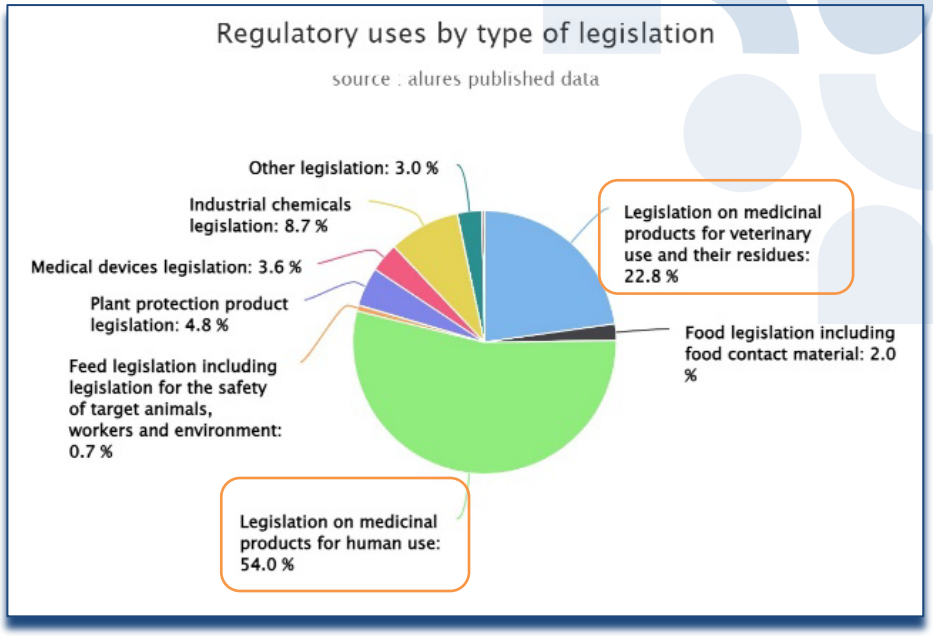
Advancing the 3Rs for Regulatory Testing of Medicines

Sonja Beken

Drivers for 3Rs in regulatory testing of medicines

Animal experimentation in Europe – regulatory use

7,9 million animals in 28 Member States
(EU-27 & Norway - 2020)
ALURES Statistical EU Database on animal use



Human Medicinal Products

Regulatory uses: Toxicity	Number of uses	Percentage
Pharmaco-dynamics (incl safety pharmacology)	54886	28.62%
Kinetics	42320	22.07%
Repeated dose toxicity	48406	25.24%
Acute and sub-acute	8494	4.43%
Skin irritation/corrosion	517	0.27%
Ecotoxicity	5869	3.06%
Skin sensitisation	4015	2.09%
Other toxicity/safety testing	1247	0.65%
Developmental toxicity	15319	7.99%
Eye irritation/corrosion	141	0.07%
Safety testing in food and feed area	1	0.00%
Genotoxicity	1850	0.96%
Reproductive toxicity	6460	3.37%
Phototoxicity	74	0.04%
Carcinogenicity	1008	0.53%
Neurotoxicity	22	0.01%
Target animal safety	1146	0.60%
Total	**191775**	**100,00%**

Regulatory uses: Quality control	Number of uses	Percentage
Batch safety testing	68571	13.21%
Batch potency testing	414764	79.88%
Other quality controls	14376	2.77%
Pyrogenicity testing	21545	4.15%
Total	**519256**	**100,00%**

Veterinary Medicinal Products

Regulatory uses: Toxicity	Number of uses	Percentage
Acute and sub-acute	17169	34.62%
Kinetics	938	1.89%
Target animal safety	24115	48.63%
Pharmaco-dynamics (incl safety pharmacology)	985	1.99%
Other toxicity/safety testing	4413	8.90%
Safety testing in food and feed area	767	1.55%
Repeated dose toxicity	204	0.41%
Skin sensitisation	574	1.16%
Ecotoxicity	246	0.50%
Skin irritation/corrosion	9	0.02%
Developmental toxicity	145	0.29%
Genotoxicity	27	0.05%
Total	**49592**	**100,00%**

Regulatory uses: Quality control	Number of uses	Percentage
Batch safety testing	68910	29.04%
Batch potency testing	162770	68.59%
Other quality controls	5187	2.19%
Pyrogenicity testing	435	0.18%
Total	**237302**	**100,00%**

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Directive 2010/63/EU of the EP and of the Council

of 22 September 2010 on the protection of animals used for scientific purposes

Article 4 clearly states that:

Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure.

Member States shall ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project.

Member States shall ensure refinement of breeding, accommodation and care, and of methods used in procedures, eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals.

Article 13 states that:

1. *Without prejudice to national legislation prohibiting certain types of methods, Member States shall ensure that a procedure is not carried out if another method or testing strategy for obtaining the result sought, not entailing the use of a live animal, is recognised under the legislation of the Union.*
2. *In choosing between procedures, those which to the greatest extent meet the following requirements shall be selected:*
   - *(a) use the minimum number of animals;*
   - *(b) involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm;*
   - *(c) cause the least pain, suffering, distress or lasting harm; and are most likely to provide satisfactory results.*

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European Parliament
2019-2024

TEXTS ADOPTED

P9_TA(2021)0387

Plans and actions to accelerate a transition to innovation without the use of animals in research, regulatory testing and education

European Parliament resolution of 16 September 2021 on plans and actions to accelerate the transition to innovation without the use of animals in research, regulatory testing and education (2021/2784(RSP))

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European Parliament
2019-2024

TEXTS ADOPTED

P9_TA(2021)0387

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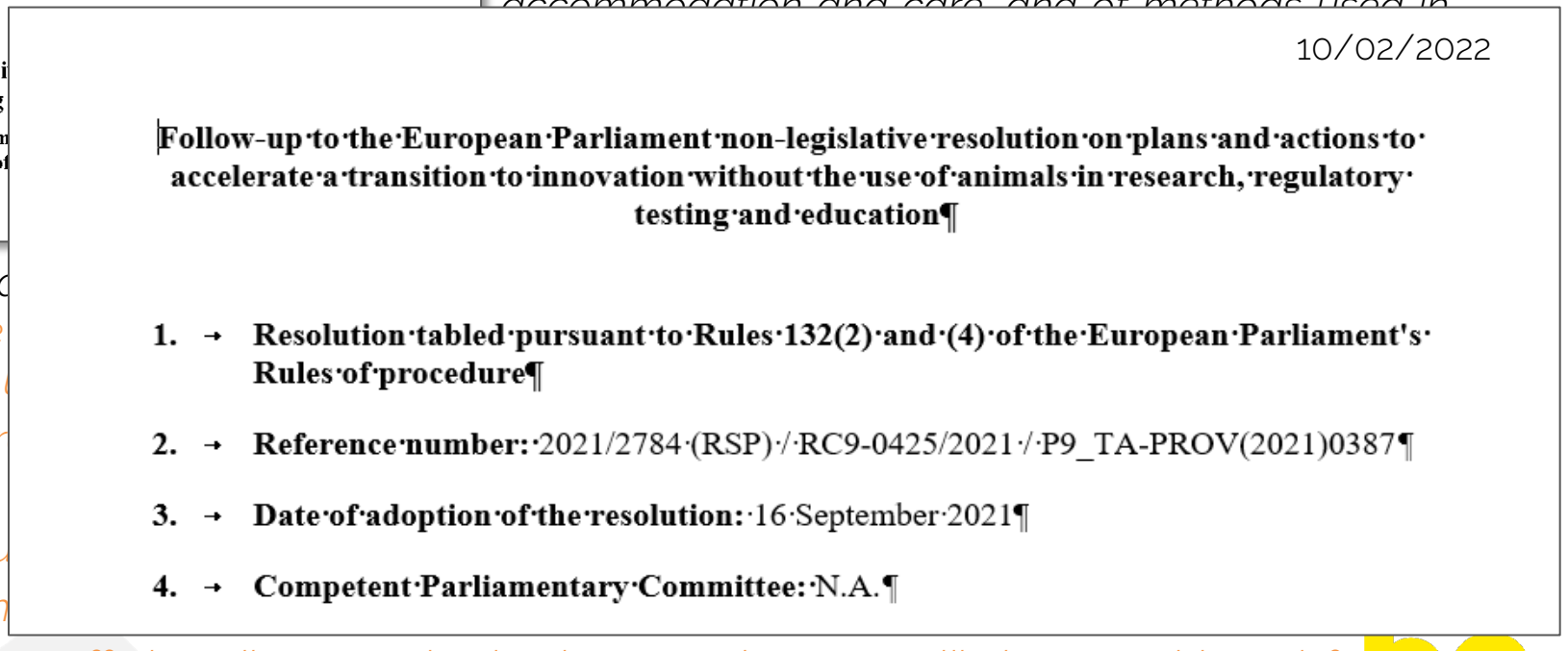

10/02/2022

Follow-up to the European Parliament non-legislative resolution on plans and actions to accelerate a transition to innovation without the use of animals in research, regulatory testing and education

1. → **Resolution tabled pursuant to Rules 132(2) and (4) of the European Parliament's Rules of procedure**
2. → **Reference number:** 2021/2784 (RSP) / RC9-0425/2021 / P9_TA-PROV(2021)0387
3. → **Date of adoption of the resolution:** 16 September 2021
4. → **Competent Parliamentary Committee:** N.A.

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Rules of procedure

Data and knowledge sharing: PARERE and other mechanisms

10/02/2022

Increased efficiency of assessing substances by grouping

One substance – One assessment, see 'ONE – Health, Environment, Society - Conference', June 2022 Brussels

3Rs in R&D of medicines EMA and 3Rs

ALURES statistical database and open-access database on non-technical summaries of authorised projects

IMI and H2020/Horizon Europe and European Research Council

EURL-ECVAM reviews on NAMs in biomedical research

Training programmes on 3Rs

EPAA as means for collaboration

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European Citizen's Initiative:

Save cruelty-free cosmetics – Commit to a Europe without animal testing


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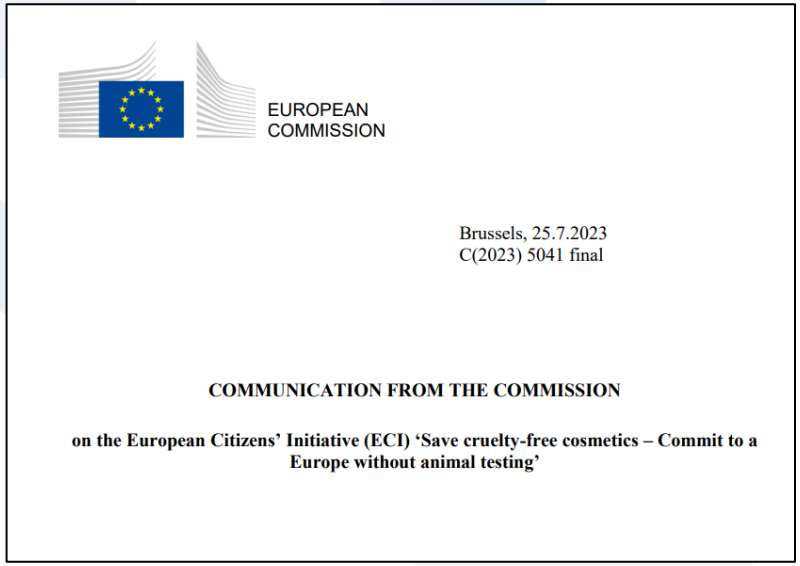
PETI / Events / European Citizens' Initiatives / ECI-Hearing 'Save cruelty-free cosmetics – Commit to a Europe without animal testing'

25-05-2023 09:00
ECI-Hearing 'Save cruelty-free cosmetics – Commit to a Europe without animal testing'

PETI ENVI AGRI

Brussels, Room: JAN - 2Q2

The hearing will be divided into three parts, corresponding the Initiative's three objectives:
1. Protect and strengthen the cosmetics animal testing ban.
2. Transform EU chemicals regulation.
3. Modernise science in the EU.


EUROPEAN
COMMISSION

Brussels, 25.7.2023
C(2023) 5041 final

COMMUNICATION FROM THE COMMISSION

on the European Citizens' Initiative (ECI) 'Save cruelty-free cosmetics – Commit to a Europe without animal testing'

EC roadmap to reduce animal testing as pre-requisite to transition towards animal free regulatory system

- Identification of short-longer term milestones and actions
- Analysis and description of necessary steps to replace animal testing in legislation that currently requires animal testing
- Outline of a path to expand and accelerate development, validation and implementation of NAMs
- Outline of the means to facilitate regulatory uptake of NAMs

Multistakeholder workshops to discuss roadmap (4Q 2023) and present & discuss progress (3-4Q 2024)

Close collaboration with agencies (e.g. EMA), MSs and relevant stakeholders

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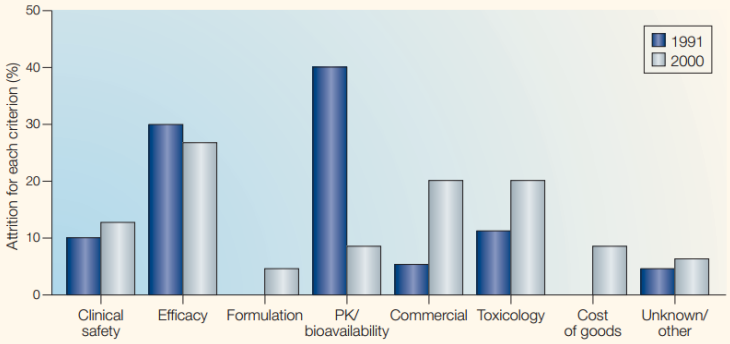
Drivers for 3Rs in regulatory testing of medicines

Reducing drug attrition through better prediction

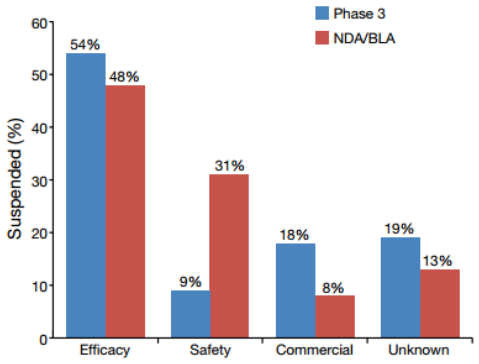
Kola and Landis 2004

Nature Reviews Drug Discovery 3, 711-715



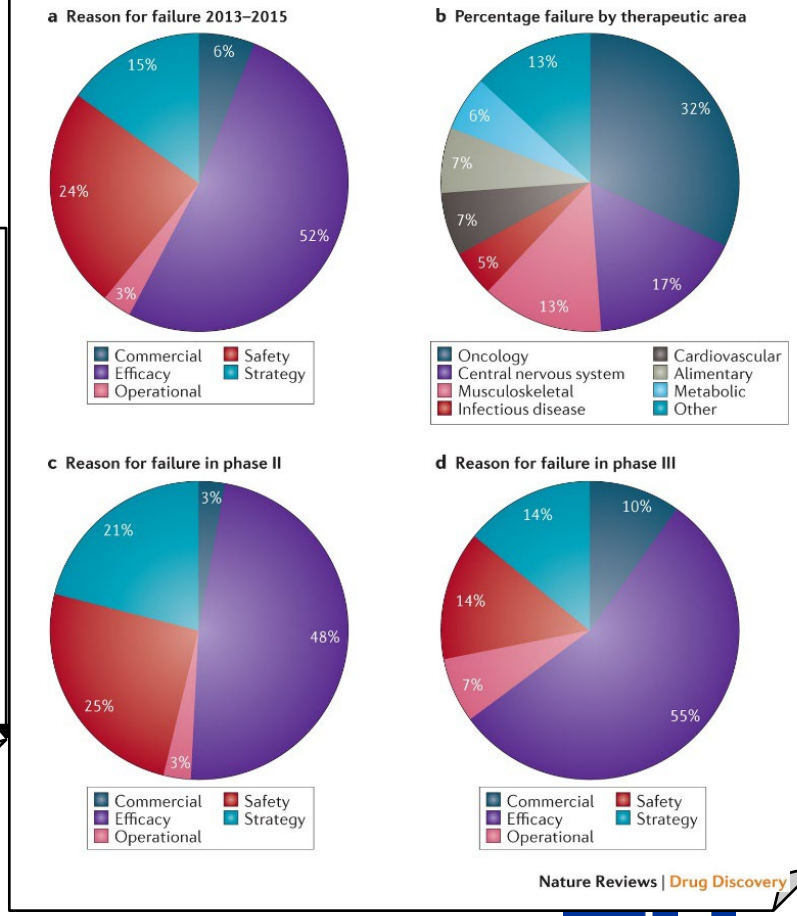
Hay et al, 2014,

Nature Biotechnology 21; 40-51



Harrison, 2016,

Nature Reviews Drug Discovery 15; 817-818



Hornberg et al 2014

Drug Discovery Today 19; 1131-1136

Most noted safety reasons for withdrawal of marketed drugs:

- *Liver toxicity*
- *Cardiovascular toxicity*
- *CNS effects*

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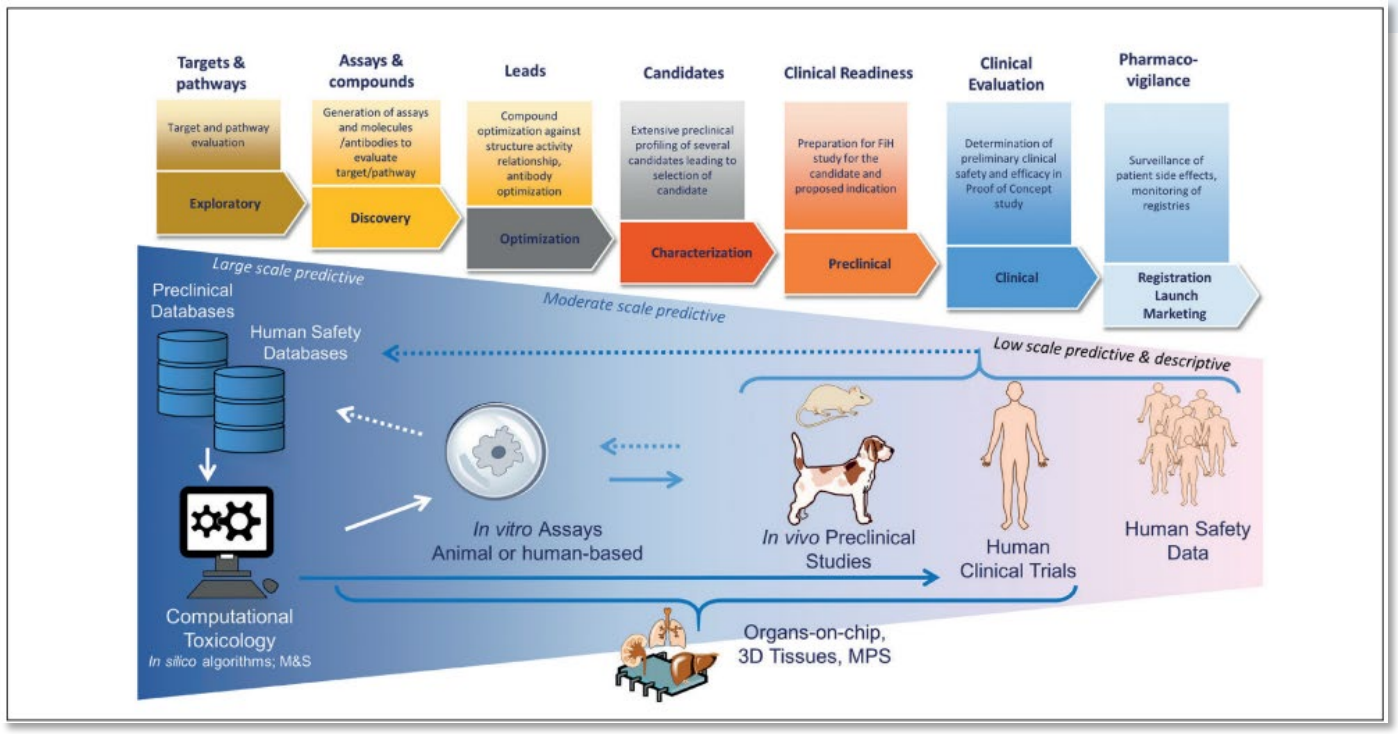
Keeping regulatory science in pace with scientific and technological progress and with the 3Rs

Evolution ongoing to a more evidence-based mechanistic and translational testing paradigms

A role for investigative toxicology combining in silico, in vitro, in vivo, and clinical data and making use of innovative technologies and novel approaches (Beilmann et al 2019, Pognan et al 2023)



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Conference on 3Rs in testing of medicines

- FAMHP contribution to the 3Rs in regulatory testing of medicines
- Stakeholders initiatives on 3Rs
- *Let's exchange!* Panel discussion
- National 3Rs initiatives

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Enjoy the Conference!

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