The vision and initiatives from the European Commission to promote animal-free research

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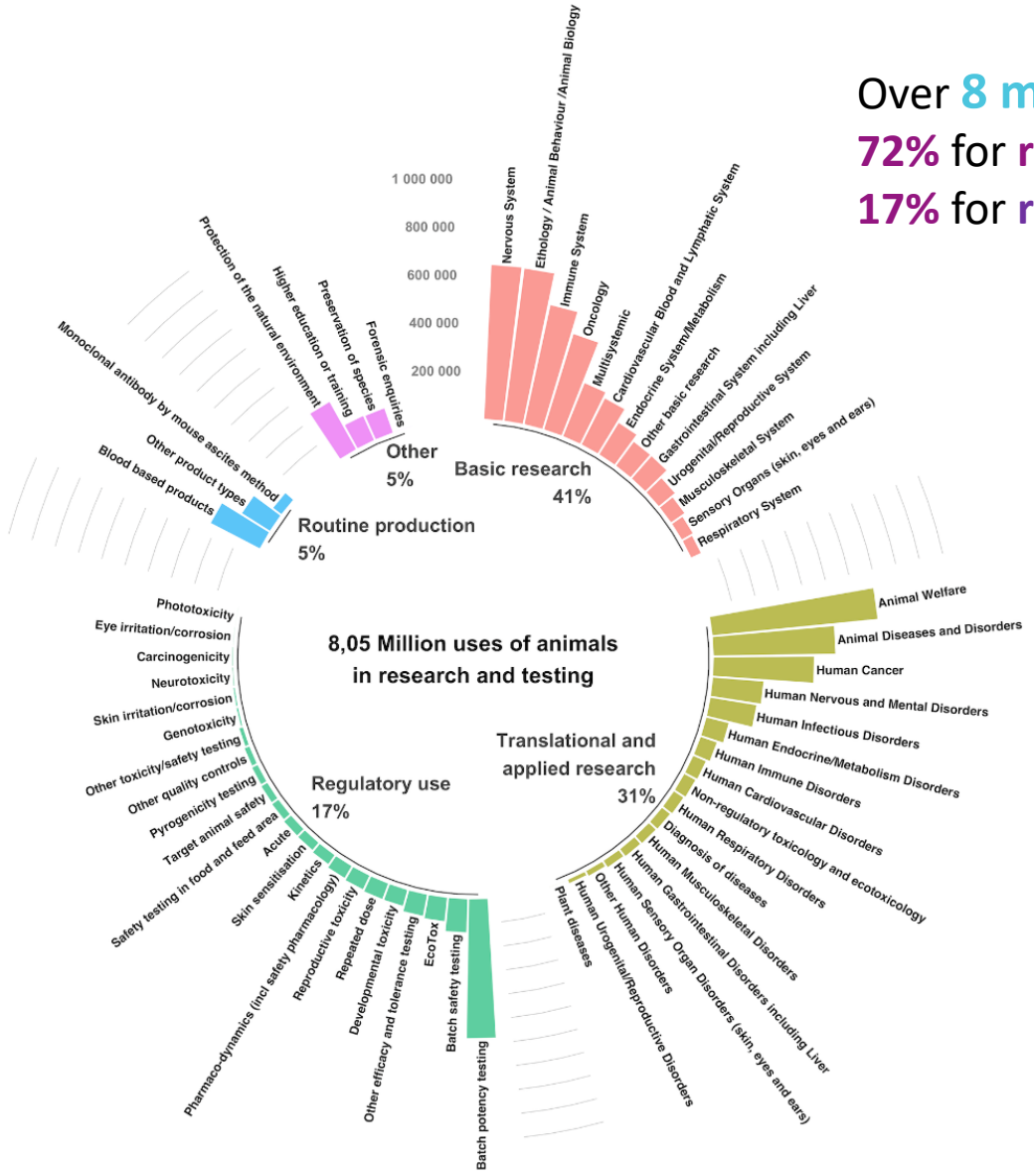
Research & Innovation DG
European Commission

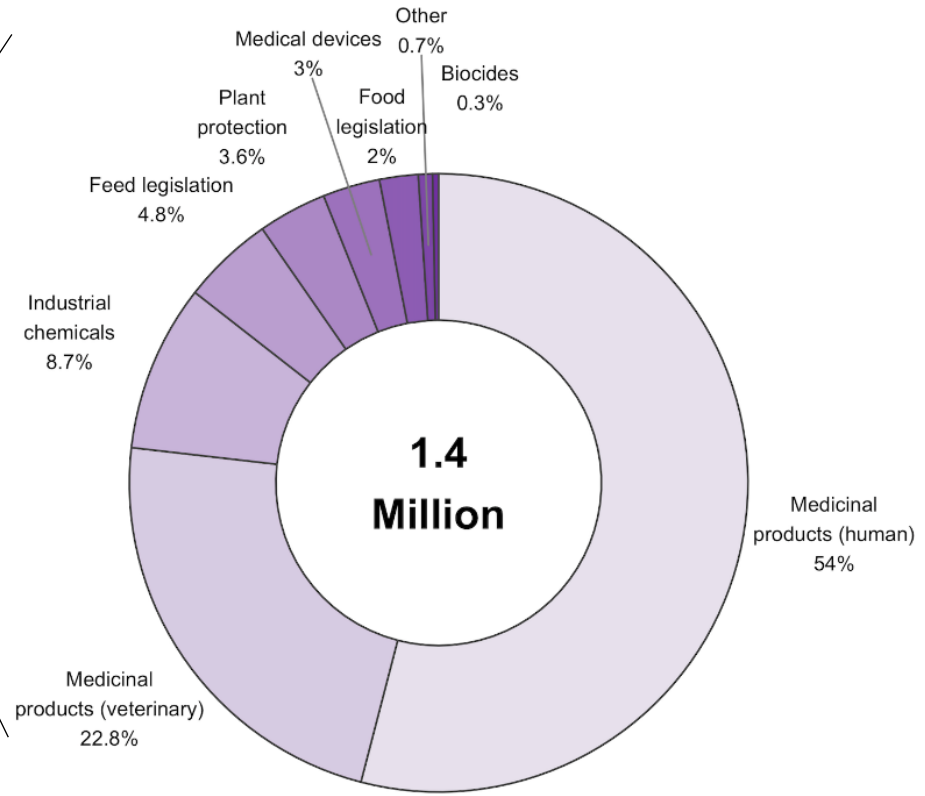
famhp, Antwerp, 31 January 2024

European Commission

Animals used for scientific purposes in 2020 (EU)

Over **8 million animals** used for scientific purposes
72% for **research**
17% for **regulatory purposes** - mostly **medicinal products (77%)**





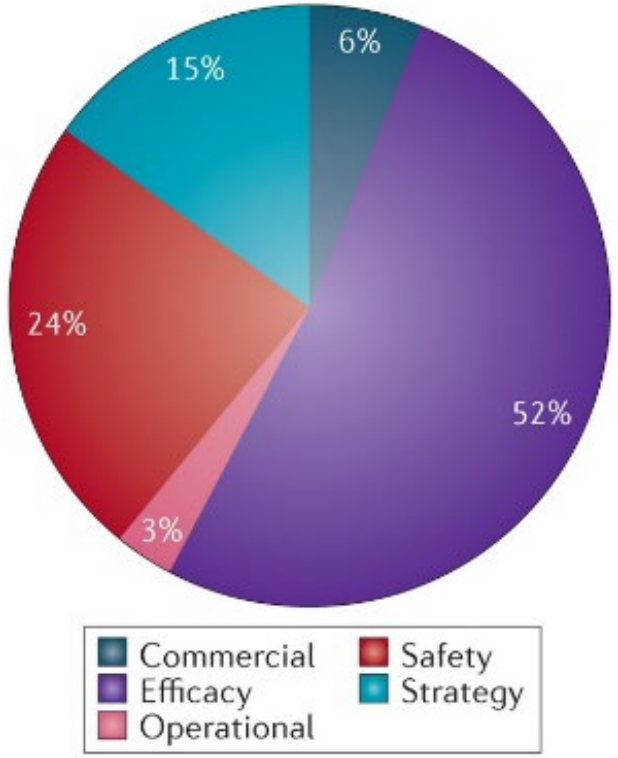
Regulatory uses by type of legislation

European Commission

Need of preclinical models which are better at predicting clinical outcomes

- It is estimated that **90% of drugs** fail clinical trials
- Probability of failure in **phase II/III is 40-70%**, mainly due to **efficacy** and **safety** reasons
- **Preclinical models** have limitations; improvements are necessary, non-animal alternative methodologies may be better at predicting clinical outcomes

Reasons for failure in Phase II/III (US data, 2013–2015)



European Commission

Graph from *Harrison et al. 2016 Nature Reviews Drug Discovery*

Alternatives to animal testing

Why are they important?

HUMAN-RELEVANT

- Improve **predictability and robustness** of studies for scientists and regulators

VERSATILE

- Answer **questions** that current methods cannot address

ETHICAL

- **Animal protection**: reduce/replace animals (3Rs)

SUSTAINABLE/AUTONOMOUS

- Independent of **shortages/issues** with animal supply

Increasing political and societal pressure to phase out animal testing

2010

Directive 2010/63
protection of animals for scientific purposes

2009-2013
ban on animal testing for cosmetics

2015

European Citizen Initiative (ECI)

STOP VIVISECTION

2018

EP resolution on **global ban** to end animal testing for cosmetics

2021

European Citizen Initiative (ECI)

Save Cruelty Free Cosmetics

2023

EP resolution to accelerate transition to innovation without animals in research, regulatory testing and education

Current actions by the EC to accelerate uptake of alternatives to animal testing

Promoting knowledge, experience and confidence in New Approach Methodologies (NAMs) is central

BRINGING STAKEHOLDERS TOGETHER

- Cross-sectorial collaboration
- Dialogue with regulatory bodies

epaa
The European Partnership for Alternative Approaches to Animal Testing

ROADMAPS ON NAMs FOR:

- Food (EFSA)
- Industrial chemicals (ECHA)
- In response to ECI for all chemicals (including pharma)

REVISION OF REACH

Package of NAMs in:

- Toxicokinetics
- Endocrine disruptors
- Bioaccumulation
- Acute toxicity

RESEARCH FUNDING

- ASPIS

Animal-Free Safety Assessment of Chemicals: Project Cluster for Implementation of Novel Strategies

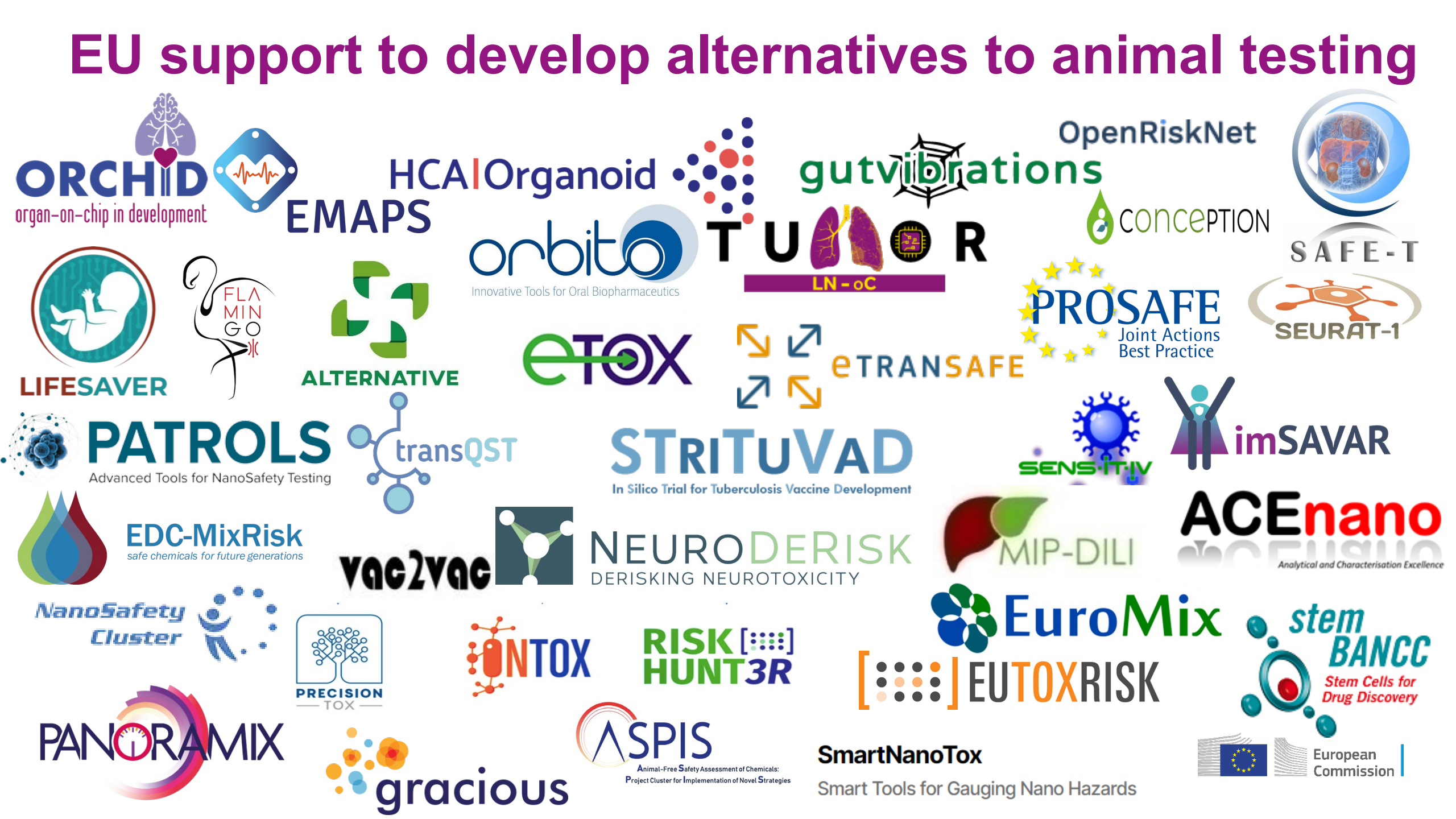
- PARC

Partnership for Assessment of Risks from Chemical

- Other research calls (IMI/IHI)

European Commission

EU support to develop alternatives to animal testing

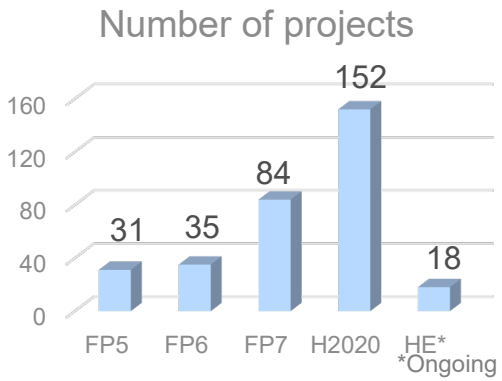


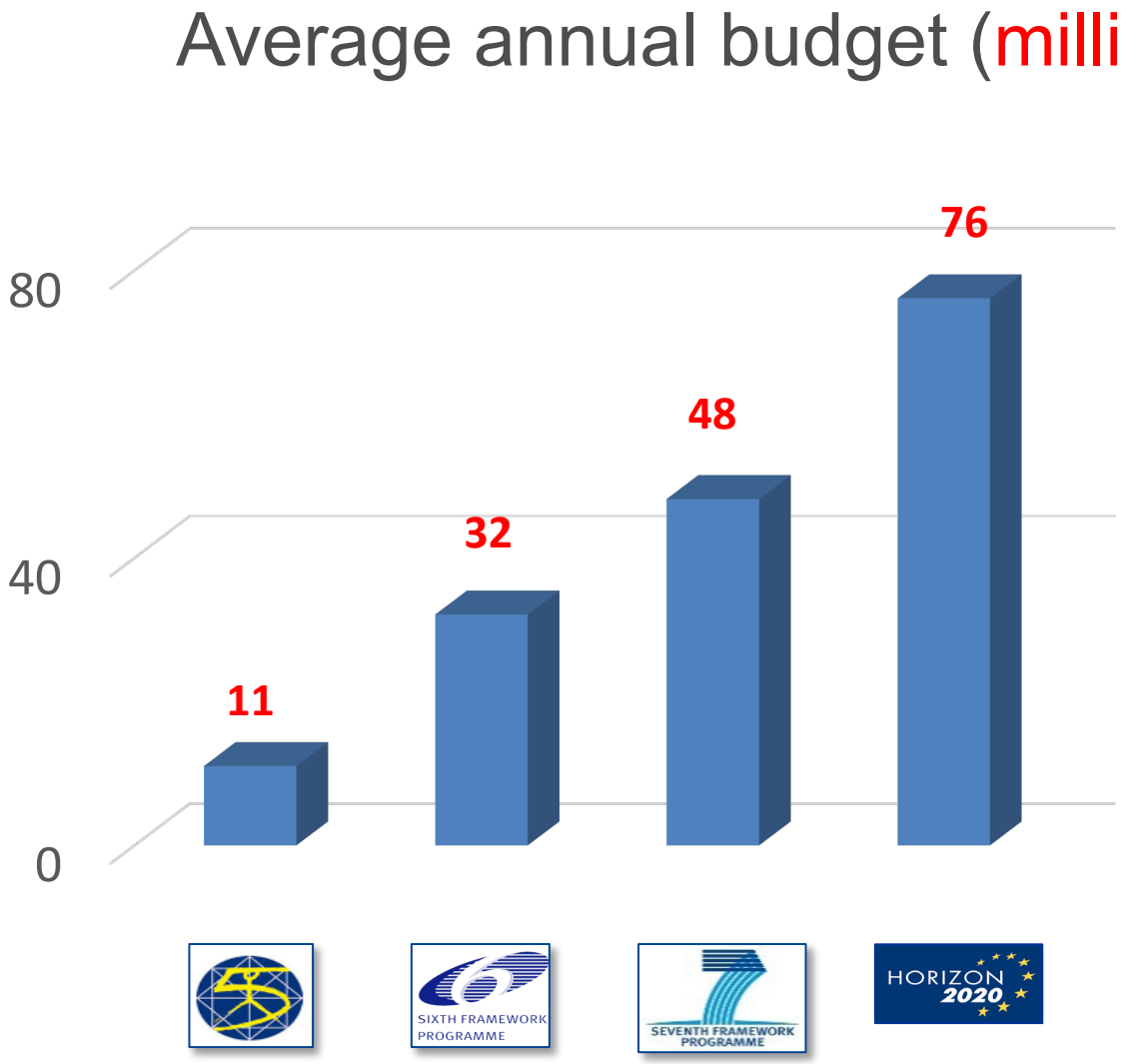
EU support to develop alternatives to animal testing

In the last two decades:

>300 projects

1 billion €





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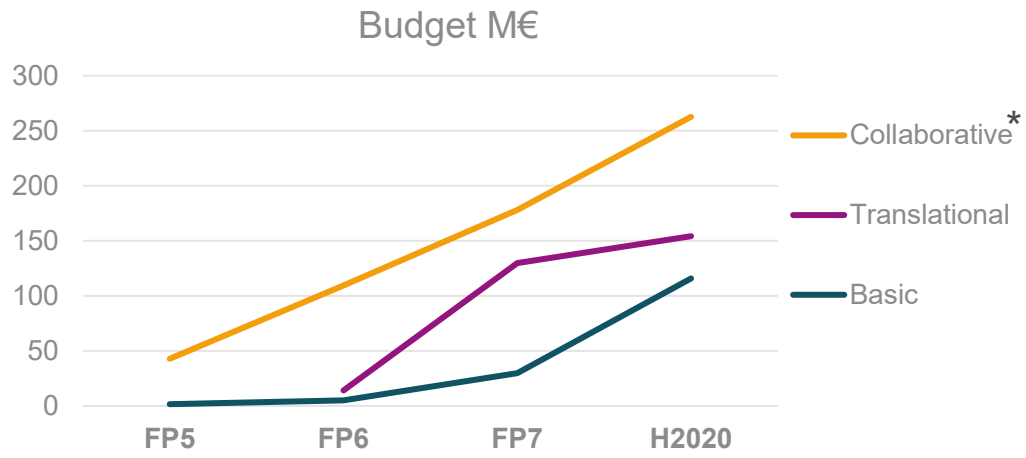
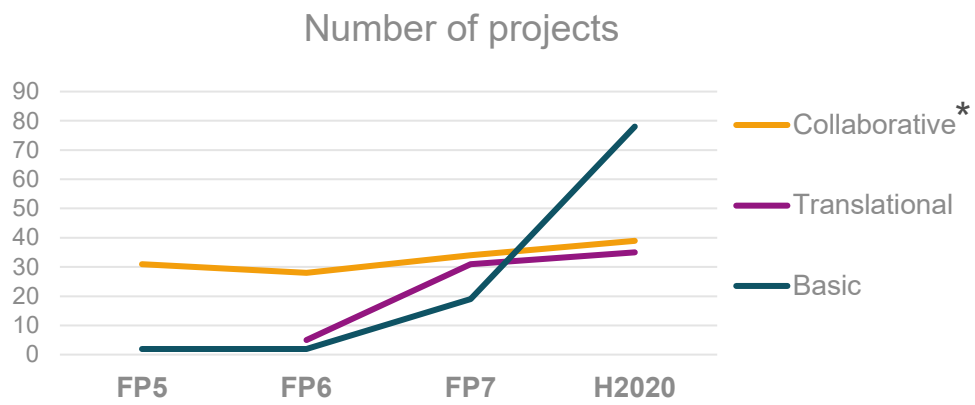
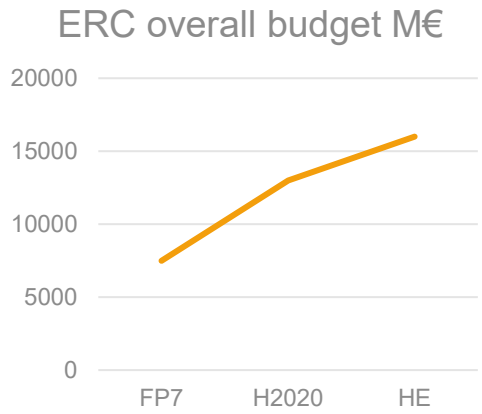
EU support to develop alternatives to animal testing

IMI1	IMI2
6 projects	5 projects
73,5M€	60,85M€

Types of grants







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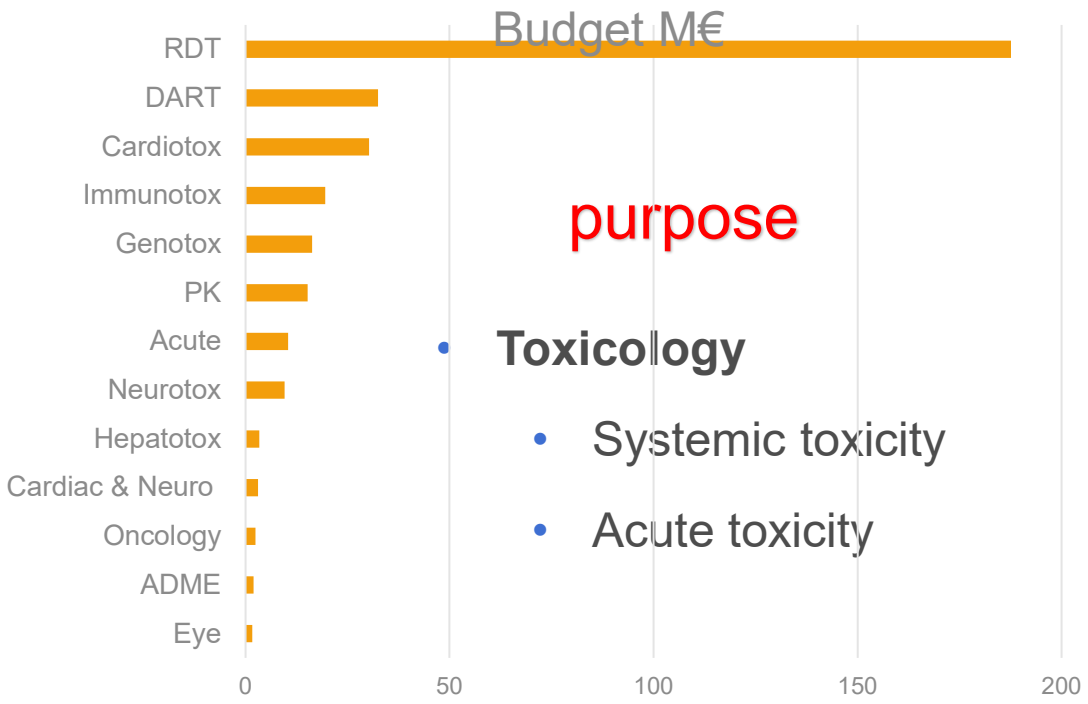
* Including IMI1 & IMI2

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**

products

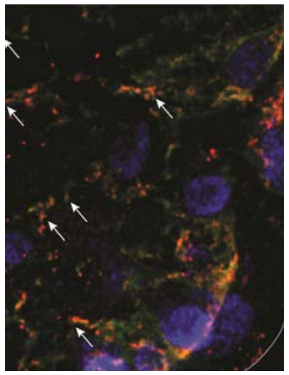
- **Chemicals**
- **Drugs**
- **Nanomaterials**
- **Vaccine**
- **Generic**

European Commission

EU projects on alternatives: immediate impact on COVID-19 research

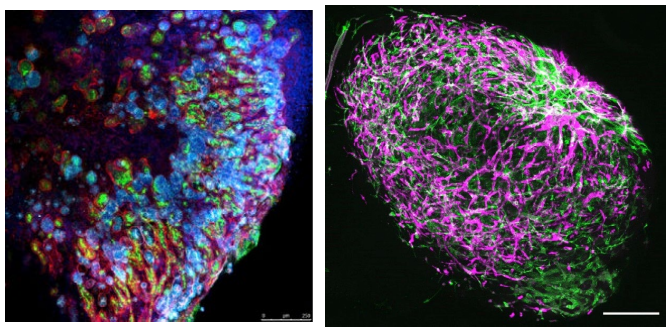
- **35% of projects on alternatives redirected activities towards COVID-19 research**
- **55% contributed through their tools to COVID-19 research**
  - Microfluidic devices
  - Air-liquid interface cultures
  - Organoids and spheroids (e.g., cardiac, lung)

liver



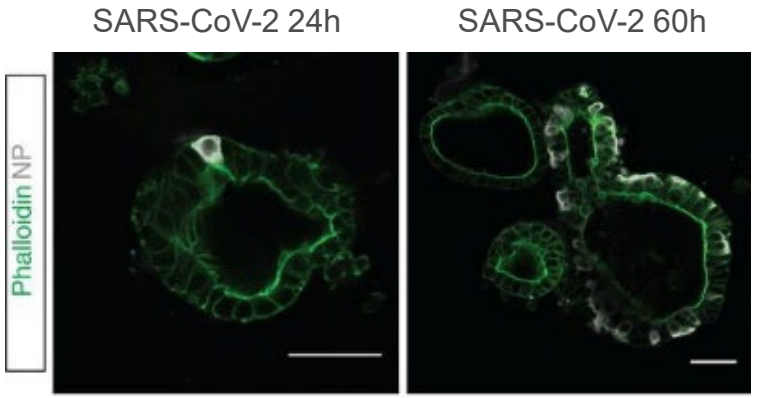
EMBO Mol Med 2020 12: e12697
H2020 ERC HEPASPHERE

kidney blood



Cell. 2020 May 181:905-913
H2020 ERC REGMANKID

intestinal



Science 2020 369: 50–54
H2020 FET Q-SORT
H2020 ERC Organoid

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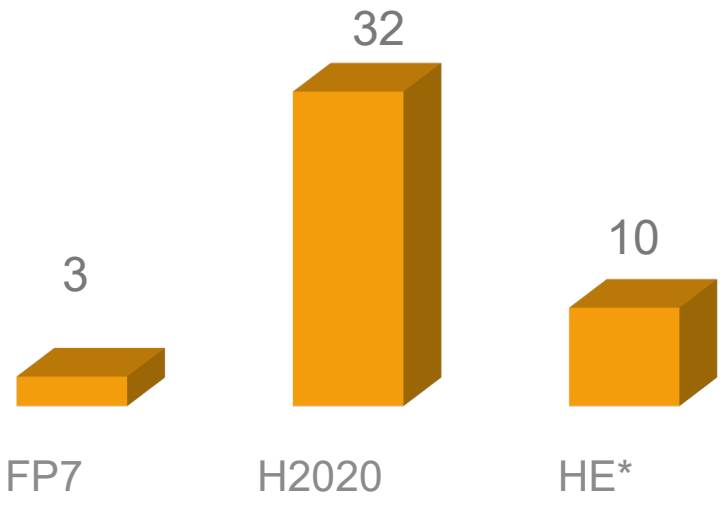
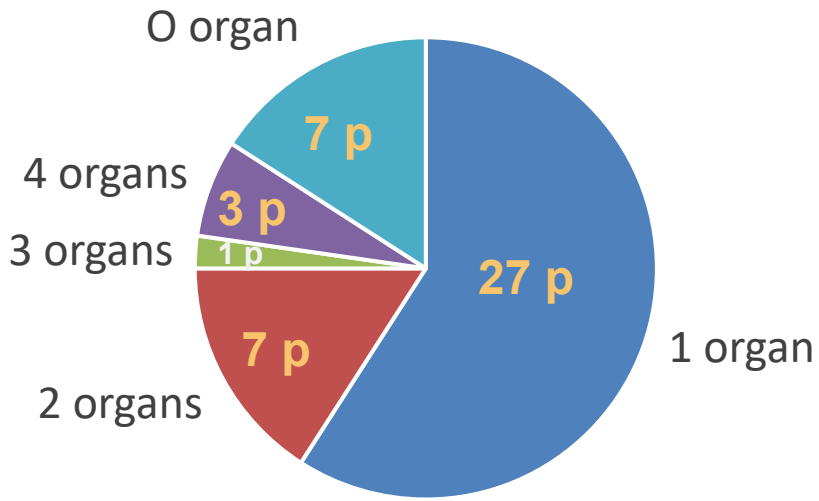
EU support to organs-on-chips (OoCs)

€ 120 million

Number of projects with OoCs



Number of linked organs



* Up to August 2023

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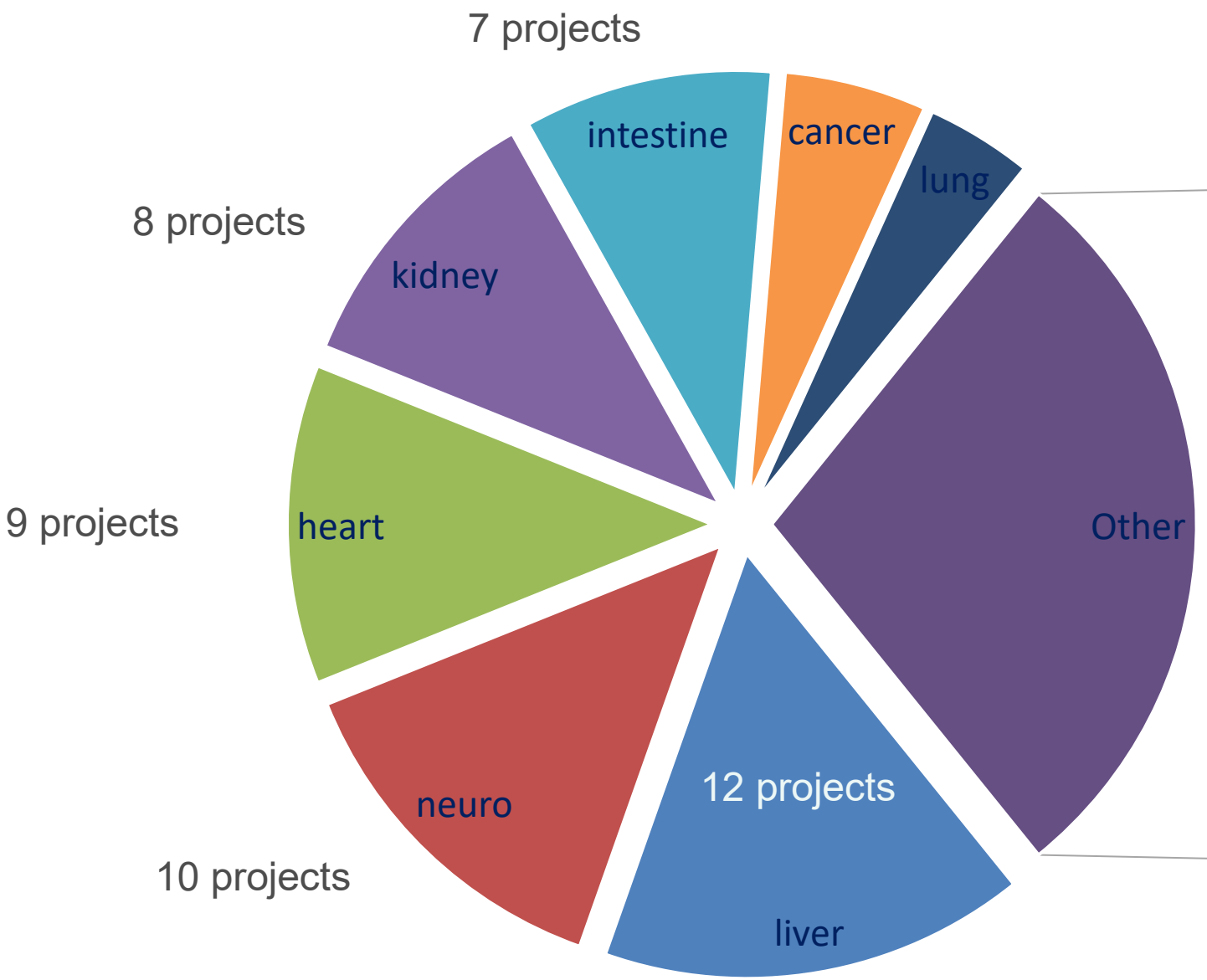
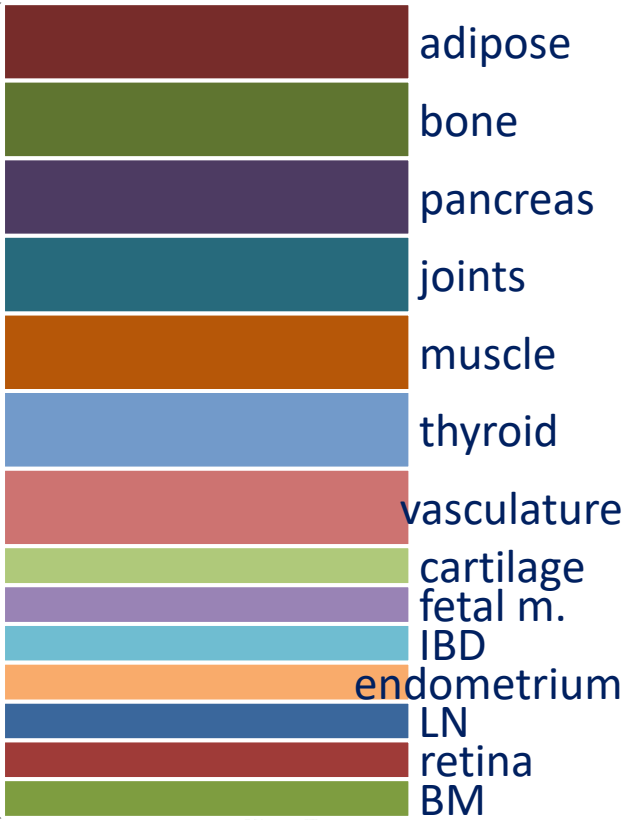
Main organs in OoC projects



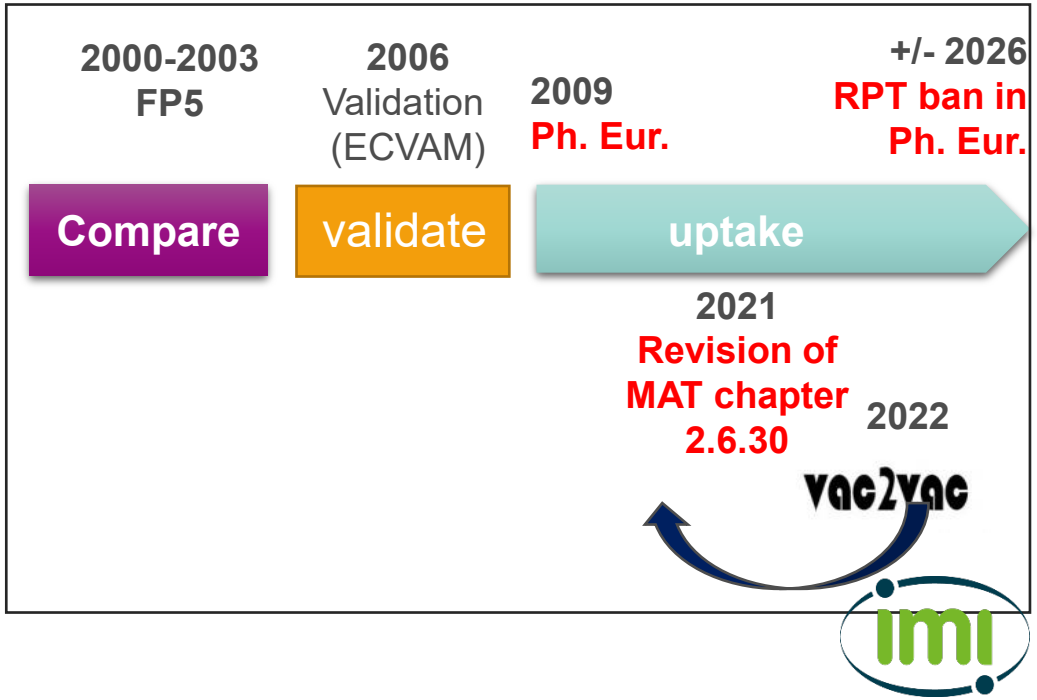


European Commission

HUMAN(E) PYROGEN TES success story

MAT: Monocyte Activation Test

- Trans-national comparison of the most promising *in vitro* models for replacing the rabbit pyrogenicity test (RPT)
- **5 in vitro pyrogen tests validated** for pyrogenicity mediated by Gram-negative endotoxins replacing rabbit pyrogen tests
- **MAT** Tests are based on **Monocyte Activation** (production of pro-inflammatory cytokines)
- MAT added to the **European Pharmacopoeia Ph. Eur. (**General chapter 2.6.30) as *in vitro* alternative to the RPT for detecting **both endotoxin and non-endotoxin pyrogens**
- MAT validated by **IMI2**VAC2VAC for pyrogenicity testing of TBEV vaccine, implemented by industry, authorized by competent regulatory authorities (AU, DE), and now accepted in EU



1,3 million EUR budget

2000-2003

10 partners

European Commission

SENS-IT-IV success story

GARDskin test

SIXTH FRAMEWORK PROGRAMME

11 Million €
Budget

2005 - 2011

26
Partners

FP6
11M€

SENS-IT-IV

2005-2011

Validation
(EURL ECVAM)
2017-2021

EU legislation
2023*

Development → **Market**

2014
Spin-off
(Lund University)

2022
OECD
Test Guideline

* Test Method Regulation

- *In vitro* assay for skin sensitization (topical dermatitis) based on expression of 200 biomarkers in human dendritic-like cells
- Outperforms the murine Local Lymph Node Assay (LLNA) test
- **Required many years** despite targeting a toxicological endpoint well understood
- **Impact**:
  - Accepted by regulators
  - Applications: chemicals, cosmetics, medicinal products and medical devices

Alternative methods for repeated dose toxicity (systemic toxicity)

Ambitious continuum of research in consecutive initiatives:

- **FP7 - SEURAT-1 (€50M)**

  Established the basis for use of New Approach Methodologies (NAMs)

- **H2020 - EUToxRisk (€30M)**

  Used NAMs for read-across (endpoint prediction between structurally/biologically similar compounds)

- **H2020 - ASPIS (€60M)**

  Extension to *ab initio* and exposure assessments

European Commission

Alternative methods for repeated dose toxicity (systemic toxicity)

Ambitious continuum of research in consecutive initiatives:

Increasing involvement of regulatory bodies earlier on

As advisory capacity in:
-SEURAT-1
-EuToxRisk
-ASPIS

As partners in:
-ASPIS

SEURAT-1

EUTOXRISK

ASPIS

EURL ECVAM (EU Reference Laboratory for alternatives to animal testing – part of the Commission's Joint Research Centre) is involved from beginning to the end in all projects.

Role of EURL ECVAM:

- Advise on **prioritization** of tests/endpoints
- **Validate** New Approach Methodologies (NAMs)
- Facilitate **uptake** by OECD

European Commission

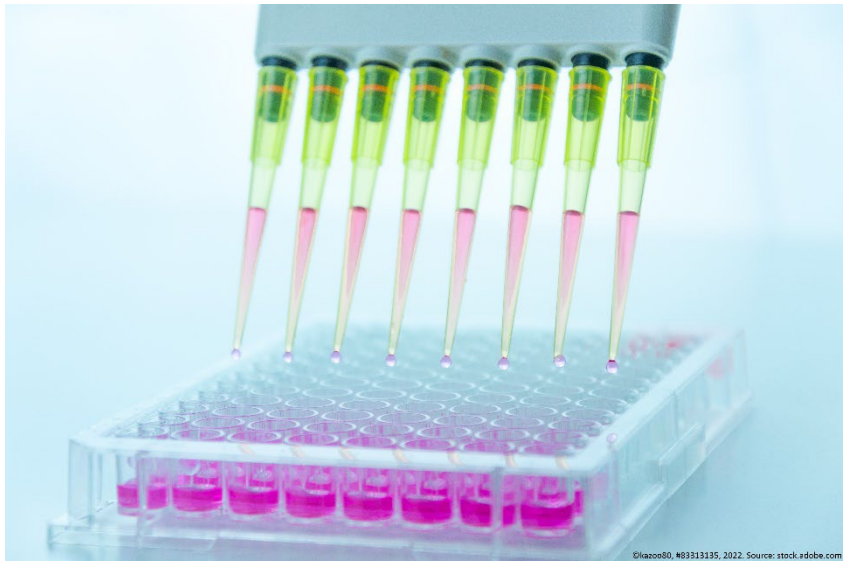
EU-ToxRisk: toxicity of the 21st century

Advisory documents on regulatory requirements for acceptance of NAM-assisted read across

- Co-designed with **regulators** from Member States and ECHA, EFSA, OECD
- Guidance applied in **case studies** co-created with industry and regulatory bodies
- Published in OECD website as part of the **Integrated Approaches to Testing and Assessment (IATA) case studies** project aimed at sharing the knowledge on new methodologies within a regulatory context

Joint development of neurotoxicity *in vitro* test battery

- Combination of **10 NAMs** using human neural cells
- Assess **changes** in:
  - Proliferation of neural progenitor cells (NPC)
  - Migration of neural crest cells, neurons and oligodendrocytes
  - Differentiation of NPC into neurons and oligodendrocytes
  - Neurite outgrowth of peripheral and central neurons
- **82% sensitivity**
- Currently under **OECD** evaluation
- **Applicability domains**: chemicals, cosmetics, medicinal products



Animal-free Safety assessment of chemicals: Project cluster for Implementation of novel Strategies

ASPIS objectives:

1. Facilitate **non-animal solutions** in various public (e.g. regulatory agencies) and private (e.g. industry) sectors
2. Translate results, methods and solutions from the scientific research community into **safety assessment practice**
3. Promote **regulatory uptake** and **commercial exploitation** of NAMs

ASPIS

PRECISION TOX

ONTOX

RISK HUNT3R

60M EUR budget

2021-2026

70 institutions, 3 projects, 16 EU countries + US + regulators as partners (RIVM in NL, BfR in DE) and other regulatory bodies in advisory capacity

European Commission

ASPA: ASPIS Safety Profiling Algorithm

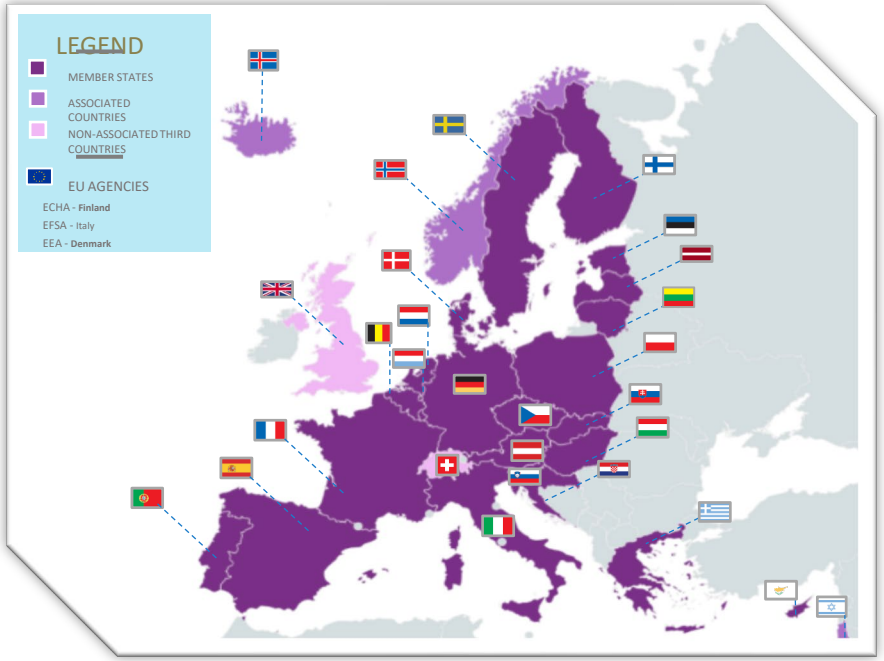
Defines a tiered approach

- on what tools/methods to use
- At which steps to obtain and evaluate data, incl. uncertainty assessment
- How to put data into a context of a hazard or risk assessment scenario
- Defines a decision logic with multiple entry and exit points, activating/deactivating specific modules, and prioritizing and filtering of information
- Modules include: toxicokinetic modelling and IVIVE, hazard identification, hazard characterization, exposure, risk assessment. Submodules under construction.
- Flexible (multiple questions and regulatory frameworks) and reproducible (same datasets used in the same block for a specific purpose should lead to the same conclusion and level of confidence

Partnership for Assessment of Risks from Chemicals

PARC Objectives:

- Establish a **Science to Policy dialogue** and interface to apply the long-term visions of European policies (notably the Chemical Strategy for Sustainability)
- Establish a **hub of excellence** enabling the transition to the Next Generation Risk Assessment
- Provide test guidelines to overcome barriers on the uptake of NAMs for regulatory purposes



>400M EUR budget (EC and MS)

2022-2029

>150 organizations, 28 countries + 3 EU agencies (EEA, EFSA, ECHA)

European Commission

UPCOMING CALLS

#HorizonEU

THE EU RESEARCH & INNOVATION PROGRAMME

2021 – 2027

Research and Innovation

The Innovative Health Initiative

Focus

- Cross-sectoral approaches to facilitate creation of new products and services to prevent, intercept, diagnose, treat and manage diseases and foster recovery more efficiently.

Goal

- Lay foundations for development of safer and more effective health care products or solutions that respond to unmet public health needs and that can be implemented into healthcare systems.

Total budget: 2.4 billion EUR over 7 years

half provided by the EU, half provided by member industry associations and contributing partners

Co-funded by the European Union

European Commission

Minipigs: a path to reduce and replace non-human primates in non-clinical safety assessment

HORIZON-JU-IHI-2023-04-02-two-stage

Budget: 8,5 million EUR (1 project)
Opening: 27 Jul 2023 / Deadlines:
8 Nov 2023 (first stage)
23 Apr 2024 (2nd stage)

innovative health initiative

Aims:

- Characterize minipig for R&D of new therapeutics and medical technologies
- Translatability of minipigs in human risk assessment following treatment with biologicals and new therapeutic modalities
- Multi-omics and imaging
- Humanized genetically modified pig models including the micro-pig
- Digital solutions for preclinical toxicity studies
- Immuno-safety assessments

Accelerate implementation of NAMs for development, testing & production of health technologies

HORIZON-JU-IHI-2023-05

Budget: 30 million EUR (12-15 million EUR /project)
Opening: 27 Jul 2023 / Deadline: 16 Jan 2024

innovative health initiative

Aims:

- Develop (or use) **non-animal tools** and strategies to improve assessment (and animal to human translation), or production processes of health technologies
- Evaluation of performance, validation, and added value
- Robustness, reliability, and applicability in industrial R&D and for regulatory decision making (engage with regulators in a timely manner)
- Gather and produce high quality sustainable datasets
- Collaboration platform between stakeholders to foster uptake or implementation in R&D and health technology development and manufacturing

Innovative non-animal human-based tools and strategies for biomedical research

HORIZON-HLTH-2024-TOOL-05-06

Budget: 25 million EUR (4-8 million EUR /project)
Opening: 30 Mar 2023 / Deadlines: 19 Sep 2023 (1st Stage)
11 Apr 2024 (2nd Stage)

Aims:

- Develop (or use) **non-animal tools** and strategies for biomedical research where animal models are currently used but of limited translational value
- For **a better understanding** of the pathogenesis of disorders leading to improved disease prediction, prevention and treatment
  - -omics and other HT procedures, human-derived cell-based material, organoids, micro-physiological systems, and *in-silico* model
- Harm and **cost-benefit** assessment & ease of **production**
- Dissemination, knowledge sharing, translation into **health policies**
- Model **qualification** and **standardization**

Gaining experience and confidence in NAMs for regulatory safety and efficacy testing

HORIZON-HLTH-2024-IND-06-09

Budget: 2 million Euro
Opening: 26 Oct 2023 / Deadline: 11 Apr 2024

Aims:

- **Bring together** NAM developers and end-users with regulators to inform on NAM solutions available and identify gaps

- Build a **framework** on how these NAMs could be most effectively used in the different decision-making contexts

  - Technical and regulatory readiness criteria
  - Technology transfer and market access
  - Standardization
  - Training (e.g. CROs, data integration and interpretation etc)
  - Legal obstacles

Research infrastructure concept development

HORIZON-INFRA-2024-DEV-01-01

Budget: 12 million EUR (1-3 million EUR /project)
Opening: 6 Dec 2023 / Deadline: 12 Mar 2024

Aims:

- Support development of new concepts for next generation of RIs of European interest (that none or few countries might individually be able to implement)
- Major upgrades of existing RIs
- Tackle all key questions on technical and conceptual feasibility of an effective RI service offer at EU level
- Identify/cover: technologies and architecture; user communities; governance options and strategy for institutions/stakeholders commitment and engagement; initial financial plans (implementation and operation), preliminary ideas for long-term sustainability; plans for data curation and preservation (FAIR principles)

ECI Objectives

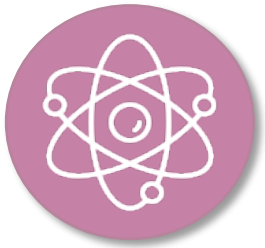
Save Cruelty Free Cosmetics

1. Protect and strenghten the cosmetics animal testing ban

initiate legislative change to achieve consumer, worker, and environmental protection for all cosmetics ingredients without testing on animals for any purpose at any time. **(GROW)**

2. Transform the EU chemicals legislation

ensure human health and the environment are protected by managing chemicals without the addition of new animal testing requirements.
(GROW and ENV)



3. Modernise science in the EU

commit to a legislative proposal plotting a roadmap to phase-out all animal testing in the EU before the end of the current legislative term.
(RTD)

Response of the Commission* to Objective 3

Action 1

Enhance coordination with Member States through a European Research Area (ERA) policy action

Action 2

Continued EU funding for alternative methods and increasing their visibility in strategic planning

Action 3

Exploratory workshop(s) to define future priority areas

Action 4

Education and training to sustain academy of young scientists in alternative testing
(H2020 APSIS cluster)

* In COMMUNICATION FROM THE COMMISSION of 25 July 2023

New ERA policy action* on Non-animal approaches (NAMs) in biomedical research and testing of pharmaceuticals

1. RESEARCH & EDUCATION

2. REGULATORY TESTING

*co-drafted with NL, SE, DE, BE and EU-LIFE

ERA Objectives

Create a forum with relevant ministries, regulatory agencies, research funders, academia, pharma and MedTech industry, CROs, to align national and regional policies for speeding up the development, validation, acceptance, and implementation of NAMs

WG1: Development of NAMs and common EU infrastructures

WG2: Validation, acceptance and implementation of NAMs

WG3: Education and training

WG4: Openness & awareness

WG1: Development of NAMs and common EU infrastructures

- Actions:
  Identification of key areas where new NAMs are most needed and expected to have the highest impact, for instance in certain disease or biological areas, or specific safety and efficacy assessment endpoints for pharmaceuticals.

  Priorities established for governments and industry to further coordinate development of NAMs and related infrastructures (also sustainability and access), taking into consideration the complementarity of scientific strengths and available expertise in the different MS and regions.

- Deliverables:
  NAM development and infrastructure **agenda** identifying the areas where NAMs are most needed and expected to have the highest impact.

  MS identify actions for possible joint support.

WG2: Validation, acceptance and implementation of NAMs

- Actions:
  Identification of the minimum criteria that NAMs need to meet to enable their acceptance and implementation in the contexts of basic and applied biomedical research, and for the regulatory assessment of pharmaceuticals.

  Priorities for the qualification and validation of NAMs in the two different contexts of use.

- Deliverables:
  NAM **implementation strategy**, which identifies criteria for the validation, qualification and acceptance of NAMs.

  MS decide to jointly support the validation of a certain number of NAMs earmarked for acceptance and implementation in regulatory testing of pharmaceuticals.

WG3: Education and training

- Actions:
  Relevant **education and training programmes** on NAMs in EU and beyond for students, researchers, and regulators are mapped, and their quality and outreach assessed.

  Suggestions to MS for jointly developing, in close collaboration with education directors at knowledge institutes, NAMs education and training modules.

- Deliverables:
  NAM **education and training plan**, identifying the various opportunities to better inform researchers and regulators on NAMs.

  MS engage to develop **common programmes** based on best practices identified in the most advanced EU or non-EU countries.

WG4: Openness & awareness

- Actions:

  Develop **common policies** to improve openness of research, publishing available NAM protocols and (positive as well as negative) results from animal experiments.

  Recommendations on how to share best practices to make sure **ethical and funding committees**, **reviewers**, and **regulators** have a similar level of awareness of NAMs.

  Improve the confidence of regulators in NAMs.

  Identification of opportunities to raise awareness of NAMs in **civil society** and **patients**.

- Deliverables:

  NAM openness and awareness programme

  Guidance to **raise** awareness of NAMs based on **best practices in the MS**.

  Plan to increase **confidence** of regulators in NAMs and involve civil society and patients.

Other responses to ECI's Objective 3

Action 2. Continued EU funding and increasing visibility in strategic planning

- **Inclusion of alternatives in Horizon Europe strategic planning 2025-2027**
- **3 currently "open" calls on alternatives (€57 million)**
- **Possible future calls in HE 2025-2027**

Action 3. Exploratory workshop to determine future priority areas of research

- **Possibly organized by mid-2025**
- **Possibly embedded in the 2 workshops 2023/2024 on phasing out animal testing for chemical safety assessments**

Action 4. Education and training – ASPIS academy of young scientists on NAMs

- **Discussion on sustainable support**
- **Discussion on integrating animal scientists to avoid silos**

Thank you!

HorizonEU

http://ec.europa.eu/horizon-europe