





Overview about recent European 3R activities with a focus on 3R Centres and the EU COST Action IMPROVE

WC13 – Rio de Janeiro, Brazil

3rd September 2025

Jeffrey Bajramovic, Adrian Smith, Anna Olsson, Arti Ahluwalia, Winfried Neuhaus

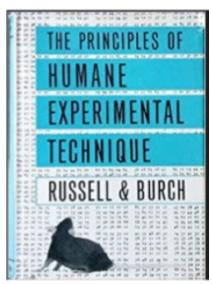


The 3Rs – a bit of history

- In the post-war period, the first experimental animal science societies emerged, which were initially mainly concerned with standardisation
- Originally, the first developments of 3R approaches in the UK in the 1950s.
- Commissioned/Contract work for the UFAW (Universities Federation for Animal Welfare): close cooperation between laboratory animal scientists, animal experimentation laboratory managers, laboratory animal breeders and scientists (so-called Lab Survey from 1952)
- In 1959, the groundbreaking book by William Russell and Rex Burch was published

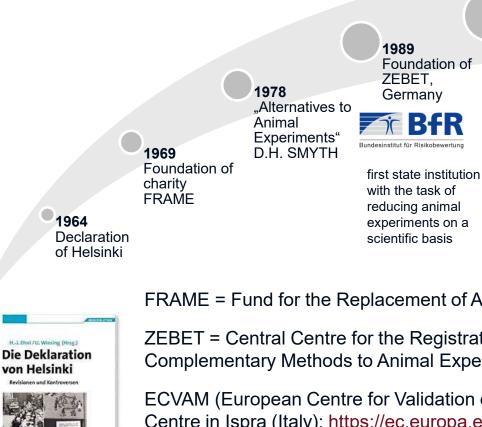
'The Principles of Humane Experimental Technique'

= is regarded as the **standard work of the 3Rs**



The 3Rs – a bit of history





1993 Foundation of the validation centre ECVAM

> 1997 Foundation of validation centre **ICCVAM**



FRAME = Fund for the Replacement of Animals in Medical Experiments

ZEBET = Central Centre for the Registration and Evaluation of Alternative and Complementary Methods to Animal Experiments

ECVAM (European Centre for Validation of Alternative Methods) at the EU Research Centre in Ispra (Italy); https://ec.europa.eu/jrc/en/eurl/ecvam

ICCVAM (Interagency Coordination Committee for the Validation of Alternative Methods) of the US federal authorities.



Key moment in the history of the 3Rs

2010: EU Regulation 'Directive 2010/63/EU' on the protection of animals used for scientific purposes.

includes a number of tasks to advance the 3Rs of animal procedures.

Directive 2010/63/EU assigns a **strong role to EU member states** to promote and implement alternative methods via reference laboratories and other coordinated initiatives in addition to EURL ECVAM.



Starting point for the establishment of 3R Centres

Power of Politics: The Rise of 3Rs Centres and platforms in Europe



Directive 2010/63/EU 30 3Rs center with huge potential to help especially on-site locally to take over 3Rs agenda centers/platforms number of 3Rs 20 Meetings 2018 organised by EUSAAT Meetings 2015/2016 organised by EURL-ECVAM 10 5 Transformation in national legislation 1995 2005 2010 2015 2020 2025

Further increase in 2022/2023: Finnish 3R Centre French 3R Centre Portuguese 3R Centre (i3S)





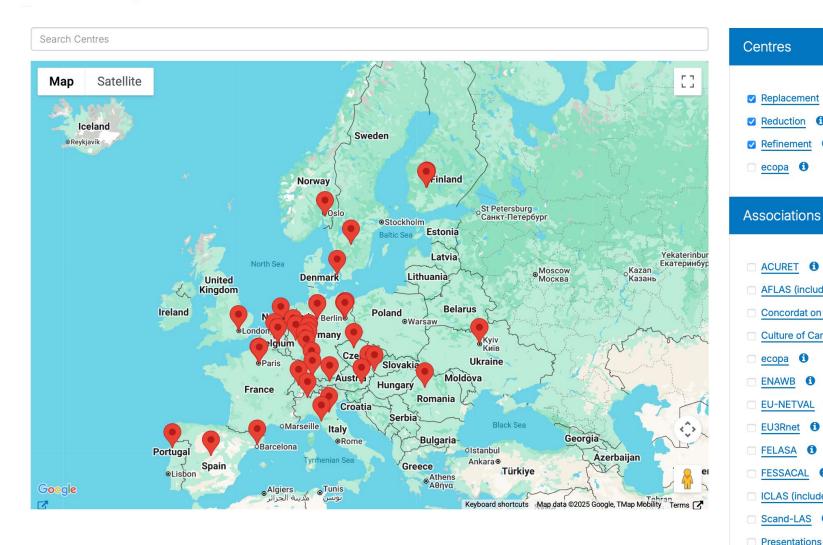


Data in table obtained from 26 3Rs centres and platforms participated in a survey of EU3Rnet (Neuhaus et al., ATLA, 2022)

The network of 3Rs centres in Europe

https://norecopa.no/EU3Rnet

norecopa.no / global3R





Number of members: ~100

✓ Refinement ① ecopa

ACURET 1

ecopa 🚯

ENAWB (1

EU3Rnet

FELASA (1)

FESSACAL 1

Scand-LAS ①

EU-NETVAL ①

AFLAS (includes South Korea) 1

ICLAS (includes South Korea) (1)

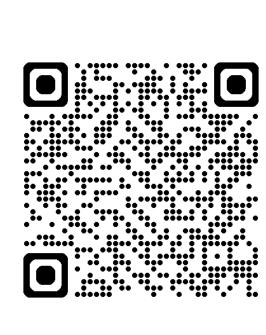
Presentations by Norecopa (1)

Concordat on Openness 1

Culture of Care Network 1

Reduction

Number of countries: 24



3Rs Centre/platform Initiative – Retrospective

IMPROVE

Platform for European 3R Centres Meeting

- Meeting Linz, EUSAAT 2018, September
 Network with 3R Centres + European Commission
- Meeting Berlin March 2019
- Meeting Prague (FELASA) June 2019
- Meeting Linz, EUSAAT 2019, October
- ✓ EU-COST Action 2020 as target
- ✓ Consensus statement of 3Rs center platform EU3Rnet
- ✓ Survey and publications about 3Rs centers activities

3Rs Initiative - Publication in ALTEX 02/2019



Invitation to all interested parties



European Society for Alternatives to Animal Testing

The European 3Rs Society

The network is a completely independent, open and free community, which is very much driven by the initiatives of its protagonists and personal efforts. It is based upon a bottom-up approach, and every 3R center or society is welcome to join.



"bottom-up approach"

of the network, since they cover many different topics and include experts on Refinement, Reduction and Replacement of animal experiments.

Major common aims were identified: to further advance the 3Rs, to help implement the aims of Directive 2010/63/EU locally, and to develop strategies and methods by which to reach out and connect with scientists in basic research. The network could also be used as a platform to exchange experience on a variety of topics, for example, how the various 3R centers and societies were established, how they organize events, how they secure funding, etc. In addition, it can also be utilized to share teaching strategies and resources to implement the 3Rs in education.

The network is a completely independent, open and free community, which is very much driven by the initiatives of its protagonists and personal efforts. It is based upon a bottom-up approach, and every 3R center or society is welcome to join.

Current coordinator: Winfried Neuhaus (winfried.neuhaus@ait.ac.at)

3Rs in Europe – EU3Rnet



Consensus Statement from the European Network of 3R Centres (EU3Rnet)

Winfried Neuhaus*

AIT - Austrian Institute of Technology GmbH, Center Health and Bioresources, Competence Unit Molecular Diagnostics, Vienna, Austria

A Network of European 3R Centres (EU3Rnet) was established in connection with the EUSAAT conference in 2018 in order to strengthen cooperation between different centres. Increased cooperation has a multitude of benefits, since many of the efforts made by local or regional centres are of national and international importance. As an important step, the members have decided to publish a consensus statement for the network.

Consensus Statement

EU3Rnet embraces *all* of the 3Rs (*Replacement*, *Reduction* and *Refinement*) throughout its work, since the 3Rs are the foundation of improved conditions for research animals and for better science.

EU3Rnet also considers it important to focus on *Non-Animal Methods*¹ as part of its collaborative efforts. *Non-Animal Methods* have largely been developed further after the introduction of the 3R concept by Russell and Burch² in 1959, thanks to technological advances in *in vitro* and *in silico* methods. EU3Rnet will therefore endeavour to promote this approach, so that researchers do not consider animal models by default when answering research questions, and instead consider the range of *Non-Animal*

Methods available, in order to avoid the unnecessary use of animal experimentation. When a relevant Non-Animal Method or an alternative Replacement method³ to an animal model does not exist, the possibilities for Reduction and Refinement of the model must be examined.

EU3Rnet considers it important that internationally relevant national efforts to develop and promote the 3Rs and *Non-Animal Methods* are disseminated within the network. The network will disseminate such information to its members, who in turn will disseminate the information further through their communication channels (which include websites, newsletters, symposia, training activities, annual reports and other channels).

EU3Rnet will emphasize the importance of involving all members of the research animal community in these efforts to develop and disseminate 3R resources. These include animal carers, technologists, veterinarians, teachers, lecturers and scientists.

All of the 3R centres in EU3Rnet pledge themselves to prioritization of their dissemination efforts. Whenever possible, they will use publically available platforms to disseminate this knowledge, in order to maximize exposure.

Participants of EU3Rnet, who agreed to the consensus statements

Institution	Country	URL		
EUSAAT - European Society for Alternatives to Animal Testing	Europe	http://www.eusaat.org/		
Unit Ethics and Human-Animal Studies, Messerli Research Institute, Vienna	Austria	https://www.vetmeduni.ac.at/en/messerli/ science/ethik/		
The RepRefRed society / Austrian 3R Center	Austria	https://www.reprefred.eu/EN		
MUI animalFree Research Cluster	Austria	https://www.i-med.ac.at/muianimalfree/		
Innovation Centre – 3R Alternatives (IC-3Rs)	Belgium	https://www.ic-3rs.org/		
3Rs Center Czech Republic	Czech Republic	http://www.szu.cz/		
The Danish 3R-Center	Denmark	https://3rcenter.dk/		
BB3R - Freie Universität Berlin	Germany	https://www.bb3r.de/		
Charité 3 ^R – Charité – Universitätsmedizin Berlin	Germany	https://charite3r.charite.de/		
Leibniz Alternatives at IUF – Leibniz Research Institute for Environmental Medicine	Germany	https://en.leibniz-alternatives.de/		
R2N - "Replace" und "Reduce" aus Niedersachsen	Germany	https://r2n.eu/		
TARC _{force} 3R - Medical University Mainz	Germany	https://www.unimedizin-mainz.de/tarc/ tarc-force-3r.html		
ICAR3R - Interdisciplinary Center for 3Rs in Animal Research	Germany	http://www.ICAR3R.de		
Comparative Medicine, Trinity College Dublin	Ireland	https://www.tcd.ie/comparativemedicine/		
Centro3R: Italian Interuniversity Center for the Promotion of the 3Rs Principles in Teaching and Research	Italy	http://www.centro3r.it/		
LIST - Luxembourg Institute of Science and Technology	Luxembourg	https://www.list.lu/		
Norecopa	Norway	https://norecopa.no/		
ROCAM - Romanian Center for Alternative Test Methods	Romania	http://rocam.usamvcluj.ro/		
Slovak National Platform for 3Rs in Research, Development and Education	Slovakia	https://www.snp3rs.com/		
CMCiB-IGTP - Comparative Medicine and Bioimage Centre of Catalonia, Germans Trias i Pujol Research Institute	Spain	http://www.cmcib.cat/		
The Swedish 3Rs Center	Sweden	https://www.jordbruksverket.se/3R		
Swiss 3RCC	Switzerland	https://www.swiss3rcc.org/en/		
3Rs-Centre of Utrecht University	The Netherlands	https://www.uu.nl/en/organisation/3rs-centre		
The National Centre for the 3Rs	UK	https://www.nc3rs.org.uk/		

Neuhaus, W. (2021) "Consensus statement from the European Network of 3R Centres (EU3Rnet)", *ALTEX - Alternatives to animal experimentation*, 38(1), pp. 138-139. doi: 10.14573/altex.2010061.

The Rise of 3Rs centres and platforms in Europe



50th Anniversary Article

The Rise of Three Rs Centres and Platforms in Europe*

Alternatives to Laboratory Animals 2022, Vol. 0(0) I-31 © The Author(s) 2022 DOI: 10.1177/02611929221099165 journals.sagepub.com/home/atl (\$)SAGE

Winfried Neuhaus¹, Birgit Reininger-Gutmann², Beate Rinner². Roberto Plasenzotti³. Doris Wilflingseder⁴, Joery De Kock⁵, Tamara Vanhae 50th Anniversary Article Dagmar Jírová⁶, Kristina Kejlová⁶, Lisbeth E. Knudsen⁷ Burkhard Kleuser⁸, Vivian Kral⁸, Christa Thöne-Reinek Giorgia Pallocca¹⁰, Marcel Leist¹⁰, Stefan Hippenstiel¹¹, The Current Status and Work of Three Rs Stephanie Krämer¹², Peter Jedlicka¹², Katharina Ameli Centres and Platforms in Europe* Julia Tigges¹³, Manuela Buettner¹⁵, Andre Bleich¹⁵, Nadi Marcus W. Meinhardt¹⁸, Rainer Spanagel¹⁸, Sabine Che Bettina Seeger²¹, Maren von Köckritz-Blickwede²², Je Viola Galligioni²³, Daniel Ruiz-Pérez²³, Dania Movia²⁴ Arti Ahluwalia²⁵, Valeria Chiono²⁶, Arno C. Gutleb²⁷, Ma Adrian Smith³³, Joanna Roszak³⁴, Maciej Stępnik^{34,35}, 2 I. Anna S. Olsson^{36,37}, Nuno Henrique Franco^{36,37}, B Helena Kandarova³⁹, Sara Capdevila⁴⁰, Jessica Johans Christopher R. Cederroth⁴², Jenny Sandström⁴², Ian Ra Horst Spielmann⁸

Alternatives to Laboratory Animal 2022, Vol. 50(6) 381-413

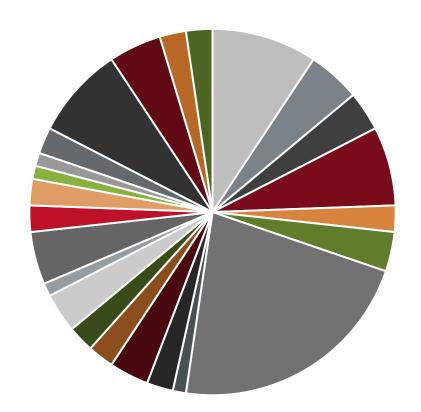
(\$)SAGE

Winfried Neuhaus¹, Birgit Reininger-Gutmann², Beate Rinner², Roberto Plasenzotti³, Doris Wilflingseder⁴, Joery De Kock⁵, Tamara Vanhaecke⁵, Vera Rogiers⁵, Dagmar Jírová⁶, Kristina Kejlová⁶, Lisbeth E. Knudsen⁷, Rasmus Normann Nielsen⁷, Leane van Weereld³⁰, Anne Kienhuis³¹, Erica van Oort Burkhard Kleuser⁸, Vivian Kral⁸, Christa Thöne-Reineke⁹, Thomas Hartung¹⁰, Giorgia Pallocca¹⁰, Costanza Rovida¹⁰, Marcel Leist¹⁰, Stefan Hippenstiel¹¹, Annemarie Lang¹¹, Ida Retter¹¹, Stephanie Krämer¹², Peter Jedlicka¹², Katharina Ameli¹², Ellen Fritsche^{13,14}, Julia Tigges¹³, Eliška Kuchovská¹³, Manuela Buettner¹⁵, Andre Bleich¹⁵, Nadine Baumgart¹⁶, Jan Baumgart¹⁷, Marcus W. Meinhardt¹⁸, Rainer Spanagel¹⁸, Sabine Chourbaji¹⁹, Bettina Kränzlin²⁰, Bettina Seeger²¹, Maren von Köckritz-Blickwede²², José M. Sánchez-Morgado²³ Viola Galligioni²⁴, Daniel Ruiz-Pérez²⁴, Dania Movia²⁵, Adriele Prina-Mello²⁶, Arti Ahluwalia²⁷, Valeria Chiono²⁸, Arno C. Gutleb²⁹, Marthe Schmit³⁰, Bea van Golen³¹, Leane van Weereld³², Anne Kienhuis³³, Erica van Oort³¹, Jan van der Valk³⁴, Adrian Smith³⁵, Joanna Roszak³⁶, Maciej Stepnik^{36,37}, Zuzanna Sobańska³⁶, Edyta Reszka³⁶, I. Anna S. Olsson^{38,39}, Nuno Henrique Franco^{38,39} Bogdan Sevastre ⁴⁰, Helena Kandarova ⁴¹, Sara Capdevila ⁴², Jessica Johansson ⁴³, Emma Svensk⁴³, Christopher R. Cederroth⁴⁴, Jenny Sandström⁴⁴, Ian Ragan⁴⁵, Nataliia Bubalo⁴⁶, Jens Kurreck⁴⁷ and Horst Spielmann⁸

Member distribution of the 3Rs platform [%]

IMPROVE

- Austria
- Belgium
- Czech Republic
- Denmark
- Estonia
- France
- Germany
- Hungary
- Ireland
- Italy
- Latvia
- Lithuania
- Luxembourg
- Norway
- Poland
- Portugal
- Romania
- Slovakia
- Spain
- Sweden
- Switzerland
- The Netherlands
- Ukraine
- United Kingdom
 - + Finland



EU3Rnet – The network of 3Rs centres in Europe



Uses (and is able to provide) educational material on the Three or training on Rs

Holds workshops Three Rs methods database

Has a searchable NAMs

Organises public Has an in vitro Rs meetings

and regular Three laboratory available for collaboration

Is a member of EU-NETVAL

Funds research

Table 2. (continued)

Name of the institution	Country	Uses (and is able to provide) educational material on the Three Rs	Holds workshops or training on Three Rs methods	Has a searchable NAMs database	Organises public and regular Three Rs meetings	Has an <i>in vitro</i> laboratory available for collaboration	Is a member of EU- NETVAL	Funds research
Norecopa	Norway	Yes	Yes	Yes	Yes			Yes
National Center for Alternative Methods to Toxicity Assessment (CMA)	Poland	Yes	Yes			Yes	Yes	
i3S	Portugal	Yes	Yes		Yes	Yes		
ROCAM	Romania	Yes						
Slovak National Platform for 3Rs- SNP3Rs	Slovak Republic	Yes	Yes					
CMCiB-IGTP-Comparative Medicine and Bioimage Centre of Catalonia, Germans Trias i Pujol Research Institute	Spain	Yes	Yes			Yes		
Swedish 3Rs Center	Sweden	Yes	Yes		Yes			
3RCC	Switzerland	Yes	Yes		Yes			Yes
National Center for the 3Rs (NC3Rs)	UK	Yes	Yes					Yes
The Ukrainian 3Rs Center	Ukraine	Yes				Yes		

EU3Rnet - Output



- Establishment of an active network of ~100 members from ~24 countries
- Interactions within the platform (Newsletter, Symposia organization)
- Publications:

Consensus statement from the EU3Rnet (ALTEX, 2021)

"The Rise of 3Rs centres and platforms in Europe" (ATLA, 2022, 50th edition) → >60 authors

"The current status and work of 3Rs centres and platforms in Europe" (ATLA, 2022, 50th edition) → 70 authors

In progress: "The future of European 3Rs centres"

COST Action IMPROVE proposal granted (~ 40 applicants, learnt to enter social sciences)





EU COST Action

a perfect tool to establish networking and future EU projects

COST Actions shall be implemented through a set of networking tools <u>such as meetings</u> (Action MC meetings, Working Groups, workshops, conferences), <u>Short-Term Scientific Missions</u> (STSMs), <u>Training Schools and Dissemination activities</u>.



Deliverables such as reports, data bases, progress in research question, new project applications, support of the field...





COST Action CA21139 3RS CONCEPTS TO IMPROVE THE QUALITY OF BIOMEDICAL SCIENCE (IMPROVE)

Therefore, the main aim of the COST Action IMPROVE is:

To establish a network which will work to refine, harmonise and promote data, documents and 3Rs concepts, in order to improve the quality of biomedical science.







3Rs concepts to improve the quality of biomedical science (IMPROVE) - Cost Action CA21139



Four working groups

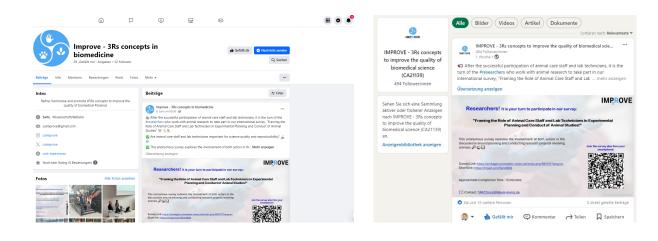


Figure 1: Main topics of the COST Action IMPROVE









150-200 k€/year for 4 years







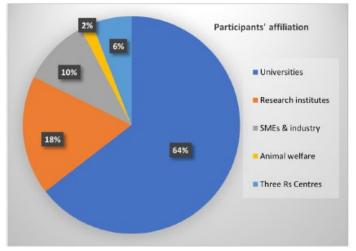
3Rs concepts to improve the quality of biomedical science (IMPROVE) - Cost Action CA21139

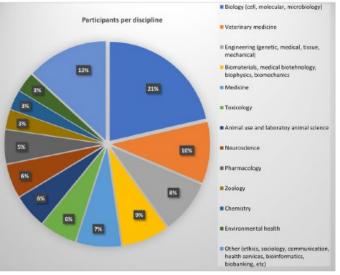


Current status of the EU COST Action IMPROVE

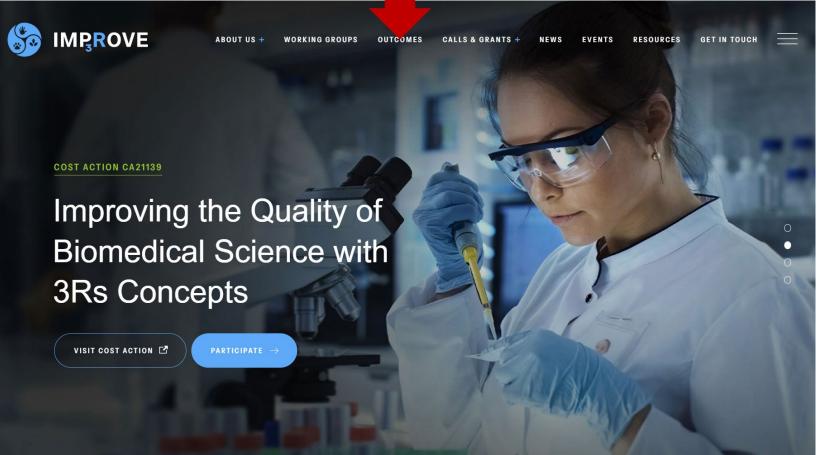
Currently grown to ~ 270 participants

- 42 countries including USA, Israel, Tunisia (21 ITC)
- 135 ITC (inclusiveness target countries)
- 148 female
- 117 Young Researchers & Innovators (under age of 40)





Kitsara et al., 2024, ATLA





78 Outcome reports until now:

FILTER BY TYPE

- All Categories
- O Conferences (6)
- O Dissemination Conference Grant (4)
- O ITC Conference grant (3)
- O Lectures & Talks (21)
- O Meetings (4)
- O Publications (23)
- O STSM (7)
- O Training Schools (2)
- O Virtual Mobility Grant (5)
- O Webinar (4)
- O Workshops (3)
- O YRI conference grant (1)







- Mindset workshop series; 3Rs webinar series in collaboration with TARCforce
- TATA Box workshop, 21.5.2024 (game about the implementation of NAMs from different perspectives)
- Career development workshop series
- STSMs (at BfR Germany, Swansea, Rome, Porto), ITC & Dissemination grants
- Austrian 3Rs Days (Dec 2023), Japanese Society for Alternatives to Animal Experiments (Nov 2023),

FENS Forum (June 2024)

 Asian 3Rs congress (Dec 2024) in New Delhi (Inauguration of the Asian Federation of 3Rs societies)







- Publications:
 - "COST Action Improve Introduction"; ATLA 2024 (Kitsara et al.)
 - "Toward a Common Interpretation of the 3Rs Principles in Animal Research"; Lab Animal 2024 (Lauwereijs *et al.*)





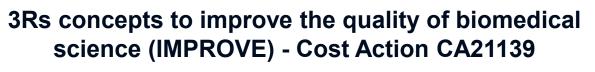
https://doi.org/10.1038/s41684-024-01476-2

Toward a common interpretation of the 3Rs principles in animal research

Jan Lauwereyns, Jeffrey Bajramovic, Bettina Bert, Samuel Camenzind, Joery De Kock, Alisa Elezović, Sevilay Erden, Fernando Gonzalez-Uarquin, Yesim Isil Ulman, Orsolya Ivett Hoffmann, Maria Kitsara, Nikolaos Kostomitsopoulos, Winfried Neuhaus, Benoit Petit-Demouliere, Simone Pollo, Brígida Riso, Sophie Schober, Athanassia Sotiropoulos, Aurélie Thomas, Augusto Vitale, Doris Wilflingseder & Arti Ahluwalia











- Surveys about
 - terms of NAMs by different stakeholders → publication in preparation
 - role of animal care takers in animal research care takers asked, separately researchers were asked → *publication in preparation*
- Topic subgroups
 - Overview about systematic reviews on Refinement
 - Systematic review on specific refinement measure(s) on the data quality of a refinement specific animal model
 - Survey on status quo of the use of housing/husbandry refinement measures across Europe
 - Pregistration of in vitro research

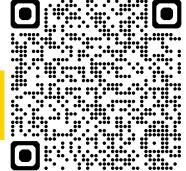






- Topic subgroups
 - Landscape analysis on "Implementation 3Rs"
 - What's in a NAM (definition paper) submitted for publication
 - A place for NAMs in biomedical research *submitted for publication*
 - NAMs expert data base poster 383
 - Survey on editorial perception of NAMs poster 386
 - Dissemination of 3Rs in Europe
 - Educational 3Rs activities within Europe
 - Evaluation of interdisciplinary research approaches to potentiate the 3Rs

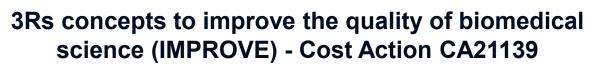






Utrecht University









Training school "3D cell models for 3R research" in Kaunas (Lithuania) on May 9-10 2024

Outcomes: Lectures, practical courses

17 participants

Talks:

- 2D vs. 3D models (focus on BBB)
- 3D reconstructed Epidermis models
- Reproducibility of 3D models
- 5D in vitro models

Practical courses:

- Skin irritation testing
- 3D tumor spheroids
- 3D fibrous scaffolds for cell culture









 WG 1+2 meeting in Utrecht (Netherlands) on June 17-18 2024, coupled with 3Rs conference on June 19 (The 3Rs and NAMs: all-inclusive?)

Outcomes: work on Working group 1+2 topics; Number of participants: 48 + ~ 20 online



https://tpi.tv/watch/132











Ethical X-over Workshop, 2./3.9.2024, Istanbul,

"Ethics, 3Rs, One Health"

Outcomes: Publications













• 3Rs centre meeting, 17.9.2024, Linz – co-organized with EU-SAAT 2024 **Outcomes:** Support of founding new 3Rs centres, Organisational development





Participant number:

- 30 + 28 online
- from > 20 countries







From September 18 – 20 at the University of Linz, Austria















• Workshop "3Rs in a CRO", Athens, Greece, 29.-30.5.2025
Outcomes: BIOEMTECH CRO Lab - Diving into preclinical research for drug discovery





Participant number:

34 on-site

Topics:

- Animal models used in theranostics
- Animal welfare when working with radiopharmaceuticals
- Visit in the facilities, focus on regulatory and safety in a CRO





Upcoming Cost Action Meetings



• 3Rs Centre Workshop, Genova, Italy, 17.-18.9.2025

 Training school for WG4 Education "Train-the-trainer", Porto, Portugal, 08.10.-10.10.2025







Benefits of the 3Rs centres network for the national authorities, national committees, competent authorities tasked with project evaluation and even to animal welfare bodies at establishment level:

- Resources of knowledge/experts (e.g. cases of questions within the network for 3Rs work)
- Bottom-up approach: very flexible/easy contacts
- Knowledge/stakeholder lists & contacts for the different specific fields
- Getting as stakeholders involved in the COST Action
- Collaboration between end-users and developers (e.g. industry, regulators, biotech companies, policy makers) increases the chance that developments meet performance criteria







Benefits of the 3Rs centres network for the national authorities, national committees, competent authorities tasked with project evaluation and even to animal welfare bodies at establishment level:

- Provide dissemination channels (outreach to (basic) scientists/ public / targeted stakeholders);
 concerted European activities (public awareness days)
- Connect educational 3Rs related activities within Europe and share experience, methodology and best practices
 - → support for the implementation in curricula
- Networking events/participation in COST Action events
- Establishment of common/European projects
- Etc.











European Society for Alternatives to Animal Testing

The European 3Rs Society

The annual EUSAAT Congress at the University of Linz, Austria

Our annual congress provides an opportunity to share scientific experience on alternatives to animal use in the life sciences, to get updated on the EU 3Rs policy and to discuss new concepts of implementing the 3Rs in academic education at the European and the international level.

LEARN MORE >



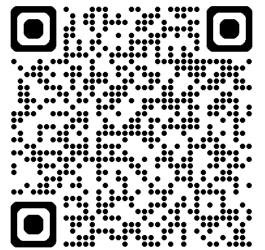








KICK OFF - Meeting of Management Committee 21.10.2022 Brussels



Interested?
Contact us – apply for Working groups online (read the MoU)!

Everyone is invited and needed (all stakeholders and various science fields)



