA
ACCELERATING THE PACE OF CHEMICAL RISK ASSESSMENT

Led by: Health Canada Santé Canada ECHA EUROPEAN CHEMICALS AGENCY UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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

2020

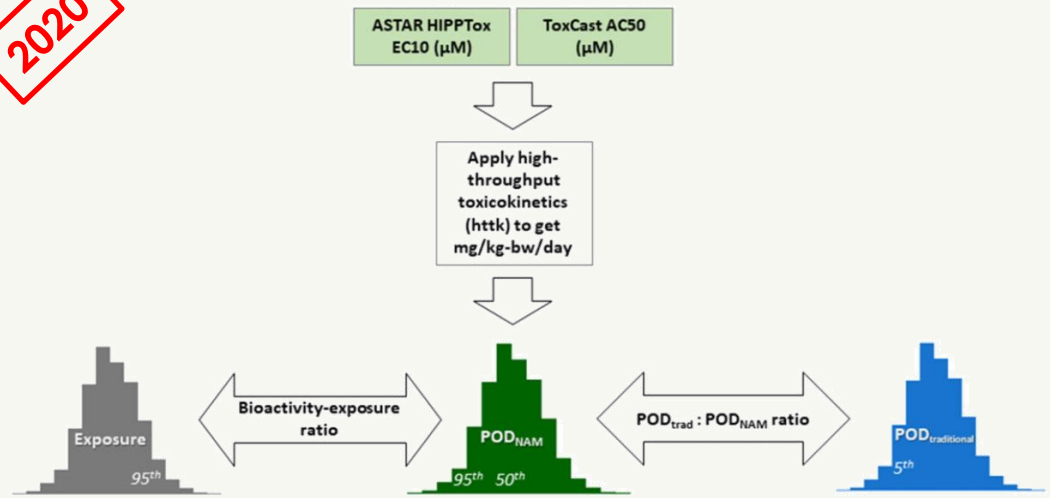

Figure 1. Overall workflow of the case study. This case study includes 448 substances with exposure predictions, *in vitro* assay data, HTTK information using the httk R package, and *in vivo* hazard information. The 50th and 95th percentile from the Monte Carlo simulation of interindividual toxicokinetic 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.

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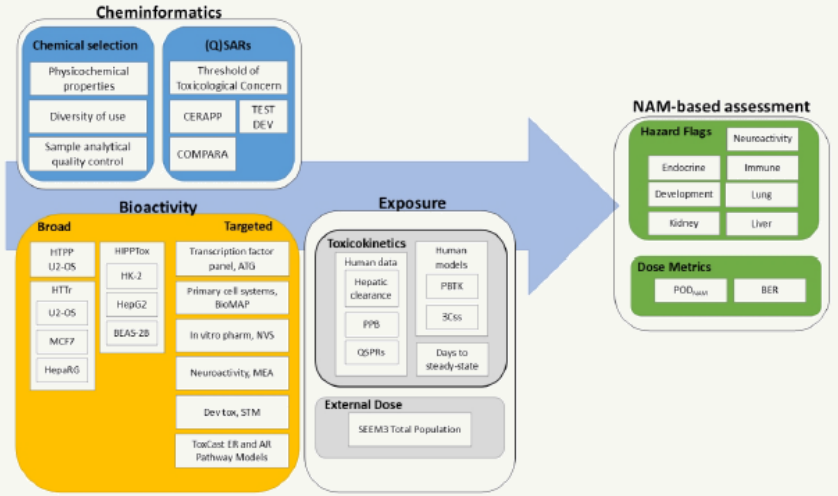

Figure 1. NAM-based assessment (NBA) workflow.
An overview of a NBA workflow that incorporates cheminformatics, broad and targeted bioactivity NAMs, via hazard flags, and exposure NAMs for internal and external exposures. The workflow culminates in a set of outputs for NBA, including hazard flags, POD¬NAM,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

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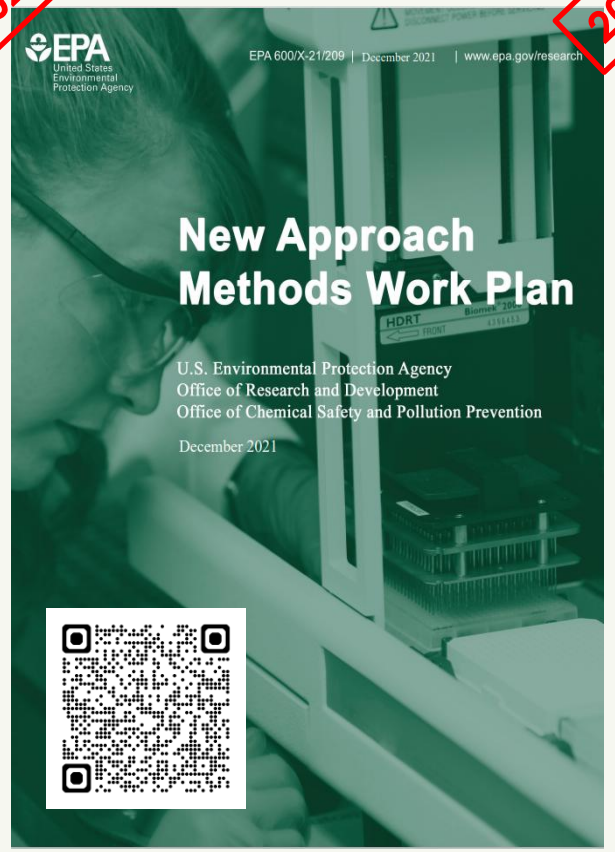
2021



New Approach Methods Work Plan

2023

towards-an-animal-free-regulatory-system-for-industrial-chemicals

2025

Strategy to replace, reduce or refine vertebrate animal testing under CEPA

2025

Replacing animals in science strategy

Government of the United Kingdom
Department for Science, Innovation and Technology

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

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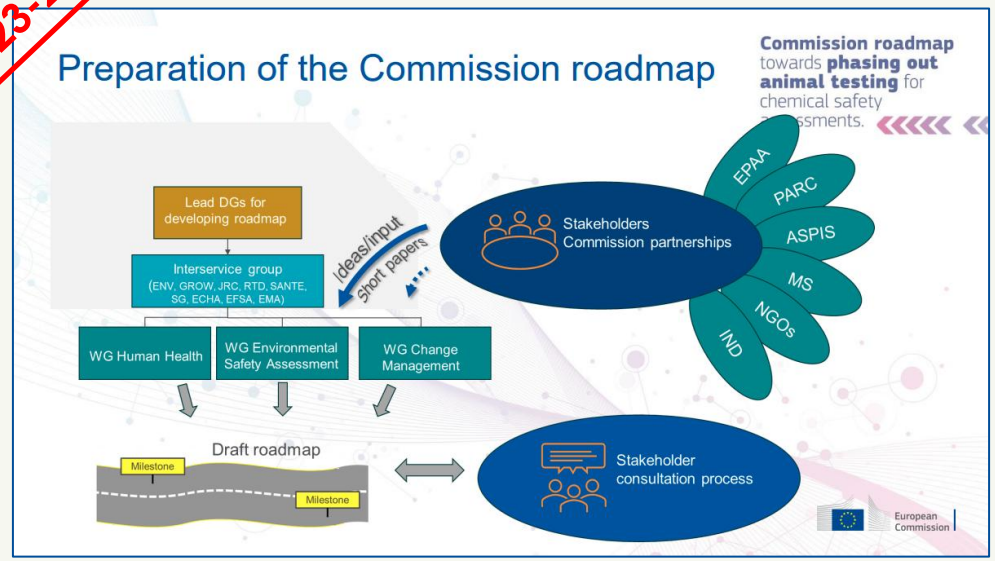
2023-26



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


Regulatory Toxicology and Pharmacology

Report of the European Commission workshop on "The roadmap towards phasing out animal testing for chemical safety assessments", Brussels, 11–12 December 2023

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

Roadmap towards phasing out animal testing

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

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

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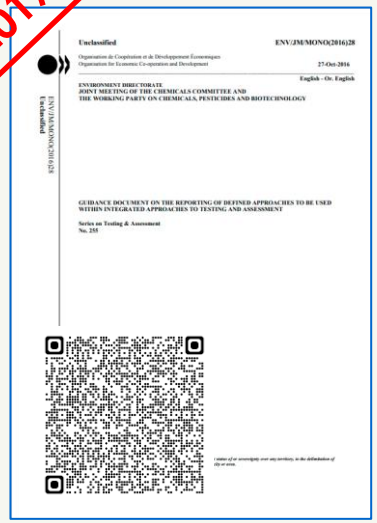
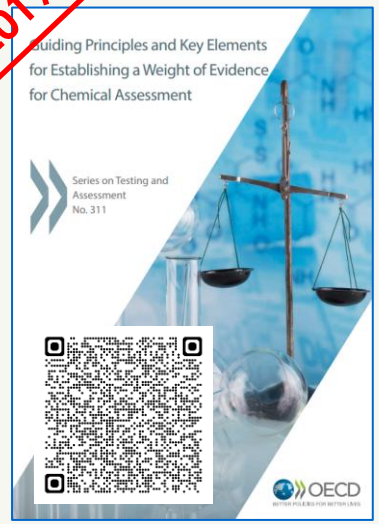
IATA combine multiple sources of information to conclude on the toxicity of chemicals and are developed to address a specific regulatory scenario or decision context.

2017



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

2019

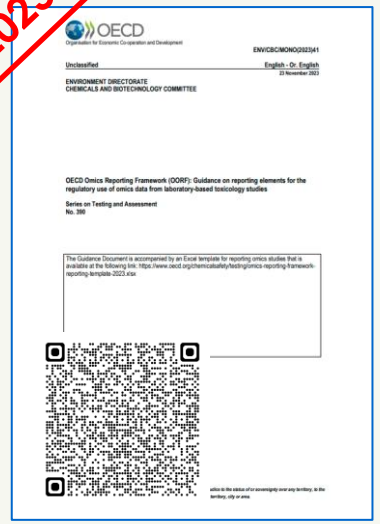


Guiding principles for establishing a **Weight of Evidence** for Chemical Assessment

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

https://www.oecd.org/en/topics/sub-issues/assessment-of-chemicals/integrated-approaches-to-testing-and-assessment.html

US FDA Roadmap to Reducing Animal Testing in Preclinical Safety Studies using New Approach Methodologies (NAMs)

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- **FDA Roadmap outlines strategic, approach to reduce animal testing in preclinical safety studies using 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

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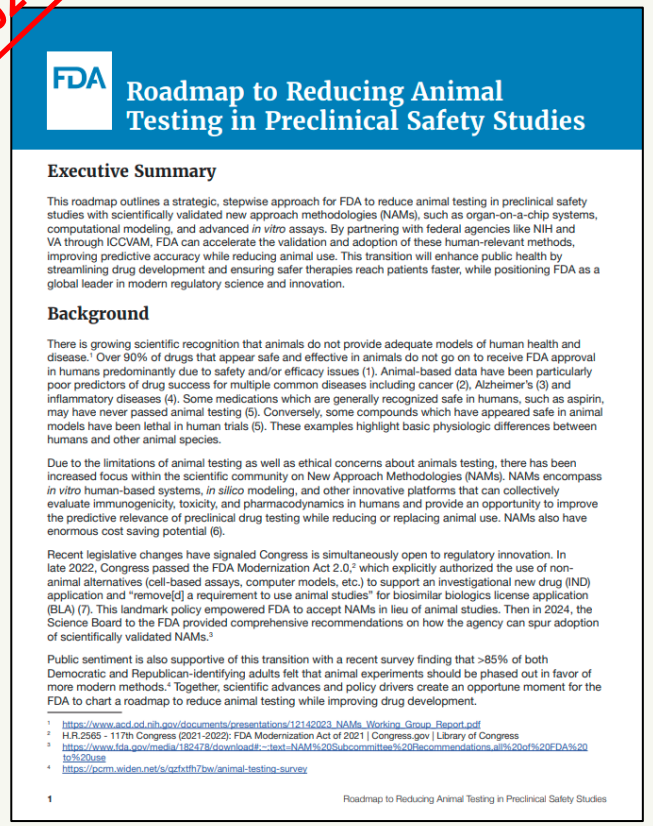


FDA

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.[1] 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]

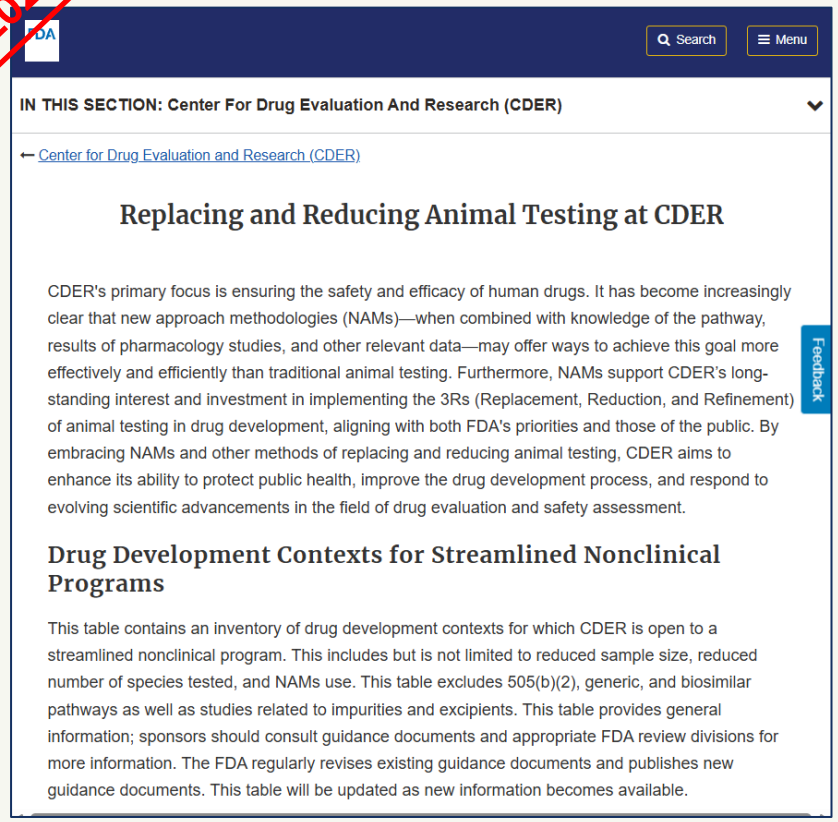
Public sentiment is also supportive of this transition with a recent survey finding that >85% of both Democratic and Republican-identifying adults felt that animal experiments should be phased out in favor of more modern methods.[4] Together, scientific advances and policy drivers create an opportune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

1 https://www.acd.od.nih.gov/documents/presentations/12142023_NAMs_Working_Group_Report.pdf
2 H.R.2565 - 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://pcrm.widen.net/s/qzfxtfh7bw/animal-testing-survey

1 Roadmap to Reducing Animal Testing in Preclinical Safety Studies

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

2025



FDA Search Menu

IN THIS SECTION: Center For Drug Evaluation And Research (CDER)

← Center for Drug Evaluation and Research (CDER)

Replacing and Reducing Animal Testing at CDER

CDER's primary focus is ensuring the safety and efficacy of human drugs. It has become increasingly clear that new approach methodologies (NAMs)—when combined with knowledge of the pathway, results of pharmacology studies, and other relevant data—may offer ways to achieve this goal more effectively and efficiently than traditional animal testing. Furthermore, NAMs support CDER's long-standing interest and investment in implementing the 3Rs (Replacement, Reduction, and Refinement) of animal testing in drug development, aligning with both FDA's priorities and those of the public. By embracing NAMs and other methods of replacing and reducing animal testing, CDER aims to enhance its ability to protect public health, improve the drug development process, and respond to evolving scientific advancements in the field of drug evaluation and safety assessment.

Drug Development Contexts for Streamlined Nonclinical Programs

This table contains an inventory of drug development contexts for which CDER is open to a streamlined nonclinical program. This includes but is not limited to reduced sample size, reduced number of species tested, and NAMs use. This table excludes 505(b)(2), generic, and biosimilar pathways as well as studies related to impurities and excipients. This table provides general information; sponsors should consult guidance documents and appropriate FDA review divisions for more information. The FDA regularly revises existing guidance documents and publishes new guidance documents. This table will be updated as new information becomes available.

Feedback

[Replacing and Reducing Animal Testing at CDER | FDA]

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

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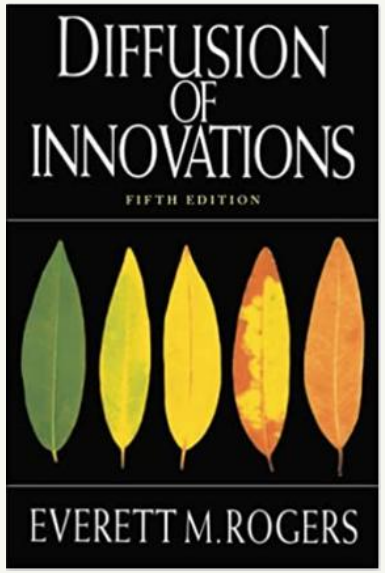
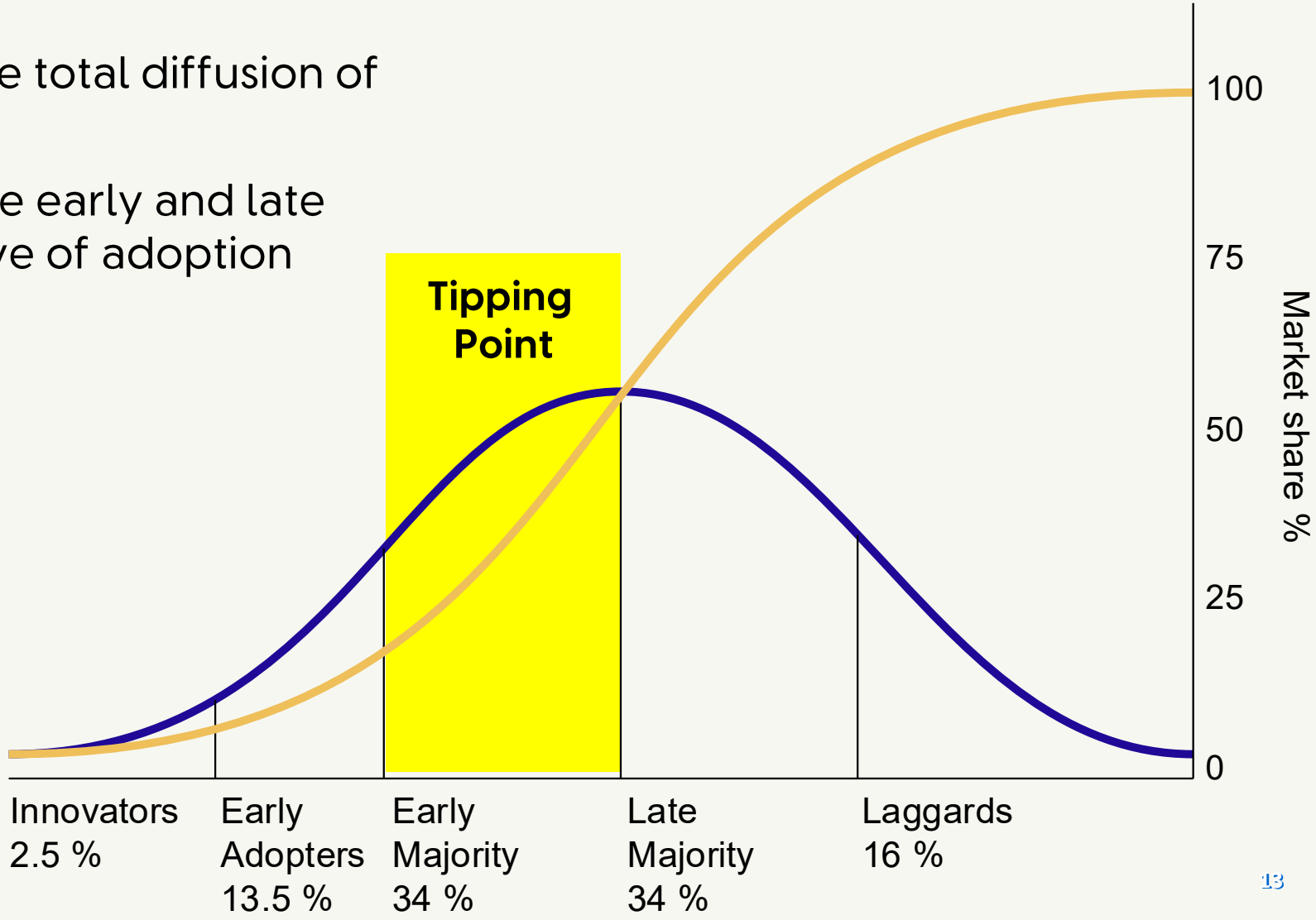
Tipping Point

- 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



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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Thank you for your attention