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Update from CHMP/CVMP 3Rs Working Party

Advancing Innovation through the 3Rs

EMA Veterinary Medicines Info Day– 13 March 2026

Sonja Beken, Chair 3Rs Working Party

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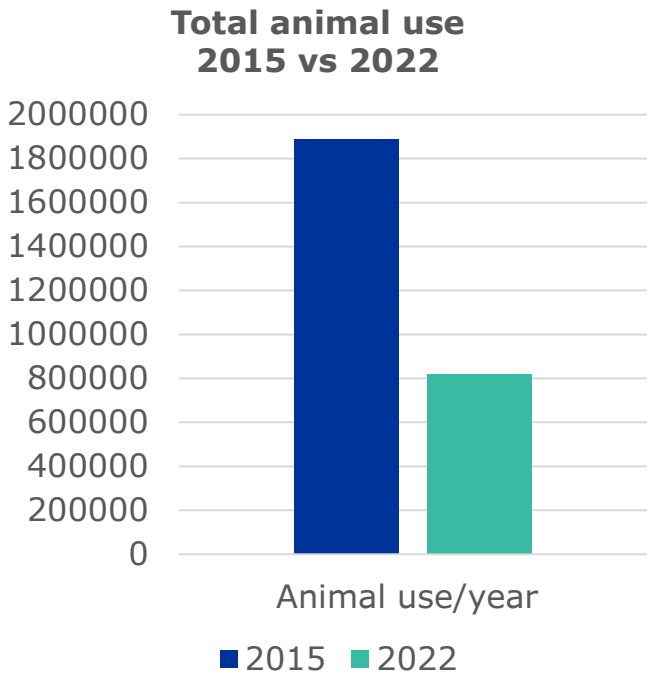
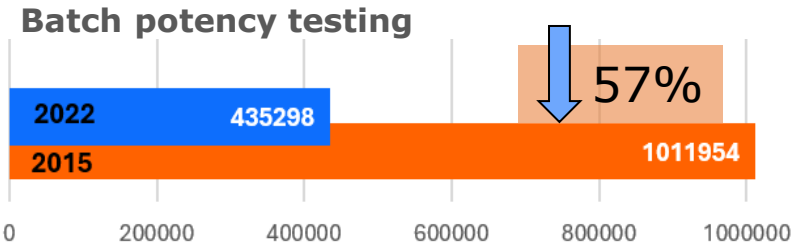
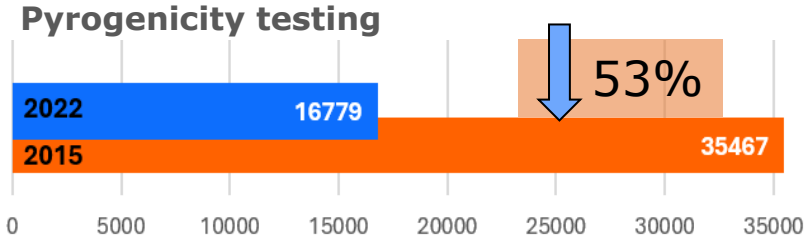
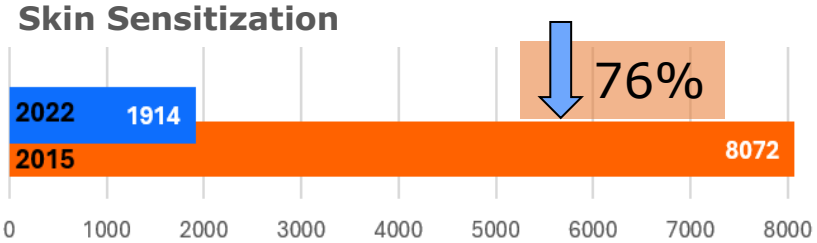
Introduction

Regulatory Use of Animals in EU - Successes









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3Rs Working Party

Share

The 3Rs Working Party (3RsWP) is a joint working party of the Committee for Medicinal Products for Human Use (CHMP) and the Committee for Veterinary Medicinal Products (CVMP). It advises these committees on all matters concerning the use of animals in the regulatory testing of medicines, with particular focus on the application of the so-called 3Rs principles - replace, reduce and refine.

Human | Veterinary | Corporate | Medicines

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The 3Rs stand for:

- **replacing** the use of animals with non-animal methods where possible;
- **reducing** the number of animals to the minimum necessary to obtain scientifically valid results;
- **refining** practices to minimise the stress and improve the welfare of study animals.

For more information on how the EMA and its 3Rs Working Party support the implementation of the 3Rs principles in the European Union, see:

- Ethical use of animals in medicine testing

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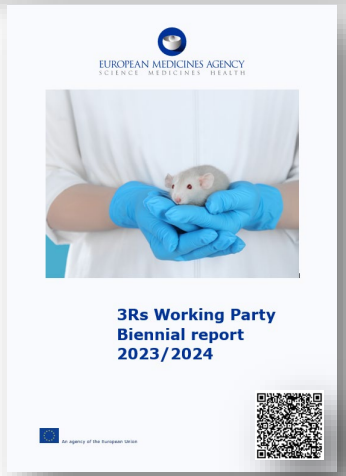
02 Dec 2024
Human Medicines Division
EMA/551442/2024

Consolidated 3-year rolling work plan for the Non-clinical domain

Domain Chairperson:	**Outi Mäki-Ikola**
Non-Clinical Working Party Chair:	Susanne Brendler-Schwaab
Non-Clinical Working Party Vice-Chair:	Karen Van Malderen
3Rs Working Party Chair:	Sonja Beken
3Rs Working Party Vice-Chair:	Sarah Adler-Flindt

Work plan period: January 2025 – December 2027 (with a first review point after one year)



EMA 3RsWP webpage
https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/3rs-working-party

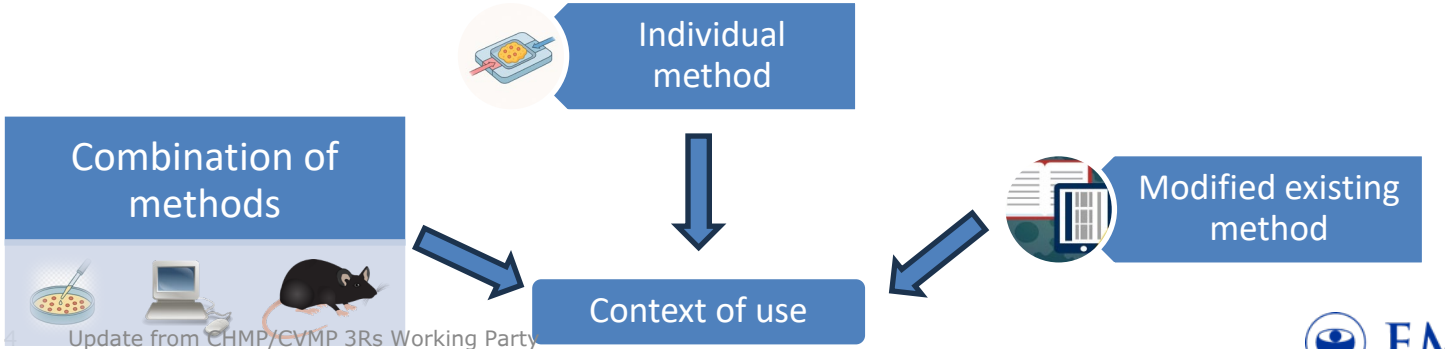
EMA webpage on "Ethical Use of Animals"
https://www.ema.europa.eu/en/human-regulatory-overview/research-development/ethical-use-animals-medicine-testing

EMA webpage on "Regulatory acceptance of NAMs"
https://www.ema.europa.eu/en/human-regulatory-overview/research-development/ethical-use-animals-medicine-testing/regulatory-acceptance-new-approach-methodologies-nams-reduce-animal-use-testing

3Rs as a Lever for Innovation

New Approach Methodologies (NAMs)

- **NAMs** are defined as **innovative** test methods or testing approaches aimed to progressively replace, reduce, and refine (**3Rs**) traditional animal studies.
- *These include in vitro, in silico, in chemico, ex vivo, refined in vivo and other advanced biology-based approaches and structured combinations of these (e.g. Weight of Evidence approaches).*
- NAMs are designed to generate **data that provide an equivalent or improved translation to support human or target species-relevant regulatory decision making.**



3RsWP Actions

- Providing Guidance
- Follow up of Quality Control and Batch Release Testing for Centrally Approved Medicinal Products
- Stakeholder Engagement
- Assessment of NAMs for Regulatory Acceptance: From Early Advice to Qualification
- Developing and Providing 3Rs Training
- Fostering International Regulatory Collaboration

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Guidance

Overview of Regulatory Testing Requirements and 3Rs

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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 3Rs

Draft

Draft agreed by 3RsWP following review by respective WPs (SWP, QWP, BWP, CAT and BMWP)	November 2024
Adopted by Committee for medicinal products for human use for release for consultation	02 December 2024
Start of Public consultation	13 February 2025
End of Public consultation (deadline for comments)	30 June 2025

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

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

Reduced non-clinical packages:

- Biological medicinal products (ICH S6)
- Products for treatment of advanced cancer (ICH S9)

Weight of evidence approaches for study waiving:

- Carcinogenicity (ICH S1B)
- Juvenile Animal Studies (ICH S11)
- Alternative assays for embryofetal tox (ICH S5)
- Chronic toxicity studies for mAbs
- *In vivo* comparative study for biosimilars

For veterinary medicinal products, see presentation by Dr. Adler-Flindt

Guiding Regulatory acceptance of NAMs

Criteria for regulatory acceptance

- Defined test methodology (protocol, endpoints).
- Relevance within a particular context of use (including accuracy).
- Context of use (including limitations).
- Reliability/robustness.
- Voluntary submission of data (safe harbour).


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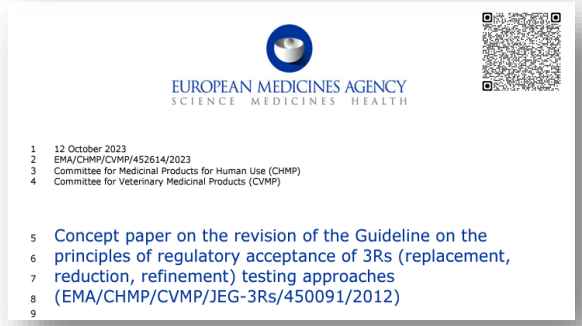
15 December 2016
EMA/CHMP/CVMP/JEG-3Rs/450091/2012
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches

Ongoing Guideline Revision

- 3Rs-related glossary and updates of body of the guideline.
- Annexes with regulatory acceptance criteria for complex in vitro models for specific contexts of use.
- Complex revision necessitates a stepwise approach:
    - *Steering group oversees GL revision.*
    - *Drafting subgroups: Terminology & Annex-specific.*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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)

Regulatory acceptance of NAMs: How?

Case-by-Case Acceptance in product submissions

- NAMs used for regulatory decision making (e.g., Clinical Trial Applications, Marketing Authorisation Application).
- Evaluation based on demonstration of scientific validity/merit and relevance to the medicinal product and target indication.

EMA Qualification for broad NAM use

- A formal EMA process to assess & endorse a novel method for a specific context of use in the development of a medicinal product.
- Provides regulatory endorsement for broader application.
- For NAMs applied for VMPS: ITF & veterinary SA.

Integration into Guidelines or PhEUR

- NAMs can be incorporated into official guidance (e.g., ICH, EMA, EDQM).
- Examples: ICH M7 allows use of (Q)SAR models for mutagenicity assessment of impurities; PhEUR adopts the MAT and BET as replacement for RPT.


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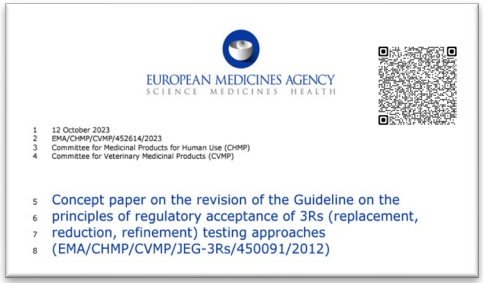
15 December 2016
EMA/CHMP/CVMP/JEG-3Rs/450091/2012
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches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1 12 October 2023
2 EMA/CHMP/CVMP/452614/2023
3 Committee for Medicinal Products for Human Use (CHMP)
4 Committee for Veterinary Medicinal Products (CVMP)

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


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10 November 2014
EMA/CHMP/SAWP/72894/2008
Revision 1: January 2012[1]
Revision 2: January 2014[2]
Revision 3: November 2014[3]
Revision 4: October 2020[4]
Scientific Advice Working Party of CHMP

Qualification of novel methodologies for drug development: guidance to applicants

Focus on reducing Non-Human Primate use

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6 October 2025
EMA/CHMP/55697/2025
European Medicines Agency

Reflection paper on non-human primates in safety testing of human medicinal products and opportunities for 3Rs implementation

Draft agreed by NcWP and 3RsWP	15 July 2025
Adopted by CHMP for release for consultation	6 October 2025
Start of public consultation	23 October 2025
End of consultation (deadline for comments)	31 January 2026

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

- Finalised public consultation
- Promotes use of NHPs only as last resort
- Leverages existing flexibility in existing guidelines
- Highlights future 3Rs opportunities
- Weight-of-Evidence Approaches
- NAM

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3Rs in Quality Control and Batch Release Testing

Batch Release Testing Operational Expert Group

VMPs:

- 67 products reviewed, 9 products still use in vivo BRT with potential 3Rs opportunities
- Response letters to MAHs adopted at CVMP in October 2025

HMPs:

- 281 products reviewed, 17 products still use in vivo BRT with potential 3Rs opportunities
- Letters will be sent to MAHs

“Lessons learned on 3Rs opportunities in batch release testing” as a future ESEC webinar

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Stakeholder Engagement

3RsWP collaborates to foster the 3Rs

3RsWP

- Annual Stakeholder meeting
- Workplan consultation
- Reflection papers 3Rs opportunities – public consultation
- Webpage on regulatory acceptance.
- ESEC to engage academia.

Interaction Mechanisms

- ITF
- Scientific Advice
- Qualification
- Portfolio and Technology meetings
- Voluntary data submission

see EMA webpage:

Collaborative fora

- EPAA
- HESI
- IMRWG3Rs
- Scientific meetings and conferences
- EC Roadmap

2025 Stakeholder meeting – Public session

- >200 participants
- Presentation of 2025-2027 workplan – 3Rs & joint NcWP/3Rs
- Slido – 75 responses

43% industry

Progress - Guidance

Prioritise - Qualification

Global - NAMs criteria

2026 stakeholder meeting – Public session

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Regulatory Acceptance of NAMs

From Early Advice to Qualification

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 or Broad Pipeline
- 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)

Voluntary Data Submission

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

Contribute to early dialogue via 3Rs EMA Innovation Task Force Briefing Meetings

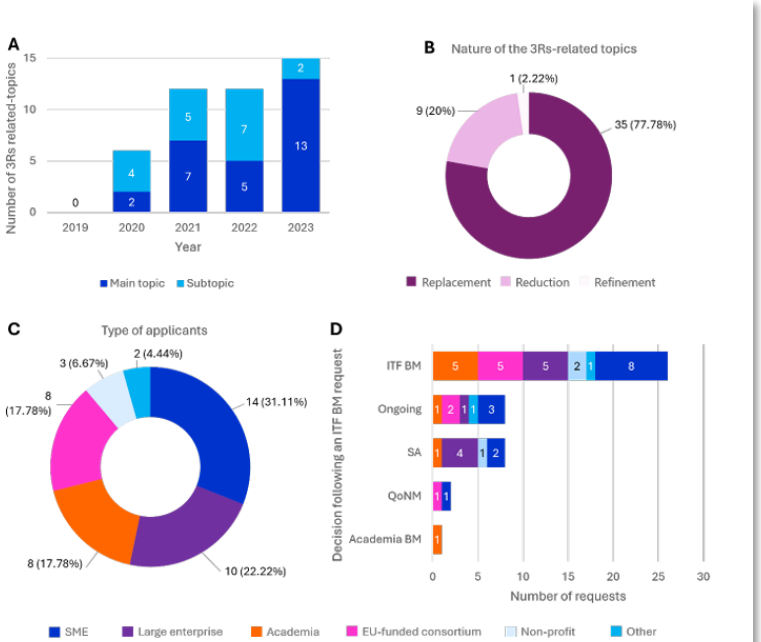


Figure 4. Number of 3Rs-related ITF briefing meetings requests received between 2019 and 2024 (A), main topics of discussion proposed (B), type of applicants (C) and advice provided by EMA ITF for the most appropriate regulatory interaction in response to the request (D).

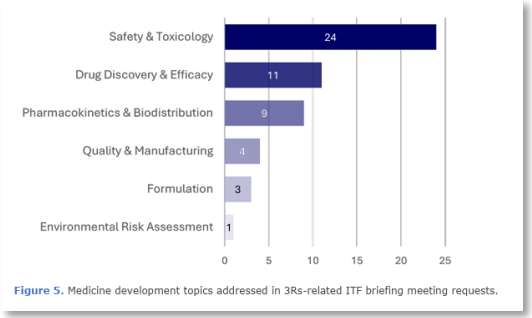


Figure 5. Medicine development topics addressed in 3Rs-related ITF briefing meeting requests.

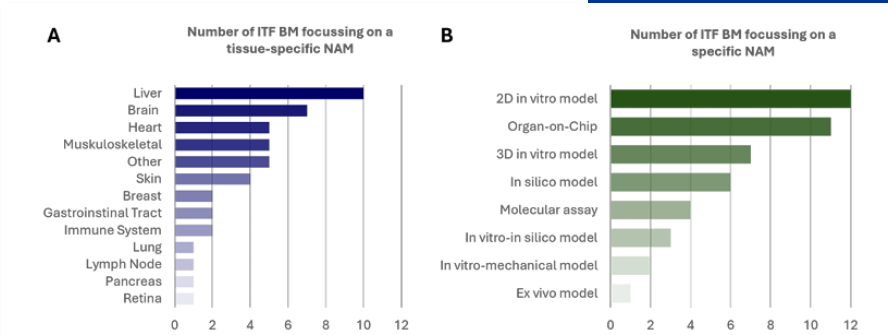
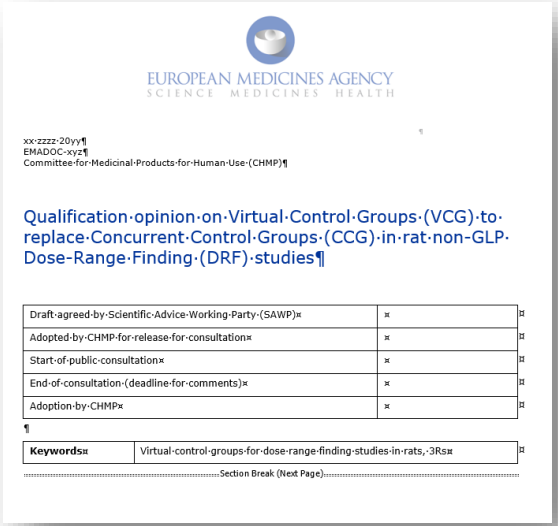


Figure 6. Number of ITF briefing meeting requests focussing on a specific tissue (A) or NAM (B).

2019-2023:

45/339 ITF Briefing Meeting Requests on 3Rs

Qualification of NAMs – The Virtual Control Groups DRAFT Qualification Opinion



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xx·zzzz·20yy¶
EMADOC·xyz¶
Committee·for·Medicinal·Products·for·Human·Use·(CHMP)¶

Qualification·opinion·on·Virtual·Control·Groups·(VCG)·to·replace·Concurrent·Control·Groups·(CCG)·in·rat·non·GLP·Dose·Range·Finding·(DRF)·studies¶

Draft·agreed·by·Scientific·Advice·Working·Party·(SAWP)¤	¤
Adopted·by·CHMP·for·release·for·consultation¤	¤
Start·of·public·consultation¤	¤
End·of·consultation·(deadline·for·comments)¤	¤
Adoption·by·CHMP¤	¤

¶

Keywords¤	Virtual·control·groups·for·dose·range·finding·studies·in·rats,·3Rs¤

Section Break (Next Page)

Qualification·Opinion·agreed·by·CHMP¶

Based·on·the·evidence·presented·by·the·Applicant·and·reviewed·by·the·SAWP·Qualification·Team,·CHMP·considers·that·Virtual·Control·Groups·(VCGs)·can·be·used·to·substitute·for·Concurrent·Control·Groups·(CCGs)·)·in·non-clinical·non-GLP·rat·dose·range·finding·(DRF)·studies·to·inform·on·dose·selection·for·subsequent·pivotal·rat·GLP-compliant·repeat-·dose·studies,·when·applied·in·accordance·to·the·SOP·(see·Appendix·1)·¶

¶

Agreed·Context·of·Use·(CoU):¶

The·Application·of·Virtual·Control·Groups·(VCGs)·according·to·the·SOP·(see·Appendix·1)·to·substitute·for·Concurrent·Control·Groups·in·non-clinical·rat·non-GLP·dose·range·finding·(DRF)·studies·to·inform·on·dose·selection·for·subsequent·pivotal·rat·GLP·repeat·dose·studies.¶

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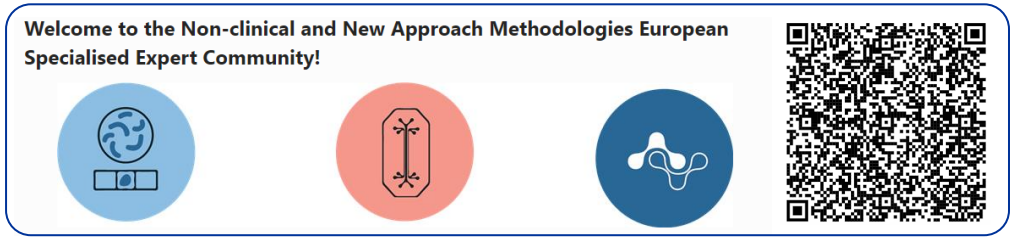
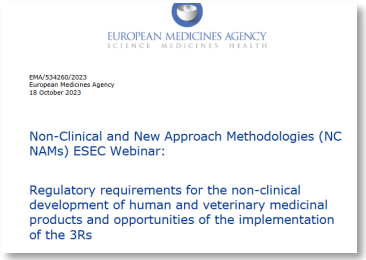
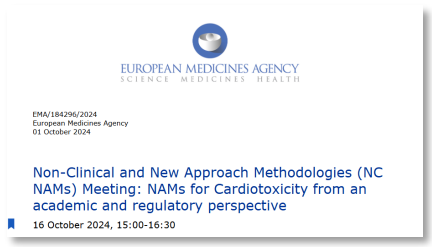
Training

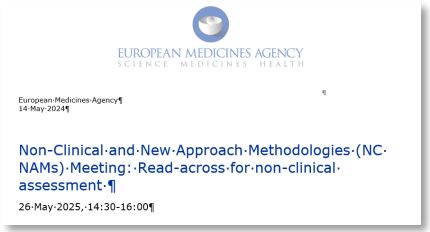
Training



- **Objective**: Information-sharing & Interactions between non-clinical & NAM experts
- **Members**: EU Regulatory Network & Academia
- **Link** with EU Network Training Centre (EU NTC)







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International Collaboration

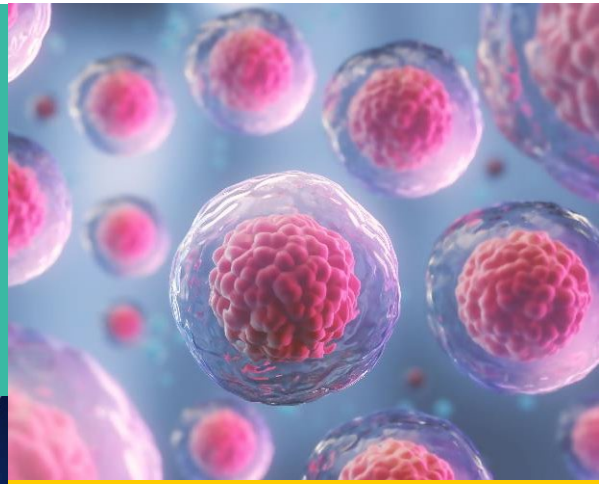
International Medicines Regulator's Working Group on 3Rs

- **Initiated by EMA**, co-chaired by EMA and Swissmedic.
- Medicines development occurs on a **global** scale – Europe **cannot work in isolation.**
- Continued reductions in animal use & promotion of the 3Rs requires global regulatory alignment to achieve harmonisation on:
  - *Acceptance criteria for NAMs*
  - *Batch release requirements*
  - *Phasing out of obsolete tests*
  - *Regulatory position statement – leading to ICH* GL
- Veterinary regulators from all regions, not by default included, but topic-based invitations are possible.

Terms of reference

Meetings in 2025

- January
- Participation of IMRWG in 3RsWP meeting, April
- July
- November



Ways of working

- Updating on regional 3Rs developments
- Sharing of NAM case studies and data
- Harmonised guidance development
- Confidence building
- Aligned stakeholder engagement

Key discussions to date

- Qualification frameworks for NAMs
- Voluntary submission of NAM data to regulators
- ICH reflection paper on NAMs
- Sharing of information on events
- Global position statement on 3Rs

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Thank you

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Annex

Animal experimentation in Europe – regulatory use

8,5 million animals in 28 Member States (EU-27 & Norway - 2022)

Human Medicinal Products

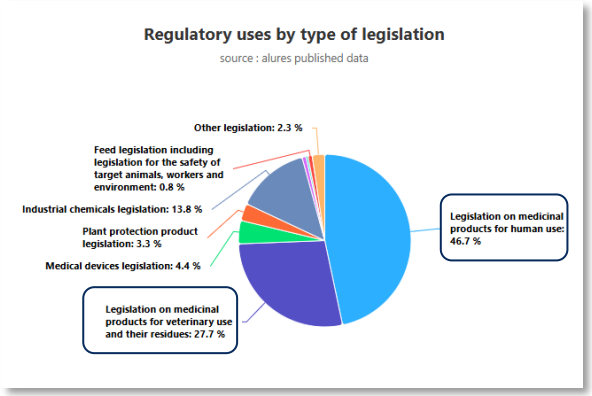
Regulatory uses: Toxicity	Number of uses	Percentage
Neurotoxicity	53	0.03%
Skin irritation/corrosion	60	0.03%
Eye irritation/corrosion	114	0.06%
Target animal safety	260	0.13%
Safety testing in food and feed area	280	0.14%
Phototoxicity	473	0.24%
Genotoxicity	1322	0.66%
Skin sensitisation	1364	0.68%
Carcinogenicity	1416	0.70%
Other toxicity/safety testing	1459	0.73%
Reproductive toxicity	8702	4.32%
Ecotoxicity	12977	6.45%
Acute and sub-acute	15281	7.59%
Pharmaco-dynamics (incl safety pharmacology)	30718	15.27%
Developmental toxicity	34303	17.05%
Kinetics	43668	21.70%
Repeated dose toxicity	48761	24.23%
Total	**201211**	**100,00%**

Regulatory uses: Quality control	Number of uses	Percentage
Other quality controls	10774	3.55%
Pyrogenicity testing	16717	5.50%
Batch safety testing	32711	10.77%
Batch potency testing	243566	80.18%
Total	**303768**	**100,00%**

Veterinary Medicinal Products

Regulatory uses: Toxicity	Number of uses	Percentage
Genotoxicity	60	0.24%
Repeated dose toxicity	168	0.66%
Skin sensitisation	550	2.17%
Ecotoxicity	648	2.56%
Other toxicity/safety testing	672	2.66%
Pharmaco-dynamics (incl safety pharmacology)	1279	5.05%
Safety testing in food and feed area	1739	6.87%
Kinetics	1754	6.93%
Target animal safety	3925	15.51%
Acute and sub-acute	14512	57.34%
Total	**25307**	**100,00%**

Regulatory uses: Quality control	Number of uses	Percentage
Pyrogenicity testing	329	0.12%
Other quality controls	7091	2.68%
Batch safety testing	48350	18.26%
Batch potency testing	209049	78.94%
Total	**264819**	**100,00%**



Publicly accessible ALURES Statistical EU Database on animal use

Animal experimentation in Europe (2015-2022)