

Veterinary Medicine

Accelerating the transition

to an animal-free regulatory system:

Let's make it happen together!

ECHA NAM workshop Helsinki 1 June 2023

Merel Ritskes-Hoitinga

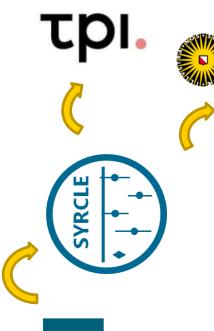
Prof in Evidence-Based Transition to Animal-Free Innovations Institute for Risk Assessment Sciences (IRAS) TOX

https://www.uu.nl/en/news/merel-ritskes-hoitinga-new-professor-of-evidence-based-transition-to-animal-free-innovations

Overview

- How did I get here?
- Where is the evidence?
- Can we act more upon scientific evidence / using systematic reviews?
- Accelerating the transition to animal-free innovations transition science
- Setting goals and leadership











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Utrecht University

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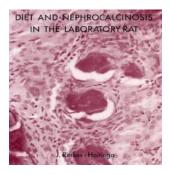
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The story of my life: from Refinement to Replacement













Where and what is the evidence behind drug legislation?

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> Altern Lab Anim. 2022 Sep;50(5):322-329. doi: 10.1177/02611929221118001. Epub 2022 Aug 1	9. FULL TEXT LINKS		Merel Ritskes-Hoitinga 1,2,* , Yari Barella 3 and Tineke Kleinhout-Vliek 4	
A History of Regulatory Animal Testing: What Can We Learn?	SAGE journals Open access full test ACTIONS	NEXT RESULT 3 of 120	 Department of Population Health Sciences, Institute for Risk Assessin Faculty of Veterinary Medicine, Utrecht University, Postbus 80163, 35 Department of Clinical Medicine, Faculty of Health Sciences, Aarhus Palle Juul Jensens Boulevard 99, 8200 Aarhus N, Denmark 	508 TD Utrecht, The Netherlands 5 University Hospital,
Doortje Swaters ¹ , Anne van Veen ² , Wim van Meurs ¹ , Janette Ellen Turner ³ , Merel Ritskes-Hoitinga ^{4, 5}	66 Cite		 ³ Faculty of Science, Radboud University, Postbus 9010, 6500 GL Nijme yaribarella.94@gmail.com ⁴ Copernicus Institute of Sustainable Development, Utrecht University, 3508 TC Utrecht, The Netherlands; Lh.kleinhout-vliek@uu.nl 	· · · · · · · · · · · · · · · · · · ·
Affiliations + expand PMID: 35983829 DOI: 10.1177/02611929221118001	Collections		* Correspondence: j.ritskes-hoitinga@uu.nl	
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The contemporary pharmaceutical industry is voicing growing concerns about the translatability and reproducibility of animal models. In addition, the usefulness of certain of the required regulatory safety tests in animals is being increasingly questioned. It remains difficult, however, to make the move toward alternative testing methods, not least because of legislative demands. A historical analysis was performed, in order to study how the mandatory animal studies in legislative requirements came about. This article reflects on the role that specific public health disasters played in the creation of (more) regulatory requirements for animal testion. It will show how the	PAGE NAVIDATION		nature > world view > article	
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Software beats animal tests at predicting toxicity of chemicals **Can we use evidence more?**

What are systematic reviews?

Systematic reviews bring us the most

objective and complete scientific evidence

and lead to better evidence-based decision making







Systematic Review results:

low publication quality

and low translation of animal studies to

humans is made transparant.

Scientific need for change.

Changes coincide with resistance.



It needs perseverance and

managing transitions:

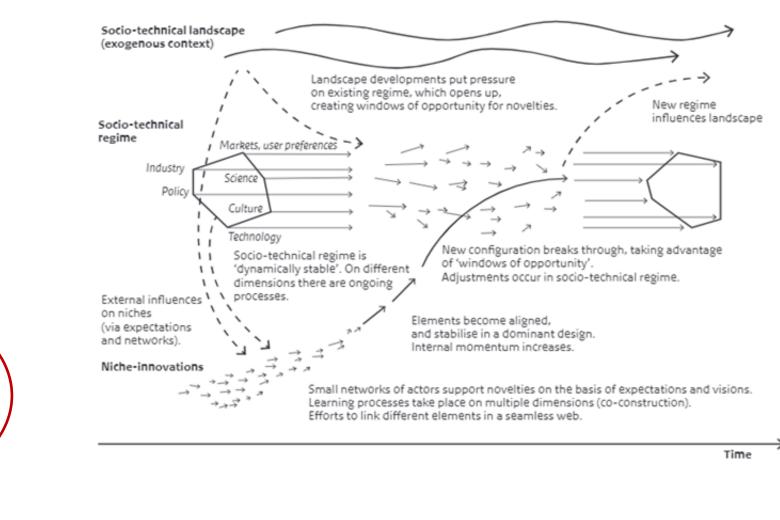
Transition science



Multi-level perspective transition analysis

Identify: Barriers, leverages and opportunities

Niche: Alternative system Regime: Dominant system Landscape: Societal trends



Radboud

Honours Geels, F. W. (2011). The multi-level perspective on sustainability transitions: Responses to seven criticisms.

Academy Environmental innovation and societal transitions, 1(1), 24-40.

Goal:

Identify

opportunities to

accelerate the transition

TPI The Dutch Transition Program to animal-free Innovations

Mission: Better predictions without (lab) animals

Ambition:

The Netherlands with TPI as a catalyst of the (inter)national transition towards animal-free innovations

Partner program founded in 2018: 11 partners (including a young TPI!)

TPI-policy is in conjunction with 3Rs policy, to ensure animal- welfare as long as animals are needed.



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PRUEFULESVIRIJ







Universities of The Netherlands



National Institute for Public Health and the Environment Ministry of Health, Welfare and Sport



Netherlands National Committee for the protection of animals used for scientific purposes



Ministry of Agriculture, Nature and Food Quality of the Netherlands

TPI International ambition and activities

European/international approach is crucial to validate, accept and implement non-animal methods (NAMs).

TPI:

- Plans to start conversations with other EU member states about validation of NAMs;
- To find common ground on what is needed to improve validation;
- Together we can accelerate our national efforts and improve our chances to a European approach!







Interested or questions ? Feel free to contact our program manager:

Erica van Oort, PhD <u>e.vanoort@minlnv.nl</u> Ministry of agriculture, nature and food quality

www.animalfreeinnovationtpi.nl





Education: Multi-level perspective transition analysis

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Co-creation

Interdisciplinary learning



Commentary

Identifying Key Factors for Accelerating the Transition to Animal-Testing-Free Medical Science through Co-Creative, Interdisciplinary Learning between Students and Teachers

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MDPI

Funding Dutch Research Agenda (NWA): Non-animal models, acceptance and implementation



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News & events > News > Three consortia awarded funding for acceptance and implementation of animal-free models in safety assessment

Three consortia awarded funding for acceptance and implementation of animalfree models in safety assessment

25 August 2022

Within the Dutch Research Agenda (NWA) 'Non-animal models: acceptance and implementation', three consortia will research on the acceptance and implementation of existing animal-free models. A total of about € 2.9mln has been awarded for this research. This programme is a collaboration between the Dutch Ministries of Infrastructure and Water Management (I&W), Public Health,



Characteristics

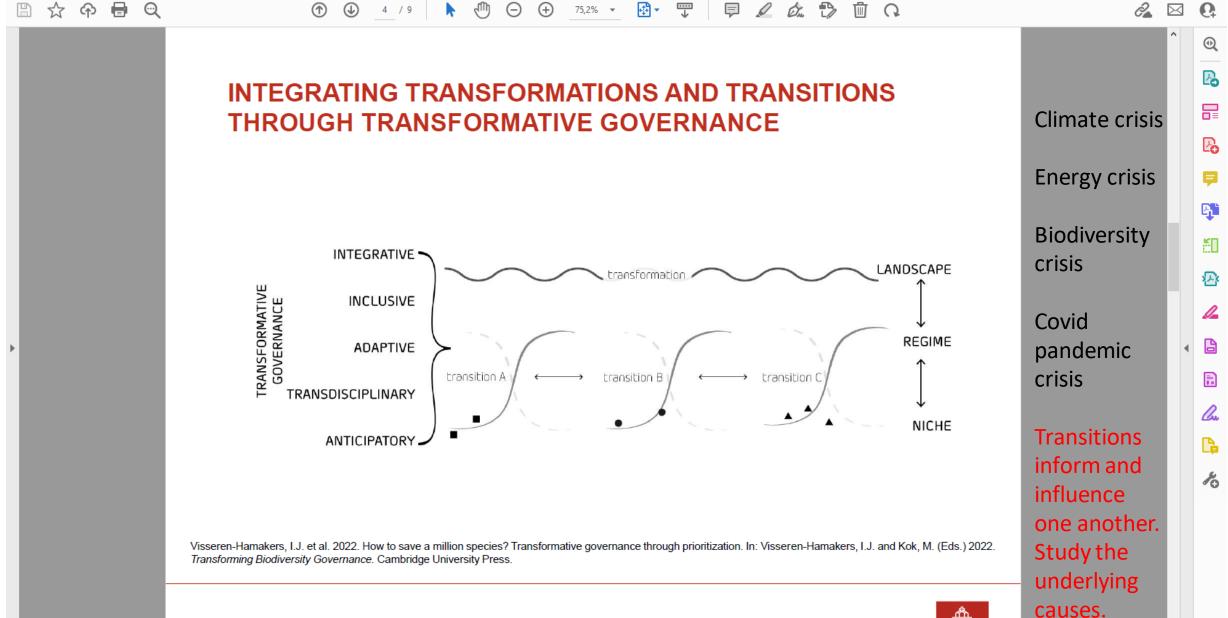
Research programme Animal-free assessment models: acceptance and implementation

Themes

Knowledge Utilisation Health Open Science Key Technologies Safety Food

Type <u>Awards</u>

SAFE = Safety Assessment through animal-free evolution



We need mixed methods research and flexible approaches: combining quantitative and qualitative research

We need inter – and transdisciplinary research

Providing scientific evidence is clearly not sufficient to make real changes





Pyrogen testing revisited on occasion of the 25th anniversary of the whole blood monocyte activation test



https://doi.org/10.14573/altex.2101

rabbit pyrogen test alternative

methods lipopolysaccharide

Published: Jan 12, 2021

DOI:

051

Keywords:

Thomas Hartung 🚳

Johns Hopkins Bloomberg School of Public Health, Center for Alternatives to Animal Testing, Baltimore, MD, USA; Center for Alternatives to Animal Testing, CAAT-Europe, University of Konstanz, Konstanz, Germany https://orxid.org/0000-0003-1359-7689

Abstract

The whole blood pyrogen test invented 25 years ago, and its variant based on cryopreserved blood one year late; brought momentum into the field of pyrogen testing, which, despite the broad application of the Limulus amebocyte lysate (LAL) assay, aka bacterial endotoxin test (BET), consumed several hundred thousand rabbits per year world-wide. The resulting international validation and lengthy acceptance and implementation process of what are called now monocyte activation tests (MATs) finally is impacting on animal numbers – at least in Europe – reducing them by more than 70% and counting. The author sees no reason for continuing any regulatory rabbit testing for pyrogens except the lack of acceptance of MATs in some regions of the world. The availability of MATs has opened also the discussion about the shortcomings of LAL/BET, namely its restriction to Gram-negative pyrogens, non-reflection of the MPS World Summit 2023 Berlin, Germany June 26-30, 2023 mpsworldsummit.com

Impact Factor 2021: 6.250

5-Year Impact Factor: 6.645

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bstract submission extended to

Monocyte activation test was validated 25 yrs ago, now finally incorporated in the European Pharmacopoiea to replace rabbit pyrogen test.

Why has this taken so long?!



Promising recent developments – transition is happening

Multi stakeholder article on building scientific confidence in New Approach Methods – van der Zalm A et al. Archives Toxicology 2022

European Citizen's initiative

European Parliament asking for a roadmap

Food and Drug Administration modernisation act

European Medicines Agency 3R working party

European Food Safety Authority roadmap

This European Chemicals Agency New Approach Methods workshop





Next generation (animal-free) risk assessment:

Human biology central Science and regulations meet

THE CHALLENGE

HUMAN-RELEVANT SCENARIOS

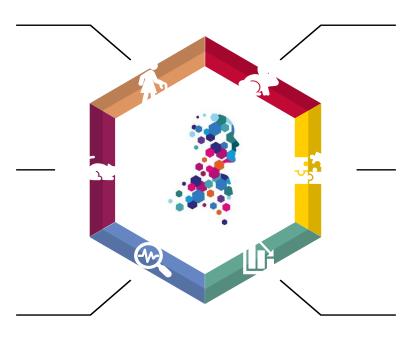
Current animal tox testing regimes do not reflect human-relevant scenarios, such as differences in susceptibility due to age, gender, timing of exposure, or disease state.

REPRODUCIBILITY

Only 25% of published results obtained with animal data can be reproduced.

PREDICTIVE VALUE

The results of a laboratory animal can only predict the results in reproductive toxicity of another species by 60%.



9,338,162 ANIMALS

Were still being used for research and testing in the EU in 2017 (about one third for toxicity testing).

INTERDISCIPLINARY APPROACH

Integrating data from new in vitro and in silico methods, data sciences and social sciences

SLOW DECREASE

In 10-years time, the use of animals is only decreased by 22% with the current approach to gradually refine, reduce and replace animal testing.



Virtual human platform for safety assessment of chemicals and pharmaceuticals

VHP4Safety project NWA 1292.19.272 is part of the NWA research program 'Research along Routes by Consortia (ORC)', which is funded by the Netherlands Organization for Scientific Research (NWO).

Let's make it happen together! Phase out animal studies and embrace alternatives asap for the benefit of animals and humans. The science and technology *are* here!

New (academic) pathways:

More evidence-based decision making

Transdisciplinary research and education – connecting stakeholders

Multilevel perspectives, transition science and transformative governance

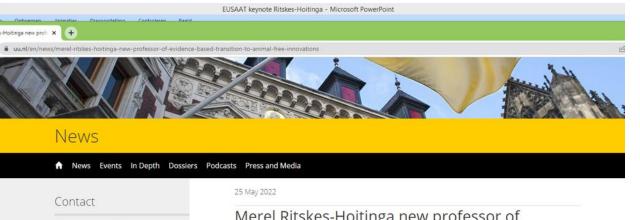


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Press Officers faculty of Veterinary

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Merel Ritskes-Hoitinga new professor of Evidence-Based Transition to Animal-free Innovations



We choose to go to the moon...

.. in this decade, not because it's easy, but because it's hard, it will serve to organise and measure the best of our energies and skills, a challenge we are willing to accept, unwilling to postpone and intend to win





We choose to go for New Approach Methods (NAM) only

.. in this decade, not because it's easy, but because it's hard, we will only use NAMs because it will serve to organise and measure the best of our energies and skills in a challenge we are willing to accept and unwilling to postpone in the interest of all living creatures and our environment



