EU initiatives to advance NAMs in research and regulatory testing

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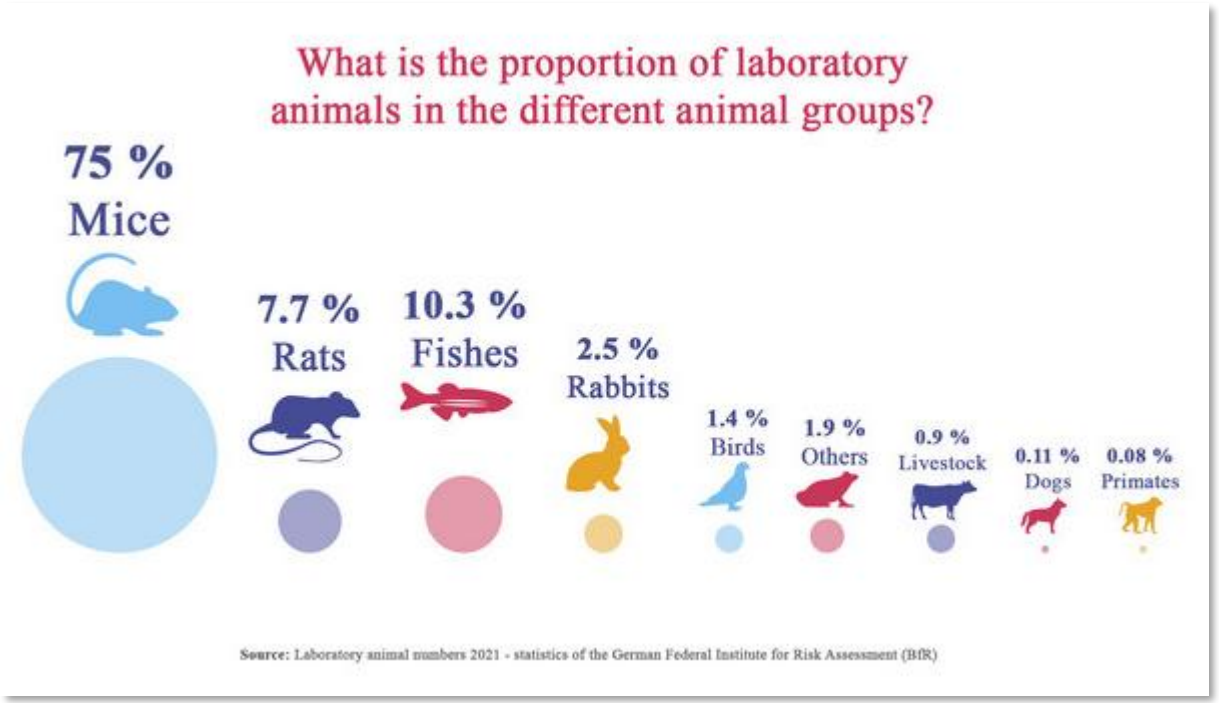
IABS-AFSA-Humane World for Animals
Bangkok, 4 December 2025

What are New Approach Methodologies (NAMs)?

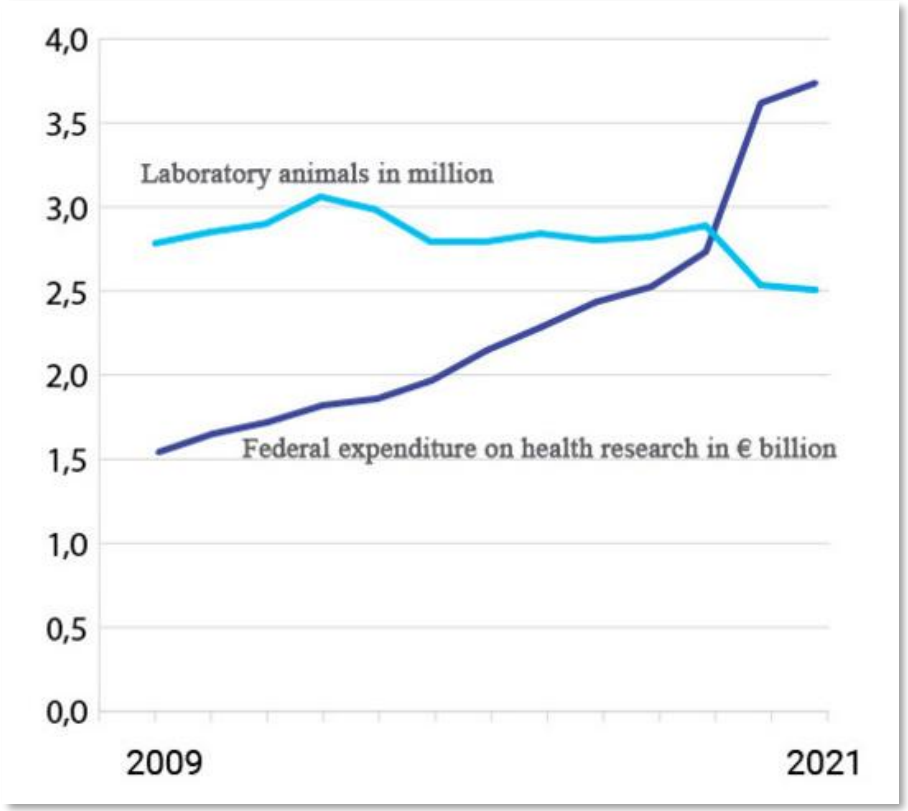
For the European Medicines Agency (EMA), NAMs *are defined as innovative methods and strategies that aim to replace, reduce, or refine the use of animals in the testing of medicinal products, aligning with the 3Rs principles. These methods encompass a range of non-animal approaches, including simple and complex human cell-based assays, microphysiological systems, in chemico methods, in silico modelling and other non-human or human biology-based test methods*

Extensive use of Experimental Animals

More than 115 million experimental animals are used each year globally (Humane Society International)



Around 750,000 animals used in EU for Quality Control (including batch safety & potency testing) (ALURES)



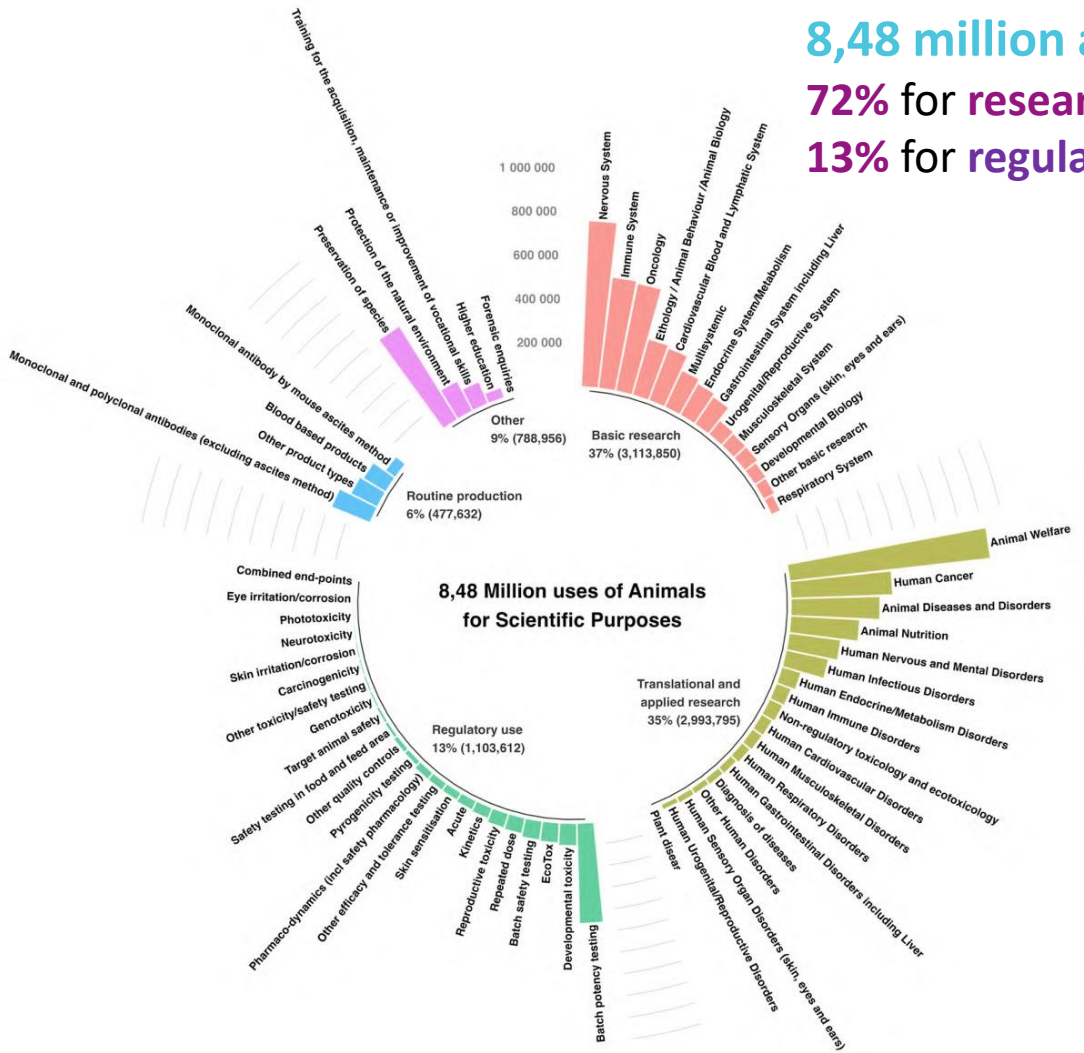
Experimental animals used in Germany

Animals used for scientific purposes in EU (2022)

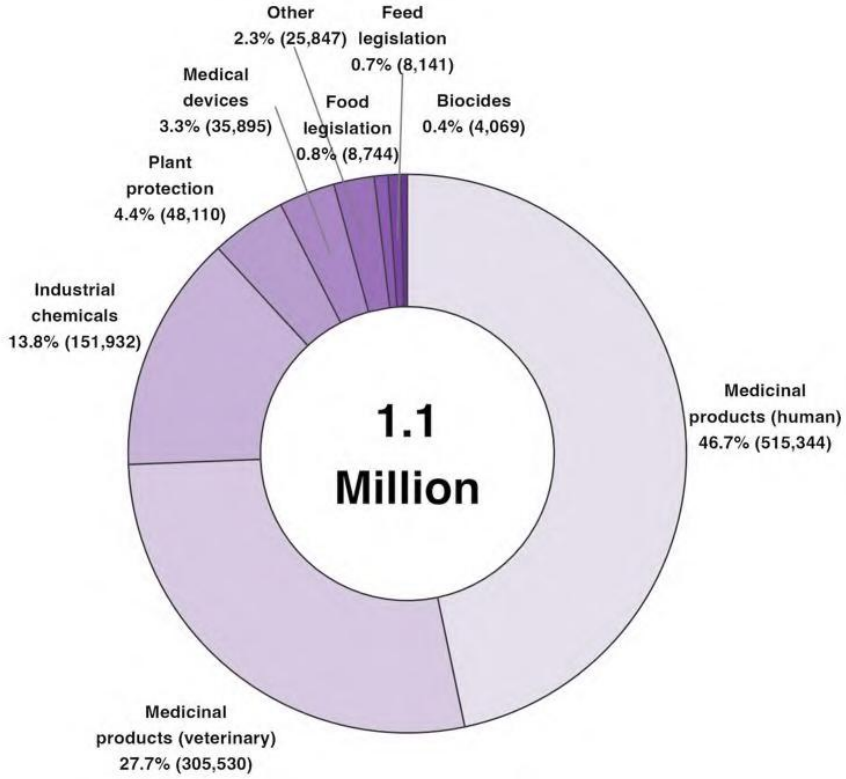
8,48 million animals used for scientific purposes

72% for **research**

13% for **regulatory purposes** - mostly **medicinal products (74%)**



All uses of animals for research and testing



Regulatory uses by legislation type

Increasing political and societal pressure to phase out animal testing

The European Partnership for Alternative Approaches to Animal Testing

European Citizen Initiative (ECI)

European Citizen Initiative (ECI)

Directive 2010/63 on protection of animals for scientific purposes

STOP VIVISECTION

Save Cruelty Free Cosmetics

2005 2010 2015

"Member States shall wherever possible, a satisfactory method o not entailing the use shall be used instead

ingredients (20), sale/marketing (2013)

EC Response:
1) Scientific conference (D
2) Active monitoring and c
3) Support to development of alternative methods
4) Dialogue, dissemination

EC Response:
1) Roadmap towards phasing out animal testing for safety assessment of chemicals (Q1-2026)
2) Modernise science in the EU:
   1) continue supporting the development of alternative approaches.
   2) exploring the possibility to coordinate the activities of EU Member States and national authorities

Roadmap towards phasing out animal testing for safety assessment of chemicals

- Roadmap will provide a **plan/schedule** to accelerate phasing out animal testing
- To be **finalised in Q1 2026**
- Applicable to **all 15 pieces of EU chemical legislation** that might lead to animal testing for **chemical safety assessments (incl pharma)**
- The roadmap will:
  - List **concrete action points** (e.g. recommendation on how to replace/reduce/refine animal testing for certain endpoints)
  - Contain **milestones** (e.g. agreement on regulatory needs for complex endpoints)
  - Define **indicators** that help to monitor the progress of the implementation
  - Define **organisational structures** that are necessary for the implementation process

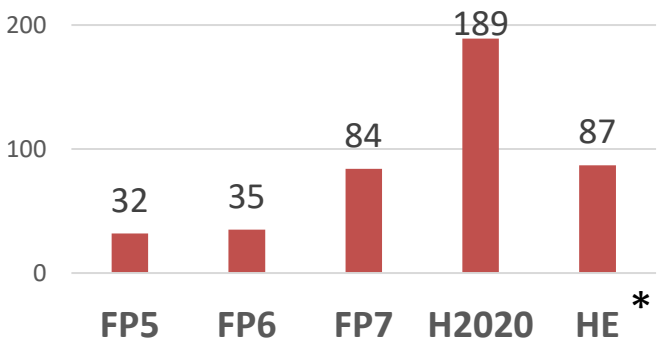
EU support to NAMs / alternatives to animal testing

Since 1998 (FP5):

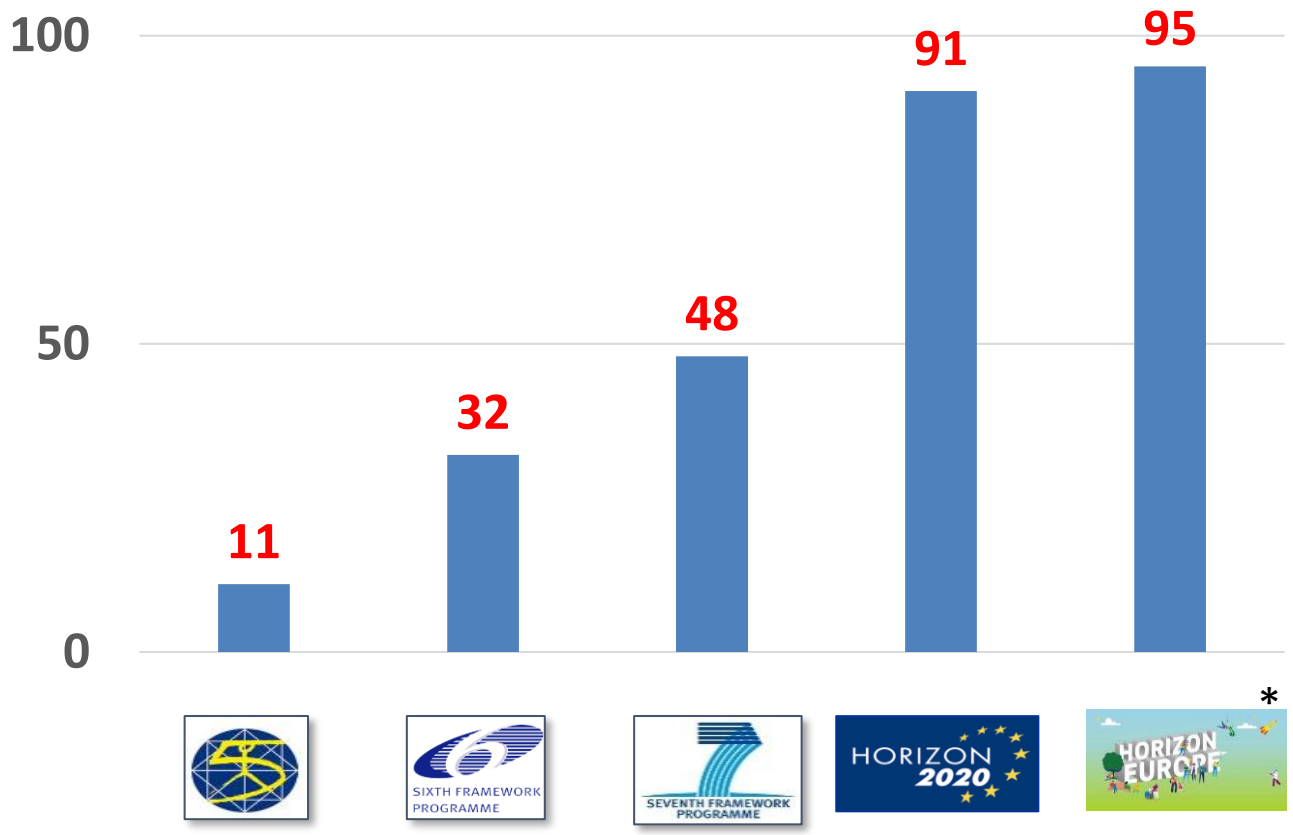
>430 projects

1,5 billion €

Number of projects

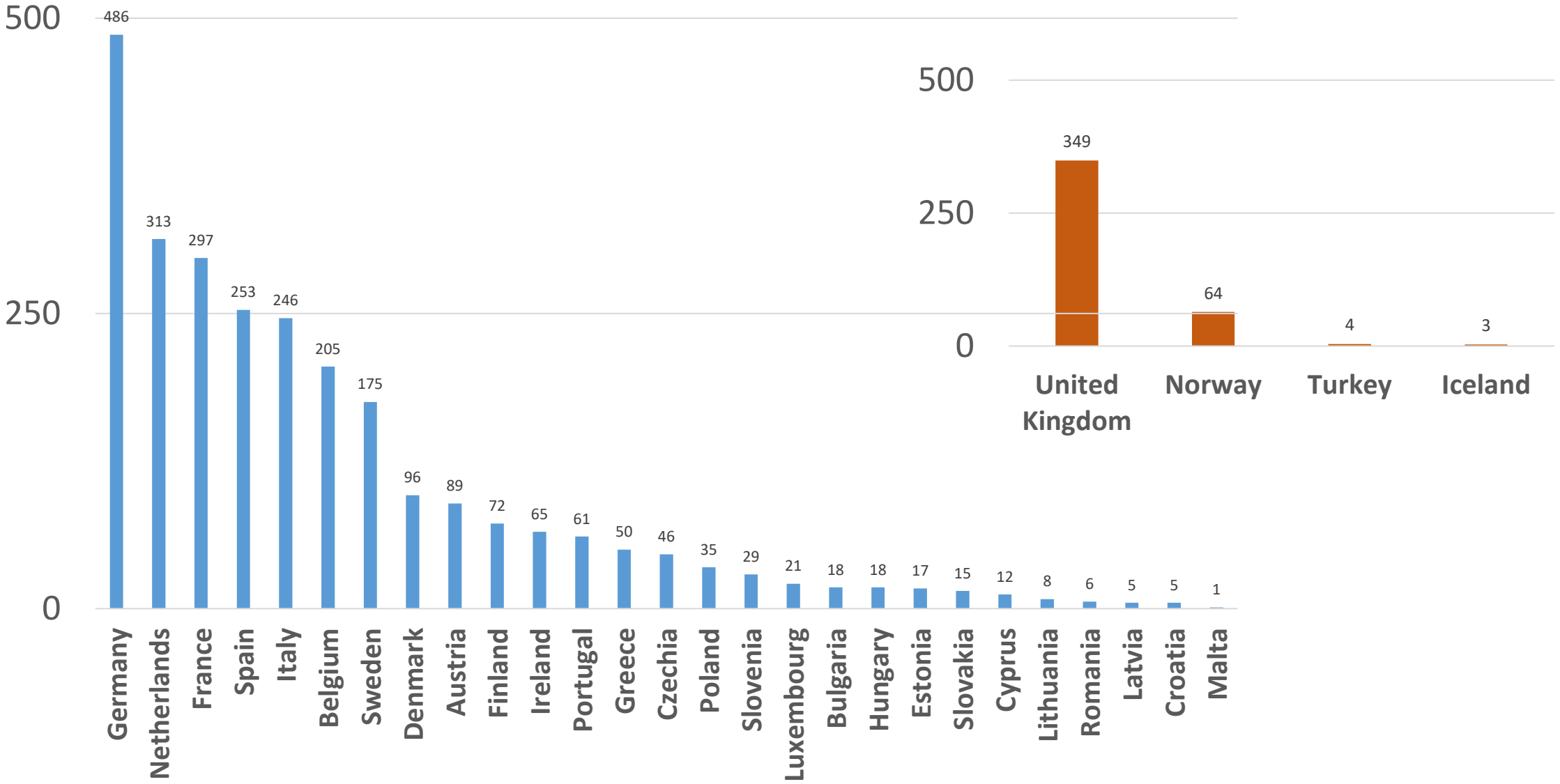


Average annual budget (million €)

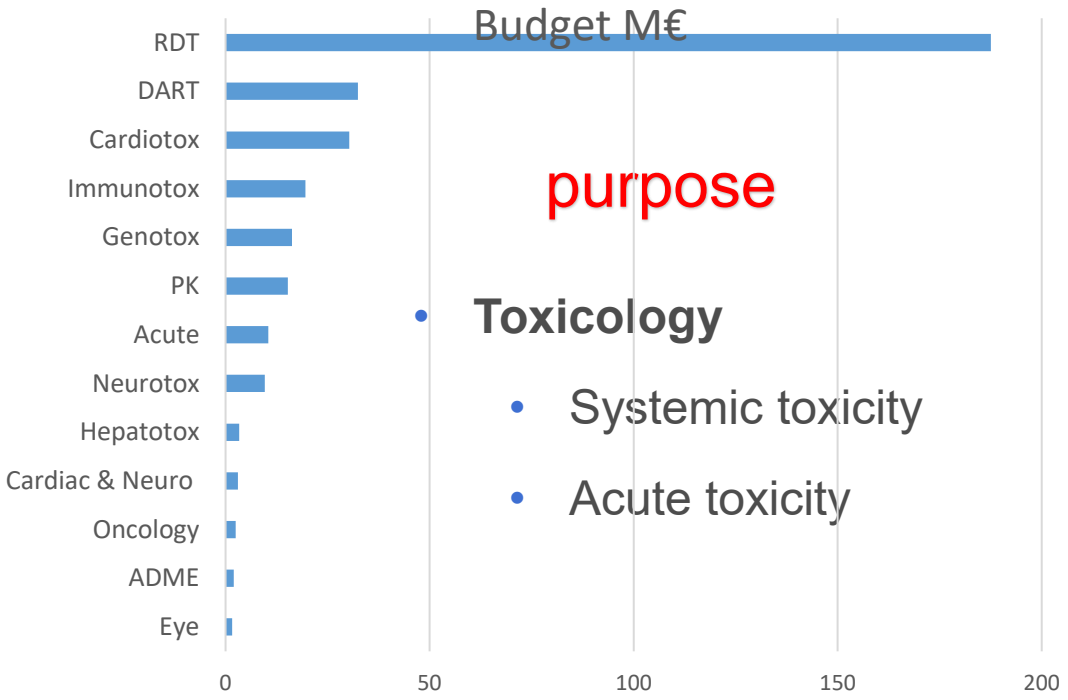


* Up to May 2025

Participants in EU funded NAMs projects



Features of EU projects on alternatives



purpose

- **Toxicology**
  - Systemic toxicity
  - Acute toxicity
- **Ecotoxicology**
- **Basic / Preclinical studies**
- **Quality assessment**
- **Training**

methods

- **In vitro cell cultures**
  - Tissues
  - Organoids
  - Organs on chips
- **Modelling**
  - QSAR
  - Virtual twins

products

- **Chemicals**
- **Drugs**
- **Nanomaterials**
- **Vaccine**

European Research Area (ERA) action on NAMs

Aim: Coordinate and streamline EU and Member States' and other stakeholders' actions on NAMs

Focus on **biomedical research and regulatory testing** of **medicinal products** and **medical devices**

All actors involved: European Commission, relevant national ministries, regulatory agencies, EMA, research funders, academia, research institutes & infrastructures, pharma and MedTech industry, CROs, journal editors, NGOs, citizens & patients

Holistic approach involving all stages of biomedical research—from the basic discovery phase to application, implementation, and regulatory testing of medicinal products and medical devices —

Targets ~80% of animal use in EU

NAM ERA structure

3 years: Q4 2025-Q4 2028

WG1: Development of NAMs and common EU infrastructures

WG2: Validation, acceptance and implementation of NAMs

WG3: Education and training

WG4: Openness & awareness

Open to:

- non-EU Associated Countries
  (Canada, South Korea, Australia)
- Others?
  (Brazil, US, Japan)

Increased interest in NAMs from EMA

3Rs Working Party established in 2022- first permanent, standing group on NAMs – covering both human and veterinary fields

Continuously review existing guidelines:

Reflection papers (“Inventory”): what is possible (“Implemented”) and what will soon be possible (“newly identified”)

Ongoing revision of “Guideline on the principles of regulatory acceptance of 3Rs”

European Specialised Expert Committee on NAMs

Operational Expert Group on batch release testing


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

02 December 2024
EMA/CHMP/CVMP/3Rs/742466/2015 Rev. 1
Committee for Medicinal Products for Human Use (CHMP)

Reflection paper on the current regulatory testing requirements for medicinal products for human use and opportunities for implementation of the 3

Draft

Draft agreed by 3RsWP following review by respective WPs (SWP, QWP, BWP, CAT and BMWP)	
Adopted by Committee for medicinal products for human use for release for consultation	
Start of Public consultation	
End of Public consultation (deadline for comments)	

Comments should be provided using this EUSurvey form. For any techr the EUSurvey Support.

Keywords	*3Rs, regulatory testing, regulatory acceptance, approach methodologies, human medicines*

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

16 January 2025
EMA/CHMP/CVMP/3Rs/164002/2016 Rev. 1
Committee for Veterinary Medicinal products (CVMP)

Reflection paper on the current regulatory testing
ary medicinal products and
entation of the 3Rs

respective WPs (QWP,	November 2024
on	16 January 2025
	13 February 2025
s)	30 June 2025

USurvey form . For any technical issues, please contact

ing, regulatory acceptance, animal tests, new approach erinary products

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 October 2023
EMA/CHMP/CVMP/452614/2023
Committee for Medicinal Products for Human Use (CHMP)
Committee for Veterinary Medicinal Products (CVMP)

Concept paper on the revision of the Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches (EMA/CHMP/CVMP/JEG-3Rs/450091/2012)

Agreed by the 3Rs Working Party	June 2023
Agreed by the Non-Clinical Working Party	June 2023
Adopted by CHMP for release for consultation	12 October 2023
Adopted by CVMP for release for consultation	
Start of public consultation	
End of consultation (deadline for comments	

Comments should be provided using this E the EUSurvey Support .

Keywords	Regulatory accepta chip, 3Rs, context

Concept paper on the revision of the Guideline published for consultation on 12 October 2023

Regulatory acceptance of NAMs?

Regulatory acceptance refers to *the official recognition by a regulatory authority (such as the EMA) that a method, tool, or dataset is scientifically valid and suitable for use in regulatory decision-making*

Integration into Guidelines

- NAMs can be incorporated into official guidance (e.g., ICH, EMA, Ph. Eur)
- Example: ICH M7 allows (Q)SAR models for mutagenicity assessment of impurities

Case-by-Case Acceptance

- NAMs used in product submissions (e.g., Clinical Trial Applications, Marketing Authorization Application) for regulatory decision making
- Evaluation on scientific merit and relevance to the product and target indication

Qualification procedure at EMA

- Formal process to assess & endorse a novel method for a specific context of use in the development of a medicinal product – can provide endorsement for broader application

Interacting with EMA on NAMs

Innovation Task Force

- Early Dialogue
- Informal exchange
- Regulatory, technical & scientific topic
- Free of charge
- Vet & Human

Portfolio and technology meetings

- Pharma companies with large medicinal product portfolios
- Issues impacting portfolio progression
- Anticipate scientific & regulatory needs
- Identify innovative technologies

Scientific Advice

- Product Specific
- Formal scientific guidance
- Study design / Methodology
- Vet & Human separate
- Reduced Fees (e.g. SME and academia)

Qualification of a Novel Methodology

- Innovative methods medicines R&D
- Acceptability of a methodology in a specific context of use
- Vet: through SA
- Reduced Fees (e.g. SME and academia)

Safe harbour

- Voluntary data submission
- Independent evaluation
- Builds regulatory confidence & experience
- Support the drafting of CoU based qualification criteria

Early dialogue @ 3Rs EMA ITF briefing meetings

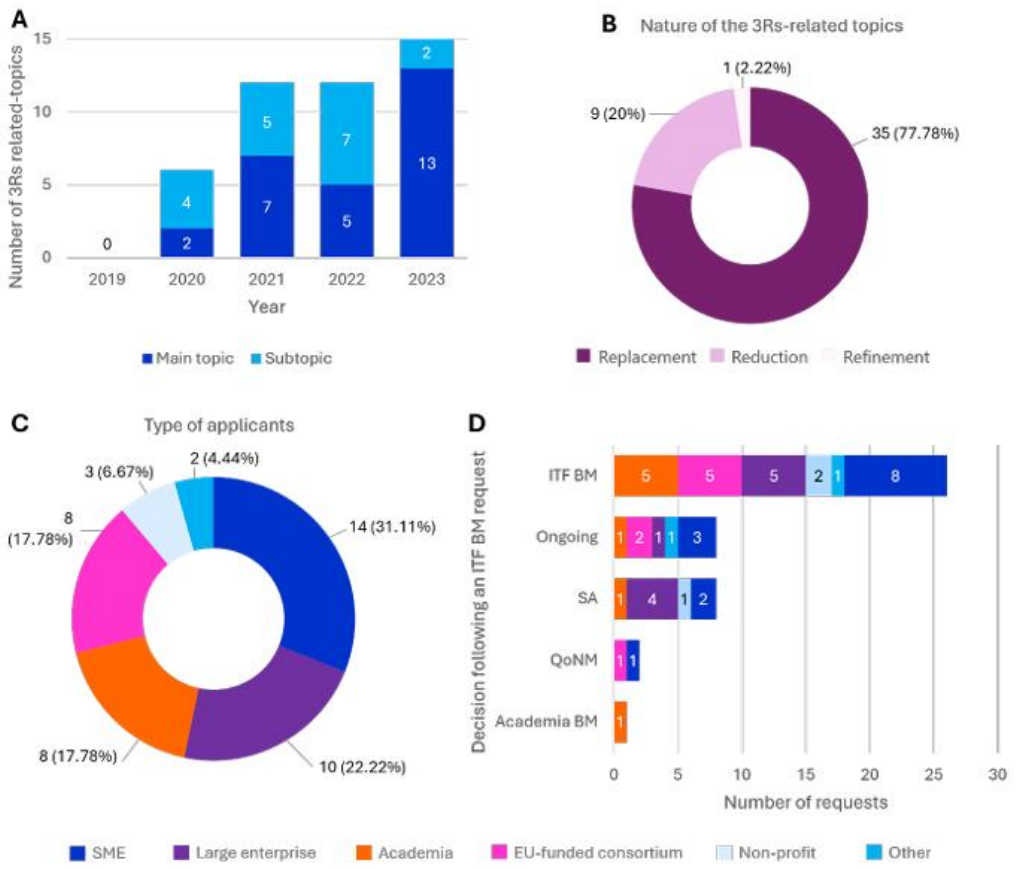


Figure 4. Number of 3Rs-related ITF briefing meetings requests received between 2019 and 2024 (A), main topics of discussion proposed (B), type of applicants (C) and advice provided by EMA ITF for the most appropriate regulatory interaction in response to the request (D).

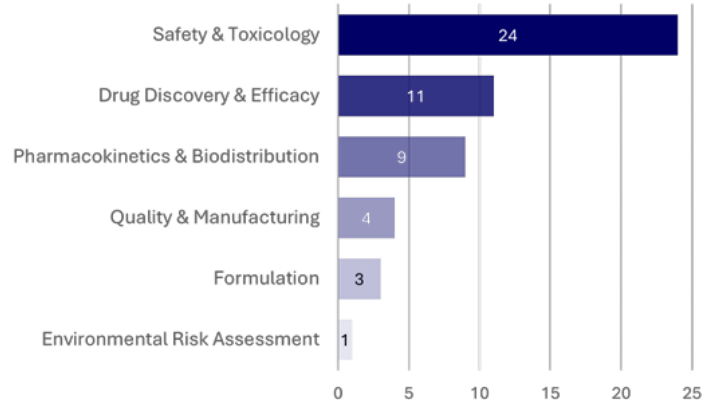


Figure 5. Medicine development topics addressed in 3Rs-related ITF briefing meeting requests.

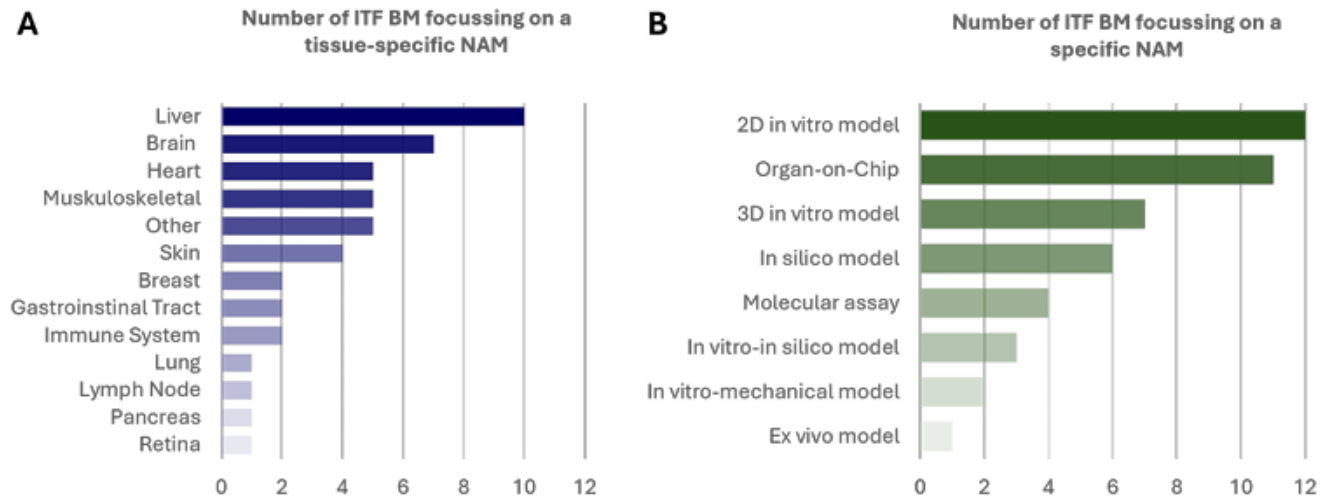


Figure 6. Number of ITF briefing meeting requests focussing on a specific tissue (A) or NAM (B).

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HMA
Heads of Medicines Agencies

New Approach Methodologies
EU-IN Horizon Scanning Report

February 2025
EMA/56850/2025

- 2019-2023:
- 45/339 ITF Briefing Meeting Requests on 3Rs

The problem with NAMs is....

Significant public investments in research and development

Large public interest (civil society) and political backing

Limited uptake in both routine R&D and regulatory testing

Little incentive for validation/qualification of NAMs:

- **Why take a risk with an unproven model?**
- **Why invest in something that may become a “public good”?**

New business model – where companies, innovators, academia and regulators can work together

Innovative Medicines Initiative: Public-Private Partnership

vac2vac

TIMELINE
01 March 2016 to
28 February 2022

COORDINATOR
European Vaccine Initiative

FUNDING
16 Mio Euro

23 Partners in 8 countries:
EFPIA/Industry: 9
Reference Labs/Public Research Orgs: 7
Academia: 3
Private non-profit organisations: 4

Observers ensure alignment within and outside of Europe

Rabbit Pyrogen Test (RPT)

- VAC2VAC objective: To replace RPT for human TBEV vaccine by the monocyte activation test (MAT)
- Pyrogens = fever inducing substances
- Groups of 3 rabbits used for initial testing (temperature rise <0.6 C)
- In 2015 (at the start of VAC2VAC), almost 50,000 rabbits were used for pyrogen testing in 14 Member States
- The monocyte-activation test (MAT) was introduced in the European Pharmacopoeia (Ph. Eur.) in 2009 as official *in vitro* alternative to RPT.
- MAT could replace RPT after product-specific validation.

What happened next?

- MAT validated according to ICH-Q2B on 3 ENCEPUR batches (Tick-Borne Encephalitis Virus vaccine) by academic partners (led by ISS, Italy);

- Method transferred to industry partner (GSK) for internal validation;
- GSK applied for approval to the German Regulator (Paul-Ehrlich Institute, PEI) at the end of 2019 (approval in May 2020). PEI was selected due to the original registration of the product.

RPT has been replaced with MAT in routine testing by GSK, later Bavarian Nordic

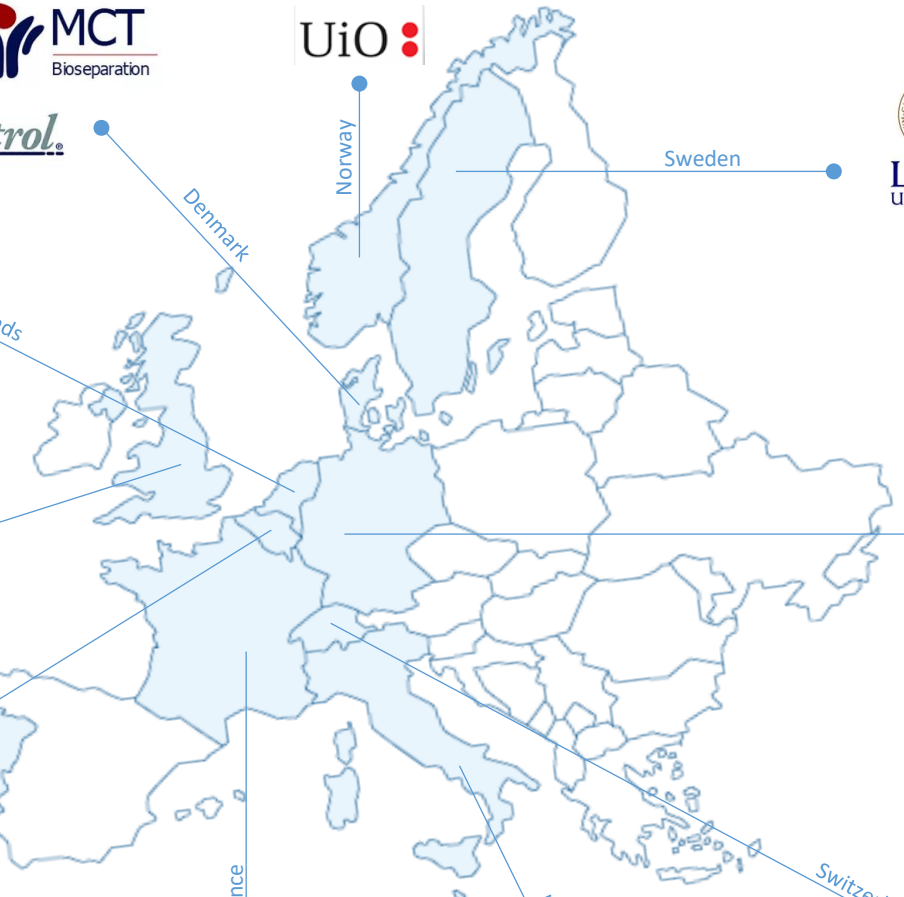
- March 2021: Request submitted (by the Italian delegation) to replace the rabbit pyrogen test by MAT in European Pharmacopoeia monograph 1375 (“tick-borne encephalitis vaccine”).
- June 2021: European Pharmacopoeia Commission decided to remove the rabbit pyrogen test from its texts by 2026 (affecting 60 Ph. Eur. texts)
- Removal from the European Pharmacopoeia became official on July 1, 2025, and the change must be implemented by January 1, 2026.
- **Between 2015 and 2020, Rabbit Pyrogen Testing decreased by 49% in Europe**

INNO4VAC

www.inno4vac.eu

FUNDING

€ 38.5 M
(€18.6M IMI, €19.9M EFPIA)



National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Utrecht University

Viroclinics DDL

ENPICOM
DECODING THE IMMUNE SYSTEM

umcg

CHDR
Centre for Human Drug Research

LUMC Leiden University Medical Center

Imperial College London

NIBSC

UCL

oxford vaccine group

University of Nottingham
Biodiscovery Institute

DTU

MCT
Bioseparation

2-control

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UiO

LUND UNIVERSITY

UNIVERSITY OF GOTHENBURG

STIFTUNG TIERÄRZTLICHE HOCHSCHULE HANNOVER

UNIVERSITÄTS KLINIKUM jena

European Vaccine Initiative

INSILICO

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1240

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VACCINES ASSOCIATION

VISMEDERI
ANALYSES FOR LIFE IMPROVEMENT

Takeda

EFPIA companies

Innovations to accelerate vaccine development and manufacture

Human in vitro mucosa models in Inno4Vac

- Development of next generation in vitro **3D models of gastrointestinal mucosa**, based on human induced pluripotent stem cells (Alexander Mosig, Jena University + Alfredo Pezzicoli, GSK)
- Next-generation **respiratory mucosal models** to evaluate vaccine-induced protective and detrimental immune responses for influenza and RSV (Puck van Kasteren, RIVM +Nathalie Mantel, Sanofi)
- Complex in **vitro 3D infection models of the urovaginal mucosa** to investigate protective effector immune mechanisms, focussing on Neisseria gonnorrhoeae and HSV-2 (Thomas Rudel, Wurtzburg University + Isabel Delany, GSK)
- **Roadmap, standardisation and guidelines** for 3D mucosa models and their use in vaccine development (Katie Huber, Paul-Ehrlich Institute, Germany)

Open Access Platform

Improve | De-risk | Accelerate | Coordinate

International dimension

- Medicines development occurs on a **global** scale – **Europe (or others) cannot work in isolation**

- Continued reductions in animal use & promotion of the 3Rs requires **global regulatory alignment** on:
  - Acceptance criteria for NAMs
  - Batch release requirements
  - Phasing out of obsolete tests
  - Regulatory position statement – ICMRA & ICH

- More involvement at earlier stage of LMIC – NGO´s like Humane World for Vaccines, IABS, European Vaccine Initiative can play important role

International medicines regulator's working group on 3Rs

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pmda 独立行政法人 医薬品医療機器総合機構 Pharmaceuticals and Medical Devices Agency

swissmedic

Santé Canada Health Canada

Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

FDA U.S. FOOD & DRUG ADMINISTRATION

Thank you!

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