European Federation of Pharmaceutical Industries and Associations

RSNN/FAST Masterclass

Bridging Innovation and Regulation: The NAMs Challenge

EFPIA pharma experience with NAMs

Bert Haenen

9 December (2025)

About EFPIA

The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the biopharmaceutical industry operating in Europe.

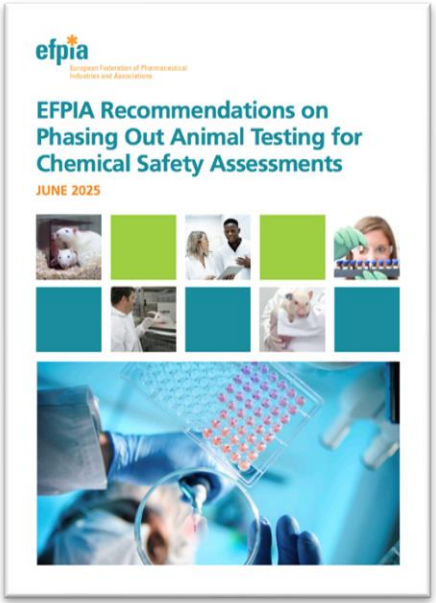
Through its direct membership of **37 national associations**, **40 leading pharmaceutical companies**, and a growing number of **small and medium-sized enterprises** (SMEs), EFPIA's mission is to create a collaborative environment that enables our members to innovate, discover, develop and deliver new therapies and vaccines for people across Europe, as well as contribute to the European economy.

More information is available on EFPIA website.

Introduction

- **16:00-17:15** - NAMs - interactieve session and panel discussie with regulators, academia and pharma
    - 16:15-16:25 EFPIA
- *What is EFPIA/pharma industry doing related to NAMs?*
    - *Roadmap to phase out animals for chemical safety testing*
        - *3 Basket Approach*

Recommendations – Roadmap to phase out animals for chemical safety testing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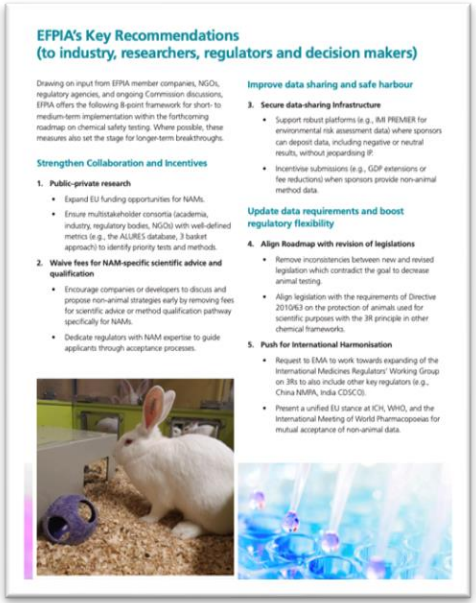
EFPIA Recommendations on Phasing Out Animal Testing for Chemical Safety Assessments

JUNE 2025


EFPIA's Key Recommendations (to industry, researchers, regulators and decision makers)

Drawing on input from EFPIA member companies, NGOs, regulatory agencies, and ongoing Commission discussions, EFPIA offers the following 8-point framework for short- to medium-term implementation within the forthcoming roadmap on chemical safety testing. Where possible, these measures also set the stage for longer-term breakthroughs.

Strengthen Collaboration and Incentives

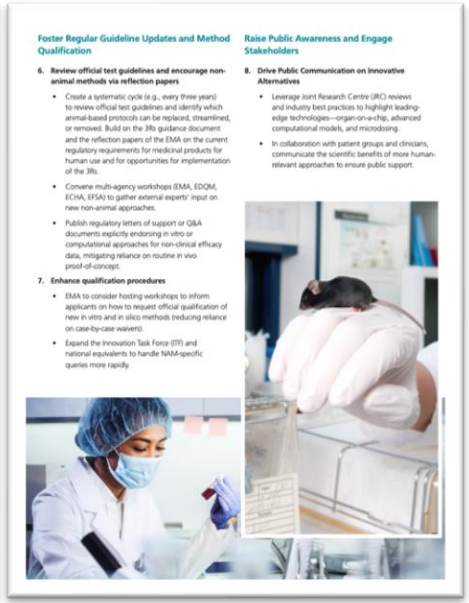
1. Public-private research
   - Expand EU funding opportunities for NAMs.
   - Ensure multistakeholder consortia (academia, industry, regulatory bodies, NGOs) with well-defined metrics (e.g., the ALURES database, 3 basket approach) to identify priority tests and methods.
2. Waive fees for NAM-specific scientific advice and qualification
   - Encourage companies or developers to discuss and propose non-animal strategies early by removing fees for scientific advice or method qualification pathway specifically for NAMs.
   - Dedicate regulators with NAM expertise to guide applicants through acceptance processes.

Improve data sharing and safe harbour

3. Secure data-sharing Infrastructure
   - Support robust platforms (e.g., IMI PREMIER for environmental risk assessment data) where sponsors can deposit data, including negative or neutral results, without jeopardising IP.
   - Incentivise submissions (e.g., GDP extensions or fee reductions) when sponsors provide non-animal method data.

Update data requirements and boost regulatory flexibility

4. Align Roadmap with revision of legislations
   - Remove inconsistencies between new and revised legislation which contradict the goal to decrease animal testing.
   - Align legislation with the requirements of Directive 2010/63 on the protection of animals used for scientific purposes with the 3R principle in other chemical frameworks.
5. Push for International Harmonisation
   - Request to EMA to work towards expanding of the International Medicines Regulators' Working Group on 3Rs to also include other key regulators (e.g., China NMPA, India CDSCO).
   - Present a unified EU stance at ICH, WHO, and the International Meeting of World Pharmacopoeias for mutual acceptance of non-animal data.


Foster Regular Guideline Updates and Method Qualification

6. Review official test guidelines and encourage non-animal methods via reflection papers
   - Create a systematic cycle (e.g., every three years) to review official test guidelines and identify which animal-based protocols can be replaced, streamlined, or removed. Build on the 3Rs guidance document and the reflection papers of the EMA on the current regulatory requirements for medicinal products for human use and for opportunities for implementation of the 3Rs.
   - Convene multi-agency workshops (EMA, EDQM, ECHA, EFSA) to gather external experts' input on new non-animal approaches.
   - Publish regulatory letters of support or Q&A documents explicitly endorsing in vitro or computational approaches for non-clinical efficacy data, mitigating reliance on routine in vivo proof-of-concept.
7. Enhance qualification procedures
   - EMA to consider hosting workshops to inform applicants on how to request official qualification of new in vitro and in silico methods (reducing reliance on case-by-case waivers).
   - Expand the Innovation Task Force (ITF) and national equivalents to handle NAM-specific queries more rapidly.

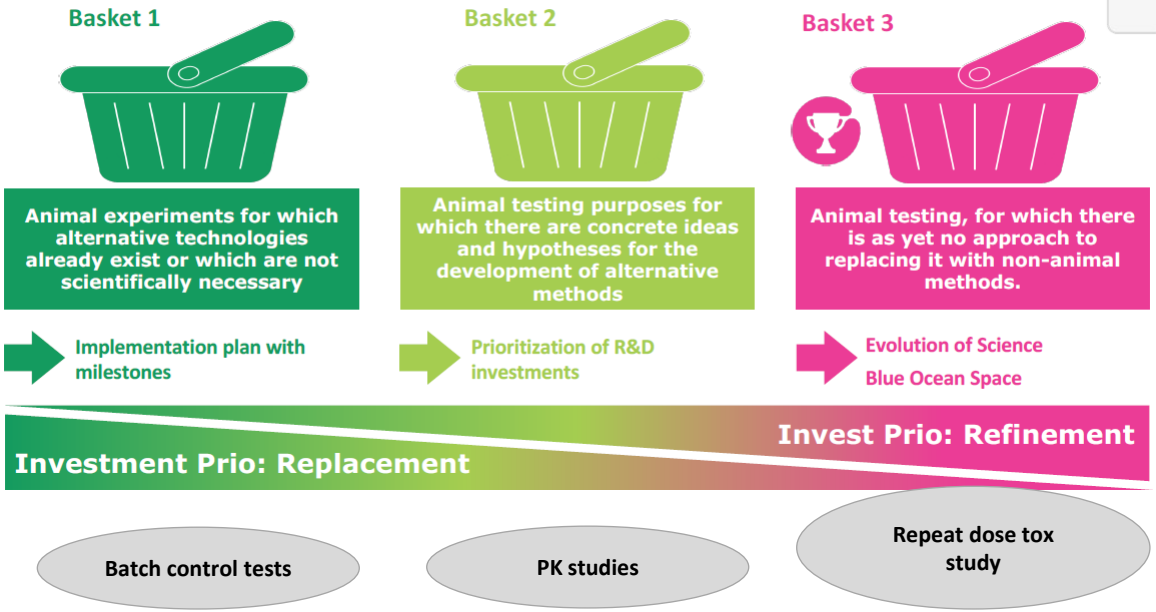
Raise Public Awareness and Engage Stakeholders

8. Drive Public Communication on Innovative Alternatives
   - Leverage Joint Research Centre (JRC) reviews and industry best practices to highlight leading-edge technologies—organ-on-a-chip, advanced computational models, and microdosing.
   - In collaboration with patient groups and clinicians, communicate the scientific benefits of more human-relevant approaches to ensure public support.

Vaccines Europe
An industry for healthy lives

https://www.efpia.eu/media/meef32ki/efpia-recommendations-on-phasing-out-animal-testing-for-chemical-safety-assessments.pdf

The 3 Basket Approach for Developing a Roadmap to Phase out Animal Testing



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    - *Publications to make the (scientific) community aware the pharma takes the task sesriously to replace, reduce and refine animal testing of drugs*
    - *EFPIA project on application of NAMs in NC safety assessment of drugs*
        - *In vitro toxicity data using human derived tissues (Beilman et al.)*

Recent publications

Review > Regul Toxicol Pharmacol. 2024 Sep:152:105683. doi: 10.1016/j.yrtph.2024.105683. Epub 2024 Aug 6.

Endeavours made by trade associations, pharmaceutical companies and regulators in the replacement, reduction and refinement of animal experimentation in safety testing of pharmaceuticals

Andrew W Harrell [1], Kirsty Reid [2], John Vahle [3], Frederic Brouta [4], Mario Beilmann [5], Graeme Young [6], Kylie A Beattie [6], Jean Pierre Valentin [4], Shajahan Shaid [6], Peter Brinck [7]

Affiliations + expand

PMID: 39117168 DOI: 10.1016/j.yrtph.2024.105683

Free article

nature reviews drug discovery

https://doi.org/10.1038/s41573-025-01182-9

Perspective

Check for updates

Application of new approach methodologies for nonclinical safety assessment of drug candidates

Mario Beilmann, Karissa Adkins, Harrie C. M. Boonen, Philip Hewitt, Wenyue Hu, Robert Mader, Susanne Moore, Payal Rana, Thomas Steger-Hartmann, Remi Villenave & Terry van Vleet

Abstract

Sections

Vaccines Europe
An industry for healthy lives

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Introduction

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  - *EFPIA project on application of NAMs in NC safety assessment of drugs (Beilman et al.)*
  - *Different type of NAMs:*
    - *In silico methods (QSARs for predicting mutagenicity: of theoretical and identified impurities)*
    - *In chemico methods (test chemical reactivity of a candidate: eg test covalent binding to proteins)*
    - *In vitro methods (high troughput screening of drug candidate toxicities using cell lines and other in vitro systems)*
    - *In vivo NAMs (non-animal scientific methods, such as organ-on-a-chip system and computational modeling like PBPK models, used to assess the safety and efficacy of substances without using whole living organisms)*
    - *Probably used: Zebra fish model (early test of developmental, neurotox, reproductive tox etc). Other models: Dev Tox NAMs (Whole Embryo Culture, mouse embryonic stem cells)*

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  - *Pharma uses NAMs mainly during the early dev't phases*
    - *In silico methods (QSARs for predicting mutagenicity: of theoretical and identified impurities)*
    - *In chemico methods (test chemical reactivity of a candidate: eg test covalent binding to proteins)*
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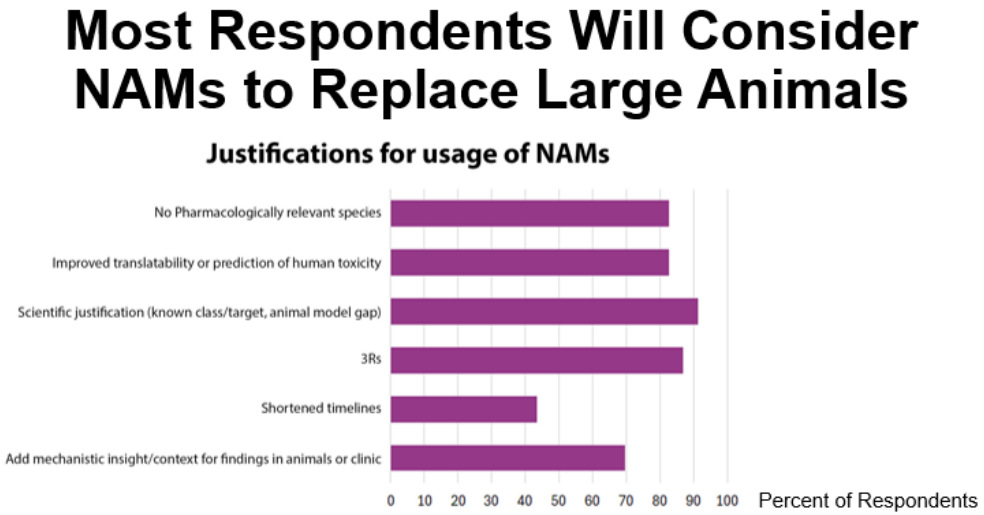
  - *Develop NAMs in different Trade Organisation WGs (IQ, EFPIA, Drusafe etc) & in-company dev't?*
    - *Intestinal and hepatic in vitro model systems for ADME studies*

Introduction

- *What is EFPIA/pharma industry doing related to NAMs?*
  - *For what purpose does pharma use NAMs (Bio survey)*



- *NAMs are predominantly used in testing drug candidates to treat Advanced Cancer*

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- *In which development phase do Pharma companies use NAMs?*
    - *NAMs are widely applied across drug modalities and disease types*
    - *Mostly during early tox (screening), sometimes in GLP dev't phase to explain a potential tox finding to regulators (instead of in an vivo study)*
    - *NAMs based MAA filings are accepted by HAs when there is no pharmacologically relevant species due to the mechanism of action or due to the pharmacological target*
    - *NAMs based filings may be appropriate when animal studies are expected to have poor translation to human and/or limited value based on one or both of the following:*

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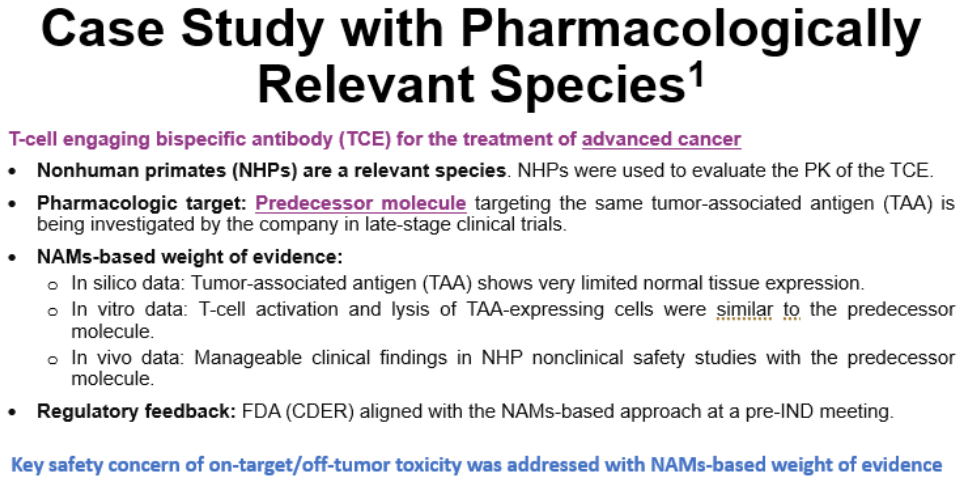

Case Study with Pharmacologically Relevant Species[1]

T-cell engaging bispecific antibody (TCE) for the treatment of advanced cancer

- **Nonhuman primates (NHPs) are a relevant species**. NHPs were used to evaluate the PK of the TCE.
- **Pharmacologic target:** Predecessor molecule targeting the same tumor-associated antigen (TAA) is being investigated by the company in late-stage clinical trials.
- **NAMs-based weight of evidence:**
  - In silico data: Tumor-associated antigen (TAA) shows very limited normal tissue expression.
  - In vitro data: T-cell activation and lysis of TAA-expressing cells were similar to the predecessor molecule.
  - In vivo data: Manageable clinical findings in NHP nonclinical safety studies with the predecessor molecule.
- **Regulatory feedback:** FDA (CDER) aligned with the NAMs-based approach at a pre-IND meeting.

Key safety concern of on-target/off-tumor toxicity was addressed with NAMs-based weight of evidence

Shenton et al 2025 (Drug Discov Today) 30(4)

- *NAMs based filings may be appropriate when animal studies are expected to have poor translation to human and/or limited value based on one or both of the following:*
  - *Modulation of target is well-characterised with a predecessor molecule*
  - *Putative risks based on the MoA and/or the pharmacological target can be addressed based on NAMs and/or clinical mitigation and monitoring*

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- *Does Pharma qualify NAMs?*
    - *Minimal qualification/validation when used during early screening.*
    - *Qualified NAMs? Not sure (Proprietary information). Validation according to OECD is indicated. Pharma is also awaiting guidance from HAs. A lot of uncertainty around regulatory acceptance of NAMs (all regions aligned?)*
    - *Based on a BIO Survey: 9 companies reported regulatory acceptance of NAMS as animal test replacements (2/3 achieving multiregional approval)*

Questions within Pharma companies related to NAMs

- *NAMs need a CoU (context of use). It is burdensome to have a cross-industry agreed COU. Can the same NAM be used for another CoU? What is the procedure then?*
- *Questions related to the validation process*
- *Validation/qualification of NAMs: what extent needed for different NAMs?*
- *“Pool efforts” of companies on developing NAMs?*
- *NAMs for batch release/quality control?*
- *Safe harbor of data? Content of submission packages of NAMs?*
- *All regions aligned on the applicability for NAMs*