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Experience with the ITF framework for 3Rs and new approach methodologies (NAMs)

Industry stakeholder platform on research and development support

11 July 2022

Presented by Stefano Ponzano on 11 July 2022

EMA and the 3Rs

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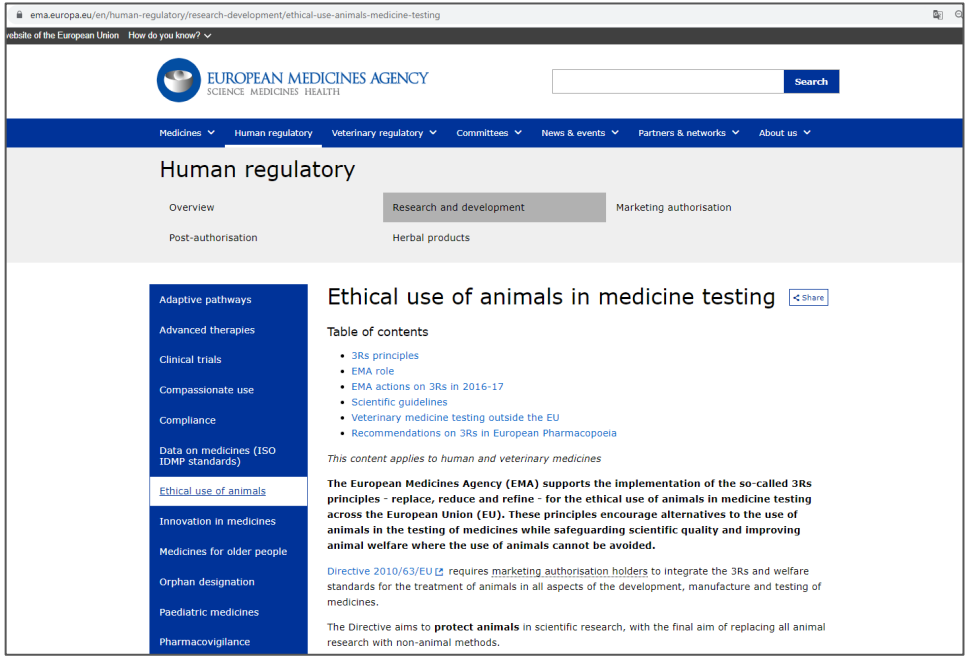

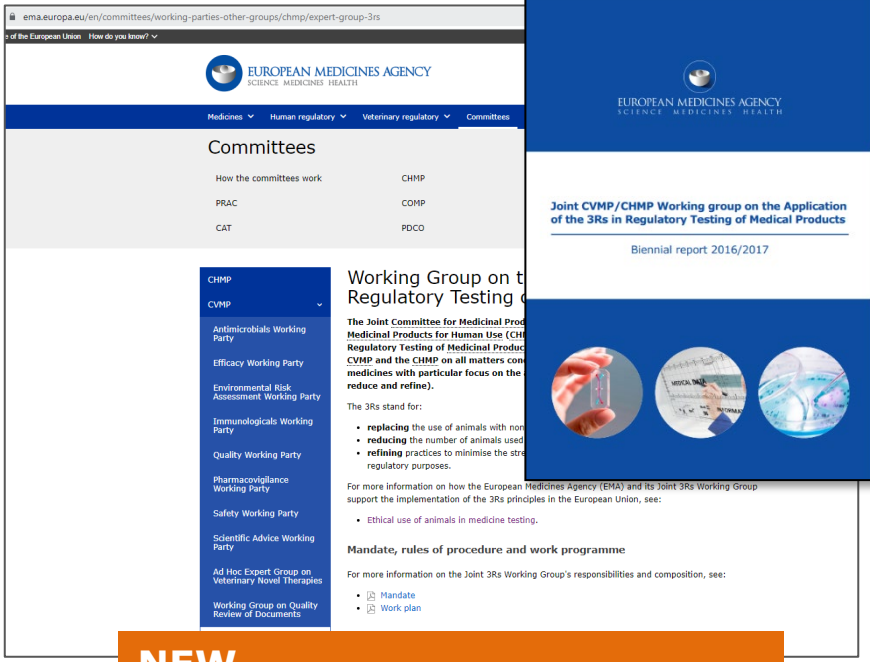

https://www.ema.europa.eu/en/human-regulatory/research-development/ethical-use-animals-medicine-testing

NEW

Start of CHMP/CVMP Joint 3Rs Working Party – Q3/4 2022

Driving the Regulatory Science and EU Network Strategy **together with all stakeholders**

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HMA
Heads of Medicines Agencies

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EMA Regulatory Science strategy 2025

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Driving collaborative evidence generation – improving the scientific quality of evaluations

Core recommendations	*Underlying actions*
Leverage non-clinical models and 3Rs principles	‣ Stimulate developers to use novel pre-clinical models where appropriate, including those adhering to the 3Rs: » Cooperate with other EU agencies/bodies to fund research and (access to) standardised repositories for alternative methods and models; » Development of clear guidance to encourage and prioritise the use of New Approach Methodologies (NAMs) that can be used to fulfil testing requirements in lieu of traditional animal tests and that take the 3Rs into serious consideration; ‣ Re-focus the role of the Joint 3Rs working group (J3R WG) to support qualification of new alternative 3R-compliant methods/models including in silico and novel in vitro assays; ‣ Implement/develop IT tools to exploit the added value of SEND for the re-analyses of non-clinical studies to support clinical trials, marketing authorisation and improved evidence generation.

- Refocus the role of the Joint 3Rs WG to **support qualification** of new alternative 3Rs methods.

https://www.ema.europa.eu/en/about-us/how-we-work/regulatory-science-strategy#regulatory-science-strategy-to-2025-section

- **core recommendation** dedicated to leverage and qualification of 3Rs methods
- EMA wants to see more 3R methods to **raise awareness** and **start discussing with developers**

Reinforce and further embed application of the 3Rs principles	‣ Apply the highest possible 3Rs standards when implementing the Veterinary Medicines Regulation (EU) 2019/6 as well as other legislative documents/guidelines to stimulate developers to use novel approaches adhering to 3Rs standards; ‣ Strengthen cooperation between all stakeholders and international partners: » Cooperate with other EU agencies/bodies to fund research and (access to) standardised repositories for alternative methods and models; ‣ Promote in silico methodology (e.g. modelling), novel in vitro assays and systematic reviews to reduce animal use, particularly in toxicology/ epidemiology and batch control: » Re-focus the role of the Joint 3Rs working group (J3R WG) to support qualification of new alternative 3R-compliant method/models including in silico and novel in vitro assays; » Development of clear guidance to encourage and prioritise the use of NAMs that can be used to fulfil testing requirements in lieu of traditional animal tests and that take the 3Rs into serious consideration; ‣ Promote regulatory acceptance and training.

Innovation Task Force (ITF)

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Multidisciplinary platform

for preparatory dialogue and orientation on

innovative methods, technologies and medicines

- Support **innovative** drug development
- **Early informal** dialogue with opinion leaders on
  - **Scientific, legal and regulatory** issues
  - Products, **methodologies and technologies**
- Free of charge
- Brainstorming "style" on innovation in areas without existing guidance
- First step to engage is submit completed 3-page template

Contact:
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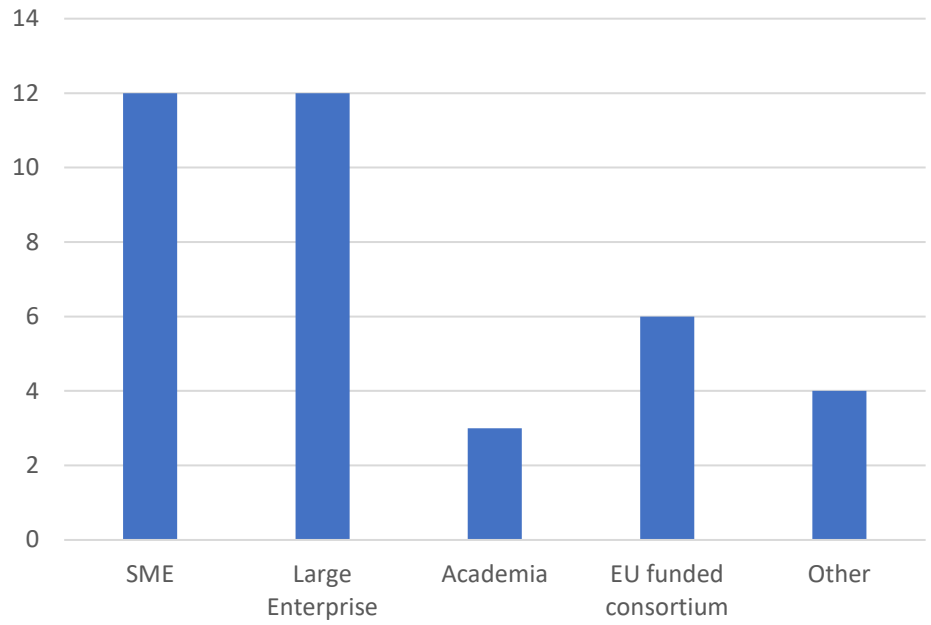
itfvet@ema.europa.eu for veterinary medicines

Number of ITF BMs in 2021 (and before)



	2017	2018	2019	2020	2021
Number of meetings	26	23	26	30	38
Number of EMA participants	166	129	167	189	251
Number of NCA participants	115	106	118	248	347
Number of Stakeholder participants	148	126	165	286	347

ITF and 3Rs (NEW)

ITF is now also focusing on the regulatory acceptance of so-called new approach methodologies (NAMs) to replace the use of animals in the testing of medicines, in line with the 3Rs principles

→ e.g., *in silico* modelling & novel *in vitro* assays (e.g. MPS/OoCs, Organoids)

Objectives:

- To increase the number of ITF meetings focused on NAMs
- To increase awareness and fill in the gap between EMA and developers
- To accelerate the integration of NAMs in the regulatory framework for the development and evaluation of medicines

Number of ITF BM requests related to 3Rs (2020 – 2022)

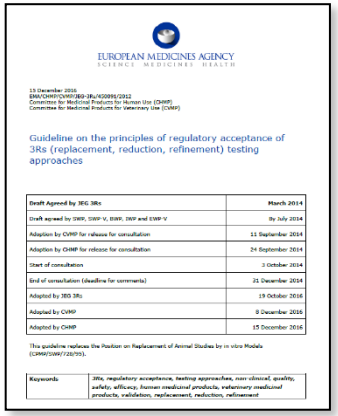
	Relation to 3Rs	Type of development
1.	New approach methodology	Organ-on-a-chip / organoid
2.	New approach methodology	Organ-on-a-chip
3.	New approach methodology	Organ-on-a-chip / 2D and 3D culture models
4.	New approach methodology	Animal-free antibody production/testing
5.	New approach methodology	Alternative transgenic animal model for the evaluation of EDs
6.	3R-related questions: Validity of *in vitro* methods for toxicity studies? Are animal studies mandatory?	Antisense oligonucleotide therapy for very rare mutations
7.	3R-related question: Validity of *in vitro* and *ex vivo* methods for toxicity studies Which read out is considered relevant for such assay?	Consortium for CAR-T Cell Therapies
8.	3R-related question: Validity of *in vitro* methods for efficacy studies	Peptidomimetics technology

What do we want to discuss in the 3Rs ITF meetings?

- ❑ Test methodology (protocol, endpoints)
- ❑ Context of use (including limitations).
- ❑ Relevance within a particular context of use
- ❑ Gold standards used per endpoint
- ❑ Applicability of biomarkers

- ➢ Need of a specific guidance for method developers on qualification
- ➢ Develop endpoint-specific performance standards incl. list of reference compounds (positive & negative controls)
- ➢ Follow-up procedures to support regulatory acceptance (e.g. SA, QA, safe harbour)

Guideline on the principles of regulatory acceptance of 3Rs testing approaches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13 December 2018
EMA/CHMP/CVMP/JEG-3Rs/450095/2012
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

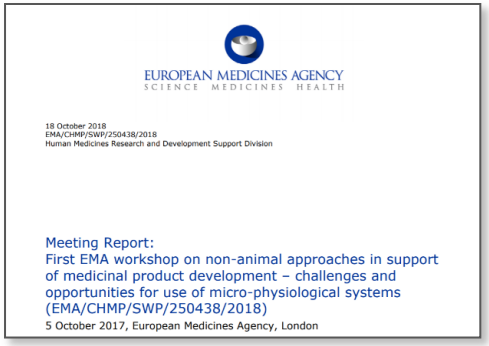
Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches

Draft Agreed by JEG 3Rs	March 2014
Draft agreed by SWP, SWP-V, BWP, IWP and EWP-V	By July 2014
Adoption by CVMP for release for consultation	11 September 2014
Adoption by CHMP for release for consultation	24 September 2014
Start of consultation	1 October 2014
End of consultation (deadline for comments)	31 December 2014
Adopted by JEG 3Rs	19 October 2016
Adopted by CVMP	8 December 2016
Adopted by CHMP	15 December 2016

This guideline replaces the Position on Replacement of Animal Studies by in vitro Models (CHMP/SWP/728/95).

Keywords	3Rs, regulatory acceptance, testing approaches, non-clinical, quality, safety, efficacy, human medicinal products, veterinary medicinal products, validation, replacement, reduction, refinement

First EMA workshop on non-animal approaches in support of medicinal product development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18 October 2018
EMA/CHMP/SWP/250438/2018
Human Medicines Research and Development Support Division

Meeting Report:
First EMA workshop on non-animal approaches in support of medicinal product development – challenges and opportunities for use of micro-physiological systems (EMA/CHMP/SWP/250438/2018)
5 October 2017, European Medicines Agency, London

Q & A session

- What are the main areas of interest to industry with regards to the regulatory acceptance of 3Rs?
- Is industry interested in presenting methods through ITF, either alone or as consortium? What are the perceived hurdles?
- Is there an interest to further interact to foster regulatory acceptance of Microphysiological systems (MPS)/Organ-on-chips (OoC)?

Special thank to:

Blanquie Oriane (ITF Office) and Falk Ehmann (ITF Office)

Any questions?

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