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EMA 3RsWP

3Rs Working Party Annual Stakeholders Meeting – Public session

Presented by Sonja Beken on 31 March 2026

3Rs Working Party (EMA)

Outline

- 3RsWP achievements
- 3RsWP Workplan 2026-2028
- Time for your thoughts – SLIDO

Outline

- 3RsWP achievements
- 3RsWP New Workplan
- Time for your thoughts - SLIDO

EMA and the 3Rs – Expanding Our Timeline

JEG3Rs — 2010

2017 — J3RsWG

BREXIT & COVID19 — 2019

2020 — EMA RSS 2025

3RsWP — 2022

First workplan published

New members — 2025

New workplan 2026-2028 — 2026


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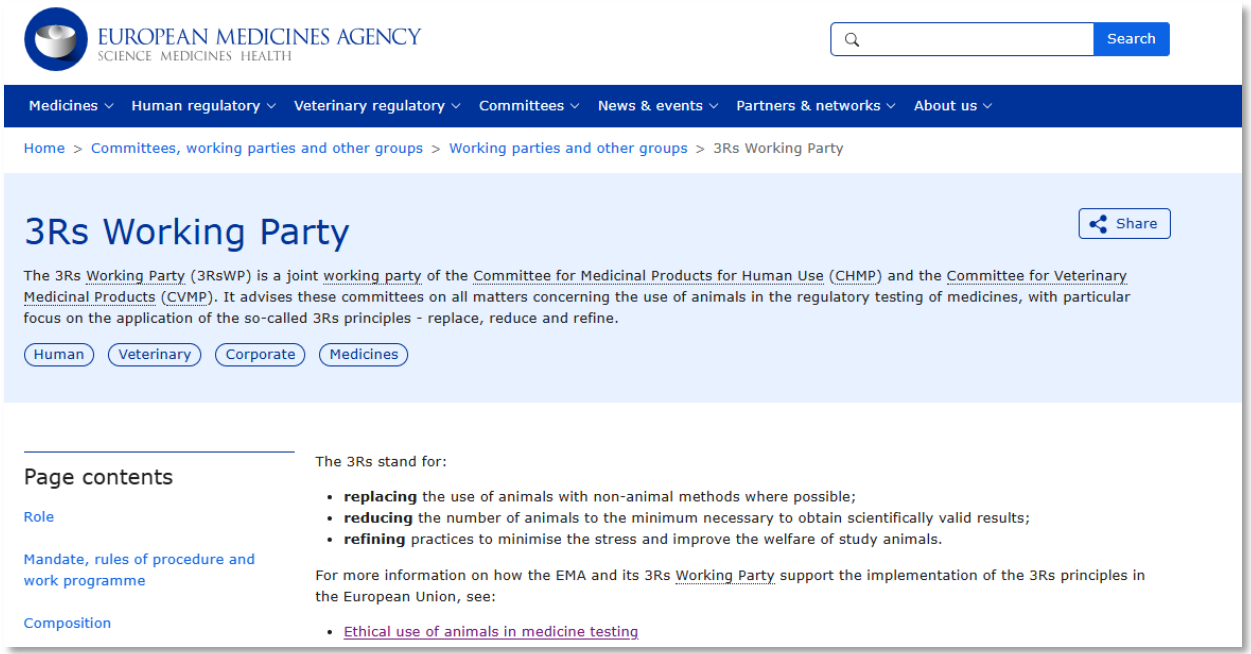
25 November 2025
Human Medicines Division
EMA/372540/2025

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 2026 – December 2028 (with a first review point after one year)



Members

- Sarah Adler-Flindt
- Kathrine Just Andersen
- Elisabeth Balks
- Sonja Beken
- Camilla Svensson
- Peter Theunissen
- Peter Van Meer
- Karen Ekkelund Petersen

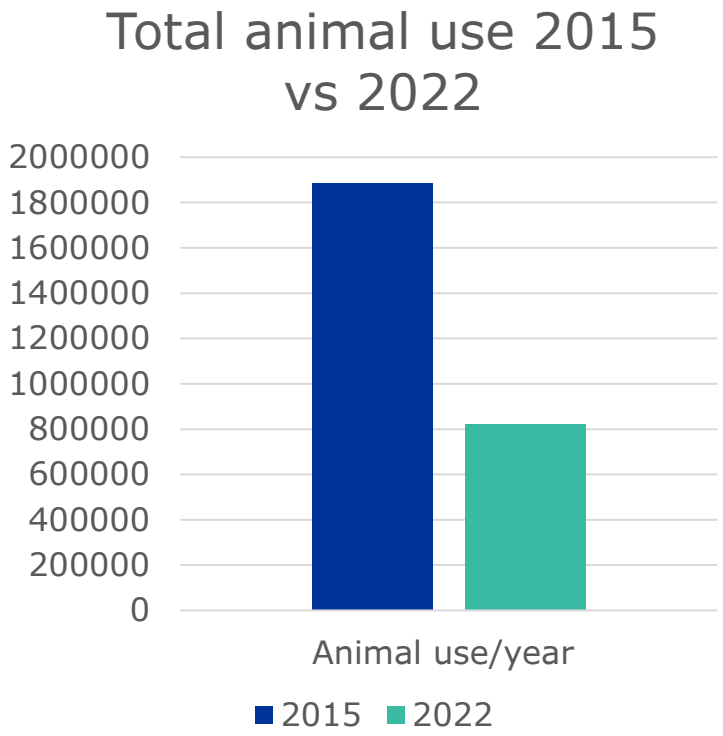
EMA 3RsWP webpage
https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/3rs-working-party

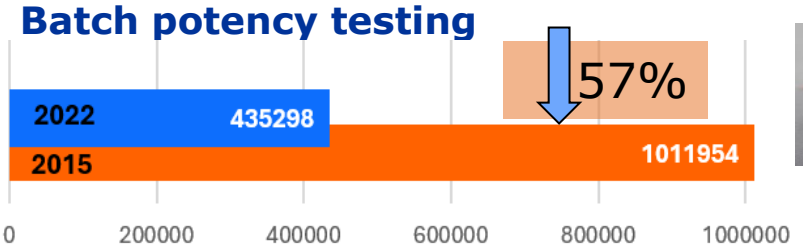
EMA webpage on "Ethical Use of Animals"
https://www.ema.europa.eu/en/human-regulatory-overview/research-development/ethical-use-animals-medicine-testing

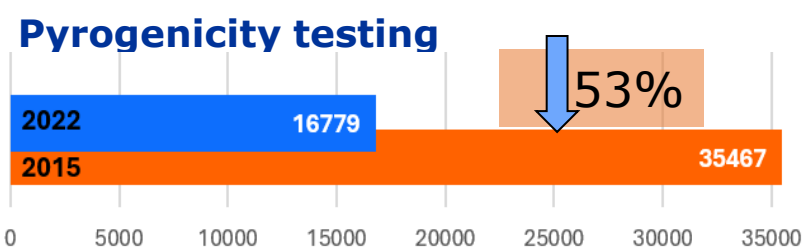
EMA webpage on "Regulatory acceptance of NAMs"
https://www.ema.europa.eu/en/human-regulatory-overview/research-development/ethical-use-animals-medicine-testing/regulatory-acceptance-new-approach-methodologies-nams-reduce-animal-use-testing

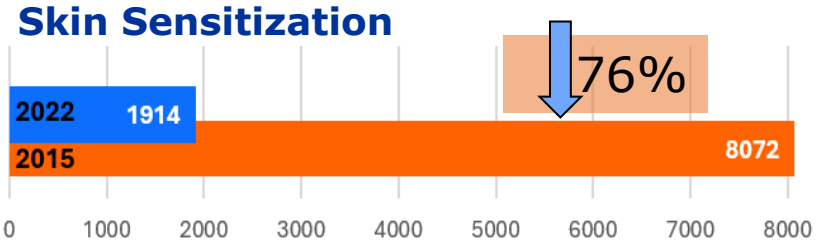
Contact us:
3Rs@ema.europa.eu

Regulatory Use of Animals in EU - Successes









*regulatory use and routine production associated with human and veterinary medicines legislation, EU requirements – ALURES database

Reinstating reporting – 3RsWP Biennial report 2023/2024

> Together, we are shaping a future where regulatory science, technological innovation, and ethical responsibility converge, ensuring the 3Rs actively drive transformation in medicines testing.
>
> **Sonja Beken**,
> EMA 3Rs Working Party Chair

Table of contents

Outline

- 3RsWP achievements
- 3RsWP New Workplan 2026-2028
- Time for your thoughts - SLIDO

3RsWP Actions

Providing **Guidance**

Follow up of **Quality Control** & **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

Reflection papers - 3Rs opportunities

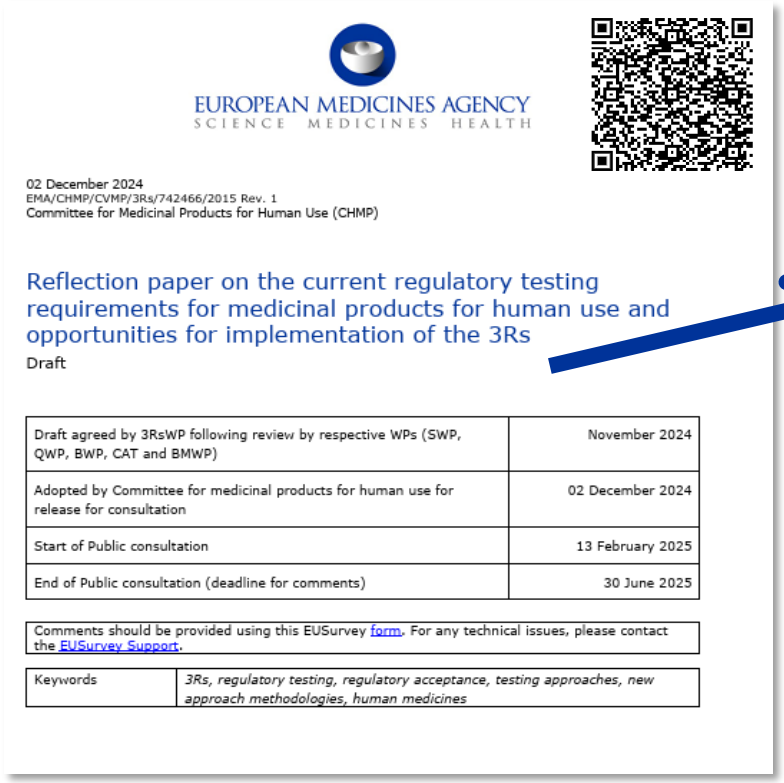
- An **inventory** of **regulatory testing requirements** for human and veterinary medicinal products and opportunities for **3Rs**
- First published in 2018, **ongoing revision** to update with state-of-the-art methods/approaches
  - Public consultation Feb 2025-June 2025
  - Over 400 comments received
  - Expected finalisation and response to comments in 2026

Implemented 3Rs opportunities: already included in guidance documents

Newly identified 3Rs opportunities: not yet included in guidance but considered acceptable for regulatory decision making (H&V) or still in development and considered promising for future implementation (H)

AIM: encourage development and submission of new 3Rs methodologies for regulatory review and acceptance

Overview of Regulatory Testing Requirements and 3Rs Human Medicinal Products



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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

Overview of Regulatory Testing Requirements and 3Rs Veterinary Medicinal Products

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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 requirements for veterinary medicinal products and opportunities for implementation of the 3Rs

Draft

Draft agreed by 3RsWP following review by respective WPs (QWP, SWP-V, NTWP, IWP, ERAWP and EWP-V)	November 2024
Adopted by CVMP for release for consultation	16 January 2025
Start of public consultation	13 February 2025
End of 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, animal tests, new approach methodologies, veterinary products*

Considerations for study waiving:

- If all in vitro genotoxicity assays clearly negative
- Standard developmental toxicity testing if no significant user exposure (companion animals)

Other safety testing opportunities:

- Limited value of single dose toxicity studies
- Use of in in vitro/in silico modelling (PK)
- Integration of multiple endpoints in single studies
- In vitro methods for batch potency testing of immunologicals

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Implemented opportunities – pyrogenicity testing

Incorporation of implemented opportunity in the revised reflection papers

3. Overview of regulatory animal testing requirements

3.1. CHMP/CVMP Quality Working Party and European Pharmacopoeia (Ph. Eur.)

Overview of animal testing requirements for active substances of synthetic, semi-synthetic, fermentation origin as well as medicinal products (Quality Working Party — CHMP/CVMP)

Topic	Regulatory provision	Animal testing requirements	Implemented 3Rs opportunities	Newly identified opportunities for 3Rs implementation
Pyrogens (rabbits)* * test also applicable to biological medicinal products	Ph. Eur. chapter 2.6.8 Pyrogens (*note: chapter 2.6.8 will be supressed from the Ph. Eur as of 1 January 2026*). Ph. Eur. chapter 5.1.13. (*note: chapter 5.1.13 pyrogenicity is to be implemented on 1 July 2025*)	Amikacin-sulfate, calcium levulinate dihydrate, colistimethate sodium, chloramphenicol sodium succinate, dicloxacillin sodium, flucloxacillin sodium, glucose, glucose monohydrate, kanamycin acid sulphate, kanamycin monosulfate, polymyxin B sulphate, sodium citrate. Besides the active substances in this table, the test was used in case of derived medicinal products and some older products.	In June 2021, the European Pharmacopoeia Commission took the decision to completely replace the rabbit pyrogen test (RPT) 2.6.8 in the Ph. Eur. with Monocyte-activation test (MAT) (2.6.30) or bacterial endotoxins test (BET) (2.6.14/2.6.32) within approximately 5 years. Subsequently, in June 2024, the Ph. Eur. Commission adopted revised text for 57 monographs where the RPT has been deleted with an implementation date of 1 July 2025. Accordingly, the requirement to carry out the RPT in the monographs for Amikacin-sulfate, Calcium levulinate dihydrate, Colistimethate	

Guiding regulatory acceptance of 3Rs testing approaches

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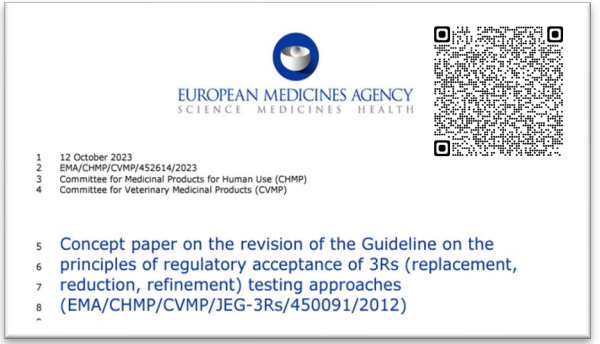
15 December 2016
EMA/CHMP/CVMP/JEG-3Rs/450091/2012
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

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)

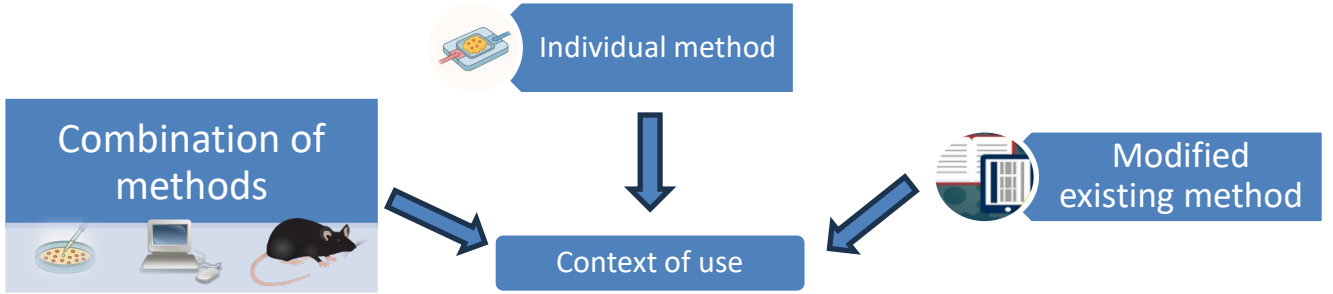
Defining Terminologies

New Approach Methodologies (NAMs) =

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.**



Other important terms - examples

Weight of Evidence
Context of use

Validation
Qualification

Formal procedures

Standardisation
Relevance
Sensitivity

How to achieve regulatory acceptance

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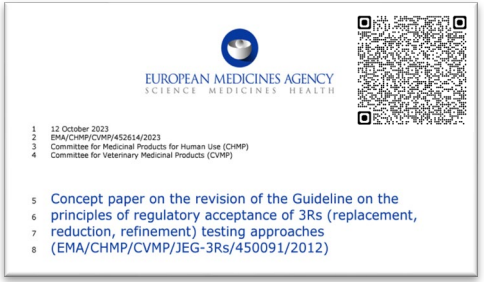
15 December 2016
EMA/CHMP/CVMP/JEG-3Rs/450091/2012
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

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


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10 November 2014
EMA/CHMP/SAWP/72894/2008
Revision 1: January 2017[1]
Revision 2: January 2019[2]
Revision 3: November 2019[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

- Finalised public consultation, over 500 comments received!
- Promotes use of NHPs only as last resort
- Leverages existing flexibility in existing guidelines
- Highlights future 3Rs opportunities
- Weight-of-Evidence Approaches
- NAMs

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Focus on local tolerance testing for human medicinal products

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22 October 2015
EMA/CHMP/SWP/2145/2000 Rev. 1, Corr. 1*
Committee for Medicinal Products for Human Use (CHMP)

Guideline on non-clinical local tolerance testing of medicinal products

Draft agreed by Safety Working Party	20 March 2014
Adopted by CHMP for release for consultation	25 April 2014
Start of public consultation	30 April 2014
End of consultation (deadline for comments)	31 July 2014
Agreed by Safety Working Party	29 September 2015
Adopted by CHMP	22 October 2015
Date for coming into effect	1 May 2016

Key aspects of revision:

- Restructure of content
- **Weight of evidence** central to determine testing strategy
- Addition of a **decision tree** for tiered testing approach
- Expanding/refining **endpoint-specific sections** to describe available *in vitro* and *in vivo* testing options (aligning with applicable OECD GLs)
- New section on **novel/state-of-the-art delivery systems**

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Focus on user safety for veterinary medicinal products

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15 March 2010
EMA/CVMP/543/03-Rev.1
Committee for medicinal products for veterinary use (CVMP)

Guideline on user safety for pharmaceutical veterinary medicinal products

Adoption by CVMP for release for consultation	12 January 2005
Date of coming into effect	13 July 2005
Revision by CVMP Safety Working Party	27 February 2009
Adoption by CVMP for release for consultation	17 April 2009
End of consultation (deadline for comments)	31 August 2009
Agreed by CVMP Safety Working Party	4 February 2010
Adoption by CVMP	10 March 2010
Date for coming into effect	1 October 2010

This guideline replaces guideline the guideline on user safety for pharmaceutical veterinary medicinal products that came into effect on 13 July 2005 (EMEA/CVMP/543/03-FINAL)

Concept paper on the revision of the guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.1)

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19 April 2018
EMA/CVMP/SWP/721059/2014
Committee for Medicinal Products for Veterinary Use (CVMP)

Guideline on user safety of topically administered veterinary medicinal products

Draft Agreed by Safety Working Party (SWP-V)	May 2016
Adoption by CVMP for release for consultation	16 June 2016
Start of public consultation	27 June 2016
End of consultation (deadline for comments)	31 December 2016
Agreed by SWP-V	February 2018
Adopted by CVMP	19 April 2018
Date for coming into effect	1 November 2018

This guideline will supplement the existing 'Guideline on user safety for pharmaceutical veterinary medicinal products' (EMA/CVMP/543/03-Rev.1).

Concept paper on the revision of the Guideline on user safety of topically administered veterinary medicinal products (EMA/CVMP/SWP/721059/2014)

Changes to both GLs:

- General 3Rs statements, e.g. step-wise testing and weight of evidence approach for quantitative risk assessment
- Reference to reflection paper
- OECD *in vitro* methods

General user safety:

- Guidance on negligible user exposure for waiving developmental toxicity studies

Topical User Safety:

- Decision tree for derivation of dermal toxicity values (TRVs)
- New section on dermal absorption

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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

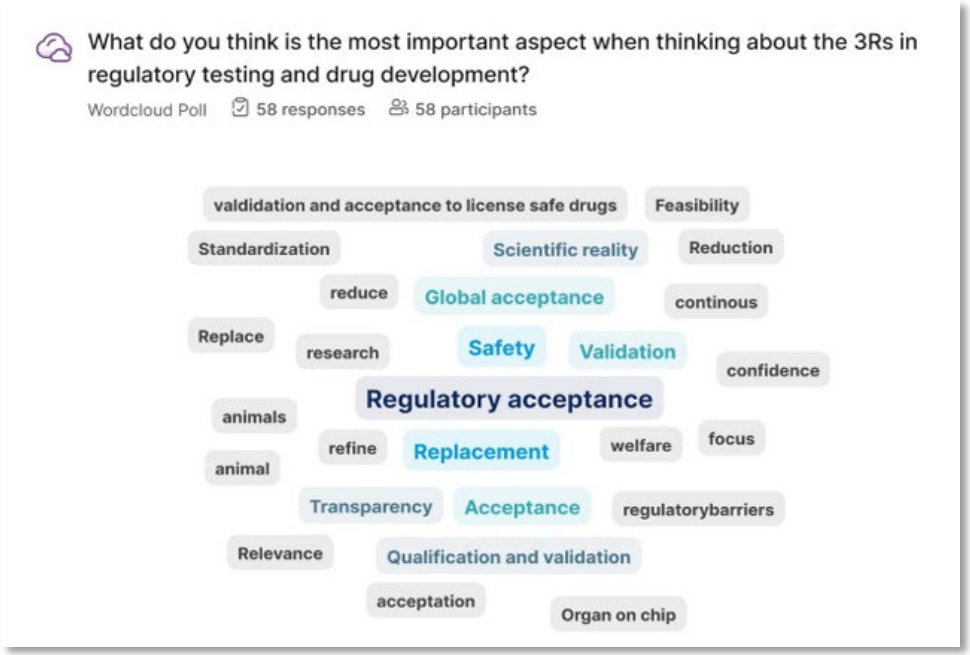
see EMA webpage:

Collaborative fora

- EPAA
- HESI
- IMRWG3Rs
- Scientific meetings and conferences
- **European Commission Roadmap**

2025 Stakeholder meeting – Public session

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



43% industry

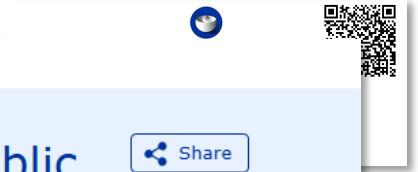
Progress - Guidance

Prioritise - Qualification

Global - NAMs criteria

2025 Stakeholder meeting – Public session

- >200 participants
-
-



Home > Events > 3Rs Working Party (3RsWP) stakeholder meeting - Public session on the 2026-2028 work plan

3Rs Working Party (3RsWP) stakeholder meeting - Public session on the 2026-2028 work plan

Share

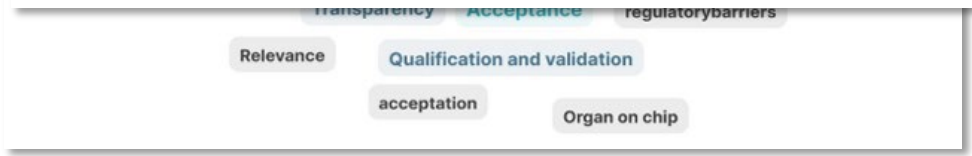
The 3RsWP is hosting this virtual public session to present the 3RsWP work plan and priorities for 2026-2028

Event | Human | Veterinary | Corporate

Add to calendar

Date: Tuesday, 31 March 2026 , 09:30 - 10:30 Amsterdam time (CEST)

Location: Online
European Medicines Agency, Amsterdam, the Netherlands
Live broadcast



Global - NAMs criteria

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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 possible

Terms of reference

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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

Ways of working

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

Meetings in 2025

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

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
- **ICMRA** position statement on 3Rs

Other outreach activities

EMA meetings

EMA workshop: Non-clinical data for regulatory decision-making on the efficacy of medical countermeasures

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Publications

New approaches in assessing potential proarrhythmic risk and cardiovascular safety during medicines development: opportunities for 3Rs application

3Rs at the European Medicines Agency: Past and future activities

Conference/Meeting participation

MPS WORLD SUMMIT
epaa The European Partnership for Alternative Approaches to Animal Testing
Safety Pharmacology Society
TOPRA
FDA
DIA
EUROoCS EUROPEAN ORGAN-ON-CHIP SOCIETY
European Commission
ECHA EUROPEAN CHEMICALS AGENCY
NIH

Media/public queries

EMA press office, ASK EMA

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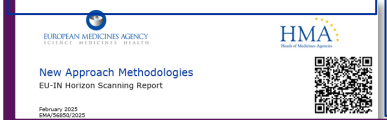
Operational Activities

Supporting 3Rs from early advice to regulatory acceptance

Fostering regulatory acceptance of 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 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

Focus on Early Advice:
3Rs EMA Innovation Task Force Briefing Meetings

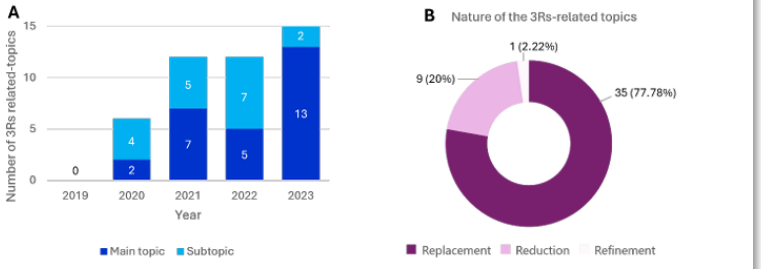


Figure 4. Number of 3Rs-related ITF briefing meetings requests received between 2019 and 2024 (A), main topics of discussion proposed (B), type of applicants (C) and advice provided by EMA ITF for the most appropriate regulatory interaction in response to the request (D).

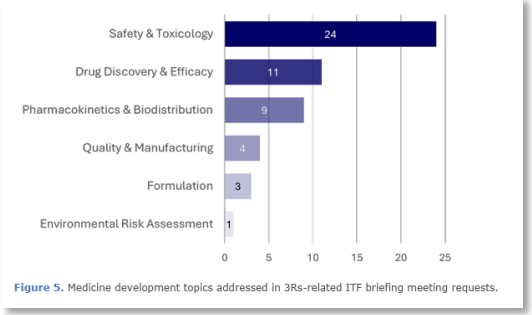


Figure 5. Medicine development topics addressed in 3Rs-related ITF briefing meeting requests.

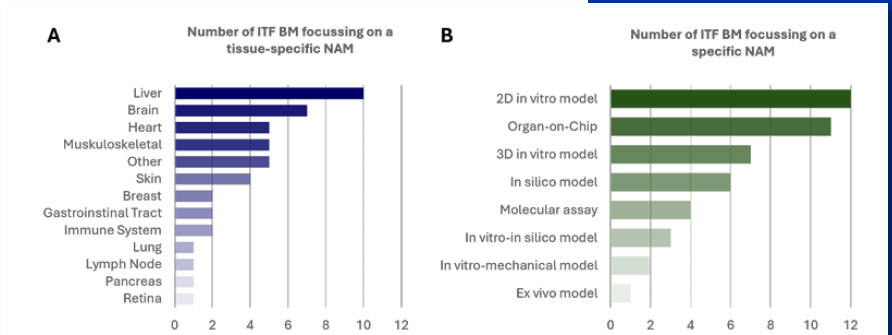


Figure 6. Number of ITF briefing meeting requests focussing on a specific tissue (A) or NAM (B).

2019-2023:

45/339 ITF Briefing Meeting Requests on 3Rs

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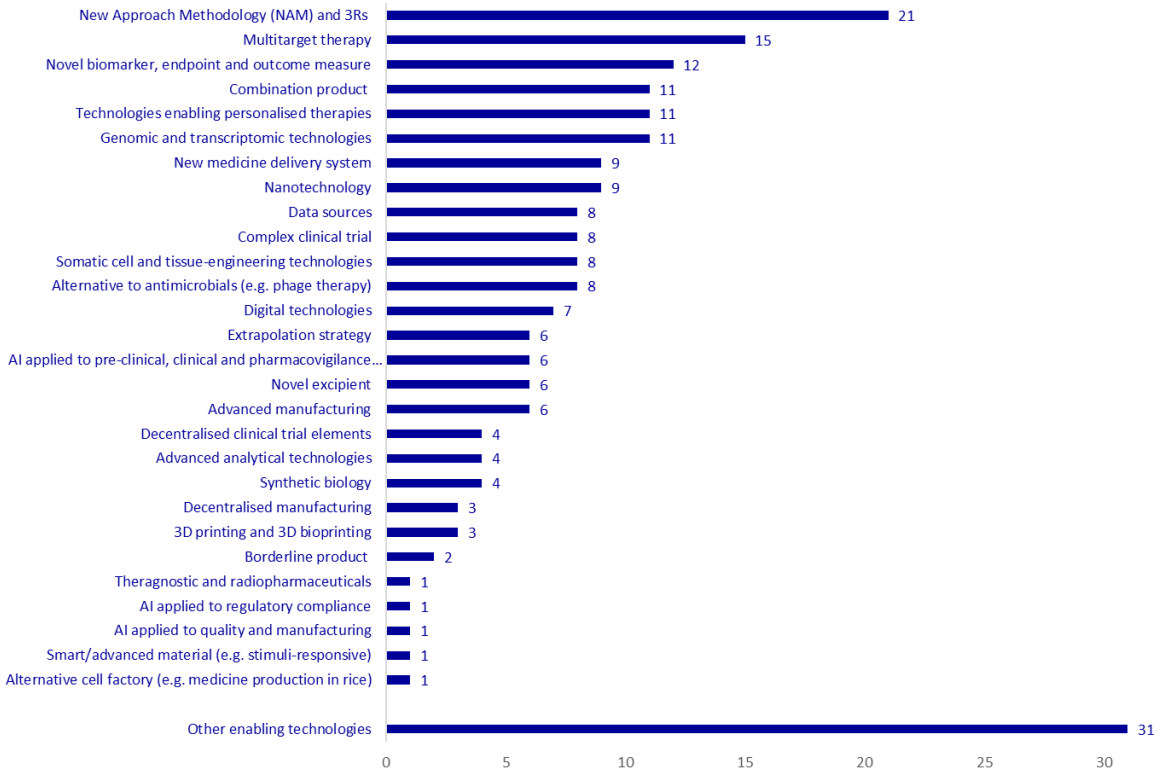
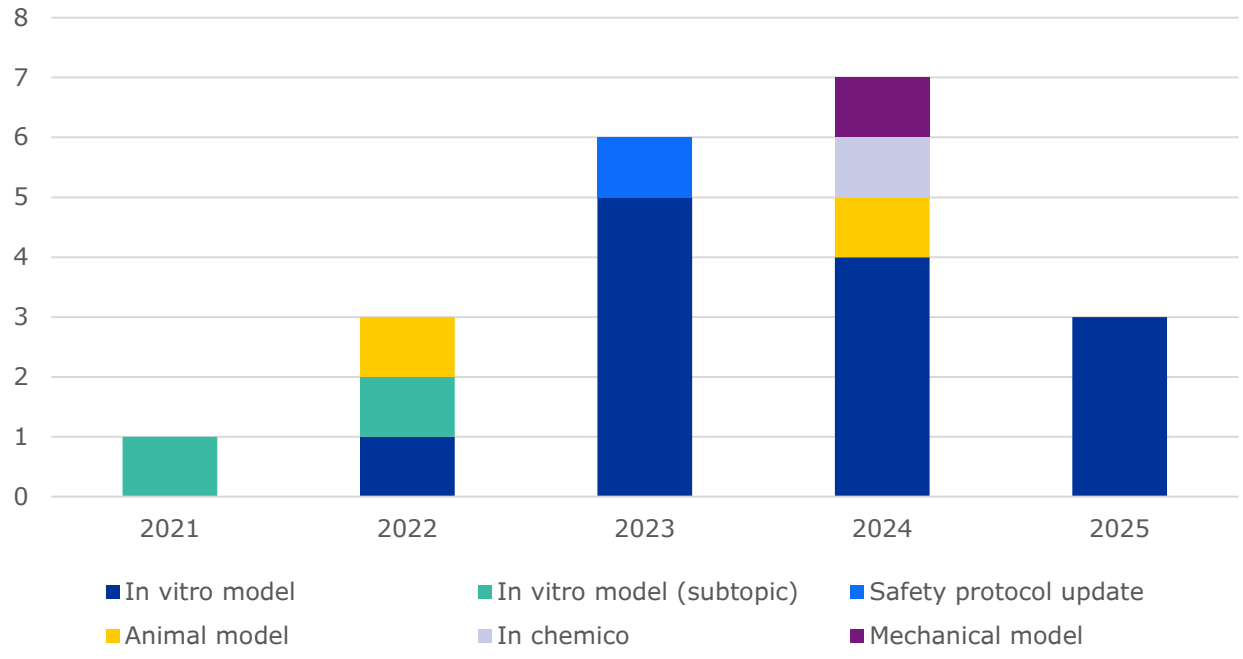
ITF – trends in 2025



For **all** applications:

NAMs was the most frequently mentioned **enabling technology**

ITF – trends in 2025



Fewer **NAM only** related ITF briefing meetings in 2025

BUT

Methods/approaches considered:

- More complex
- Of significant regulatory relevance
- Advanced in terms of readiness (e.g. suitable to progress towards qualification

AND

- High-level of 3RsWP participation in ITFs overall (e.g. non-clinical with 3Rs questions)

Focus on Qualification of NAMs:
The Virtual Control Groups DRAFT Qualification Opinion

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SCIENCE MEDICINES HEALTH

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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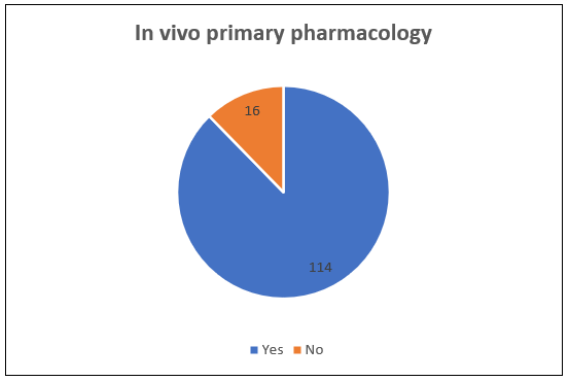
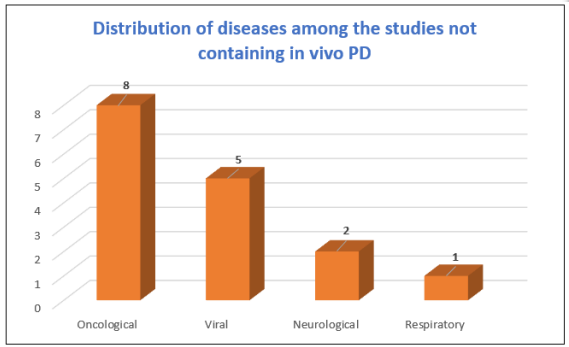
Focus on Case-by-Case Acceptance: Analysing Clinical Trials for 3Rs approaches



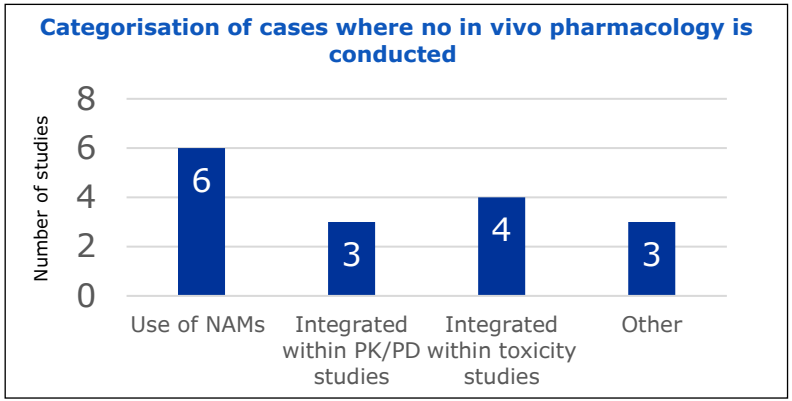


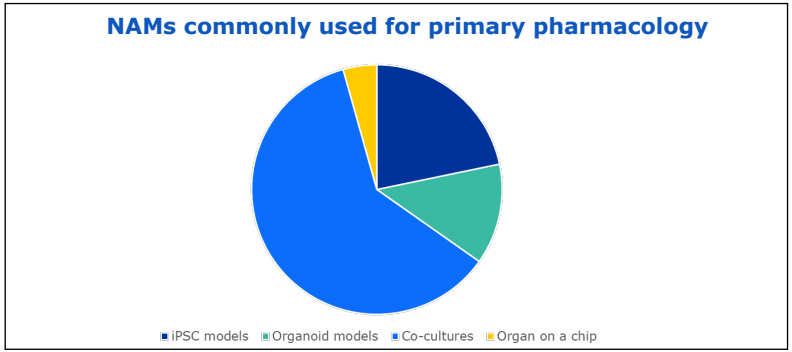
Where are NAMs used for pharmacology?

- No relevant species
- Exogenous target

When can studies be avoided?

- Incorporation of endpoints in other studies (PK/PD, toxicity)
- Use of microdosing





Focus on Data Sharing: The Voluntary Data Submission Pilot

Current issues

- **Qualification of NAMs** is slow, and **little data is seen in MAA dossiers** using the safe harbour approach
- By the time of MAA some NAMs could be outdated - not latest advancements
- *Sometimes industry may fear NAM data will be negatively considered in regulatory decisions* (EFPIA presentation at EPAA meeting)
- Regulators struggle to develop regulatory acceptance criteria for a CoU/RAA without having access to the data

Reframing the VDS procedure

Decouple the procedure from MAA and product specific procedures

Specific call for data to address a particular context of use

Safe space: confidential data only used for supporting regulatory acceptance of NAMs

Ad-hoc group of experts from EU network and EMA staff will review the data

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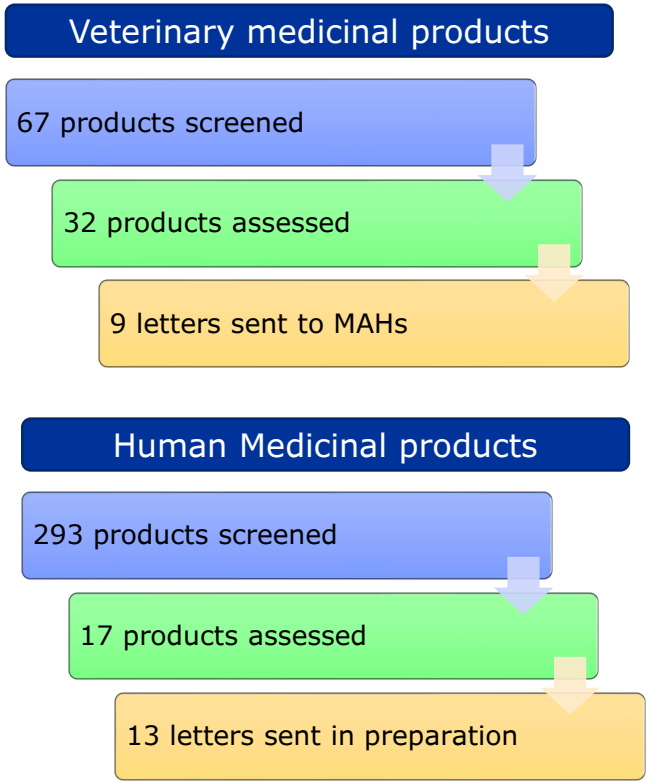
3Rs in Quality Control and Batch Release Testing

Batch release Testing Operational Expert Group (BRT-OEG)

Mandate and Objective

- **Review** quality control & batch release testing protocols for **centrally authorised human and veterinary medicinal products** (2013-2023)
- **Identify** opportunities for use of **3Rs**-compliant methods
- Where *in vivo* testing in use and 3Rs opportunities are identified - letter sent to the **MAH** to **encourage use/development of alternative methods to replace, reduce, or refine**



BRT-OEG Current Status

Veterinary products – sample outcomes

- Ongoing validation of alternative (timeline proposed) **REPLACEMENT**
- Development of alternative in initial phase and will engage with ITF **REPLACEMENT**
- Proposal to EDQM for revision of monographs based on the assessment outcomes (*in vitro* alternative already in use) **REPLACEMENT**
- Agreement to reduce number of animals used "*without impacting the robustness, the statistical power of the test or reliability of batch release decisions*" **REDUCTION**

Human products – sample recommendations

- Rabbit pyrogenicity testing **REPLACEMENT**
  - ***Implement*** *suitable in vitro alternative*
- Test for absence of tetanus toxin **REPLACEMENT**
  - *Consider suitable in vitro alternative*
- *In vivo* potency assay
  - *Consider development of an alternative*
  - *Apply humane endpoints* **REFINEMENT**
- Release and stability testing
  - *Consider development of an alternative*
  - *Consider reducing numbers used* **REDUCTION**

Model letters

MAH name
Street and number
Postal code
City
Country

DATE
EMA/CHMP/CVMP/3Rs/XXXX/XXXX
<Committee for Veterinary Medicinal Products (CVMP)> <Committee for Medicinal Products for Human Use (CHMP)>

Dear Dr XXX

Subject: Request for information concerning the batch release testing and the application of 3R methods for <product name>

I am writing to you with reference to a specific request for information concerning the batch release testing methods used for the above-mentioned centrally authorised medicinal product<s>.

The Joint CVMP/CHMP 3Rs Working Party (3RsWP) provides advice and recommendations to the CHMP and CVMP on all matters relating to the use of animals and the application of the '3R' principles (replacement, reduction and refinement) in the testing of medicines for regulatory purposes.

In line with the 3RsWP work plan, the "Batch Release Testing Operational Experts Group" (BRT OEG) is undertaking a review of the currently approved test methods used in batch release testing of all centrally authorised medicines on behalf of the 3RsWP. The group has reviewed veterinary and human medicinal products authorised since 2014.

Replacement

The review revealed that the <potency> <other> test authorised for <product name> involves *in vivo* methods. <Insert details on *in vivo* methods used>. <This same <potency> <other> test is used for the other products within the <product name> range>.

While this method was accepted at the time of the initial authorisation, there is less justification for maintaining such a method knowing that <development of an alternative method may be possible.> <the use of an alternative method, such as <method>, is now possible.> Therefore, it is essential for manufacturers to prioritise the development and implementation of suitable 3Rs-compliant methods as alternatives to animal testing, particularly for batch release.

Directive 2010/63/EU states that animal procedures should not be used if another scientifically satisfactory 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. Alternatives to in vivo test methods should be employed whenever possible. Furthermore, if an animal procedure is necessary, then the method chosen should be such as to use the minimum number of animals and to cause the least pain, suffering, distress or lasting harm. Death as an endpoint should be avoided as far as possible.

The development of alternative methods to replace the use of animals in the testing of medicines is encouraged and supported by EMA's Innovation Task Force (ITF). The ITF's service is free of charge and any methods adhering to the 3Rs principles that can be used to fulfil testing requirements are eligible for consideration.

The <CHMP> <CVMP> would also like to know if the company has plans to develop and implement a method in line with the 3Rs principles and Directive 2010/63/EU.

I would be grateful if you would direct your response to this letter to the following email address: 3Rs@ema.europa.eu by <date>.

Yours sincerely,

<name of Committee chair>, on behalf of the <CVMP> <CHMP>

This letter has been produced electronically and consequently does not bear the signature of the authorised signatory.

Reduction/refinement

The review revealed that the <potency> <other> test authorised for <product name> involves *in vivo* methods. <Insert details on *in vivo* methods used>. <This same <potency> <other> test is used for the other products within the <product name> range>.

In consideration of test specifications, <reduction><and/or><refinement> could be considered in <include relevant details for proposal><unless otherwise statistically justified>.

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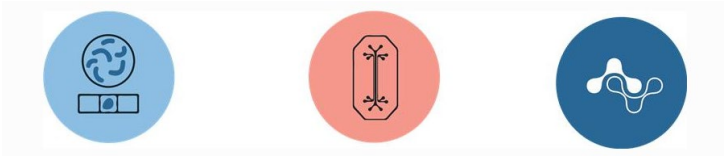
Training

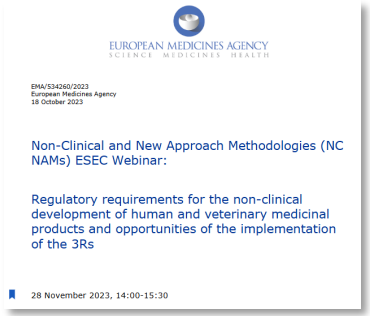
Training: ESEC

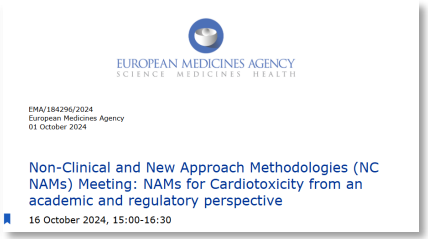
Welcome to the Non-Clinical and New Approach Methodologies Expert Community!



Objective: Information-sharing & Interactions between non-clinical & NAM experts

Members: EU Regulatory Network & Academia





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Training: EU-NTC

EU Network Training Centre (EU NTC)

Share

The European Union Network Training Centre (EU NTC) is a platform offering training opportunities to the staff of medicines regulatory authorities in the European medicines regulatory network, in the fields of human and veterinary medicines. It is overseen by the European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA).

- Training platform for EU **assessors**
- Existing **Non-clinical** curriculum
- Working on development of a **dedicated 3Rs curriculum**
    - 3Rs trainings consolidated for easy access
    - Divided by topics of interest: e.g. **Foundations**, **Weight of Evidence Approaches**, **Quality Control and Batch Release**

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Thank you

Any Questions / Suggestions?

3Rs@ema.europa.eu

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