The A S C
Animals in Science Committee

AWERB Hub Workshop

2 April 2025
13:00–16:00

Welcome — we will be starting shortly!

Agenda

Time	Topic	Presenter(s)
13.00 – 13.10	Welcome, Introductions and Workshop Protocol	Caroline Chadwick
13:10 – 13:25	Update on the work of the Animals in Science Committee	Wendy Jarrett
13:25 – 13:40	Update from the NC3Rs	Nathalie Percie du Sert
13:40 – 14:30	Introduction to alternative methods	Barney Reed Dharaminder Singh Cathy Merry
14:30 – 14:40	Break	
14:40 – 15:55	Practical advice for AWERBs on assessing replacement	Adrian Smith Elaine Blair
15:55 – 16:00	Final thoughts and feedback	Caroline Chadwick

Workshop Protocols

Remain on mute when not speaking

Ask questions during dedicated Q&A time using the chat function

Attendees are welcome to use chat and reaction functions

In breakout rooms, please use hands-up feature

Briefly introduce yourself before speaking

Audience contributions during plenary will be recorded for writing the workshop report – this does not apply to breakout rooms

The ASC
Animals in Science Committee

Poll

What is your role within your AWERB? (select all that apply)

- ☐ Chair
- ☐ Secretary
- ☐ PIL holder
- ☐ PPL holder
- ☐ NVS
- ☐ NACWO
- ☐ NTCO
- ☐ NPRC
- ☐ NIO
- ☐ HOLC
- ☐ Lay member
- ☐ Statistician
- ☐ Other (tell us in the chat!)

Poll

How long have you been an AWERB member?

1. < 6 months
2. 6 months–1 year
3. 1–2 years
4. 2–5 years
5. 5–10 years
6. 10+ years

The ASC
Animals in Science Committee

The A S C
Animals in Science Committee

Update on the work of the Animals in Science Committee

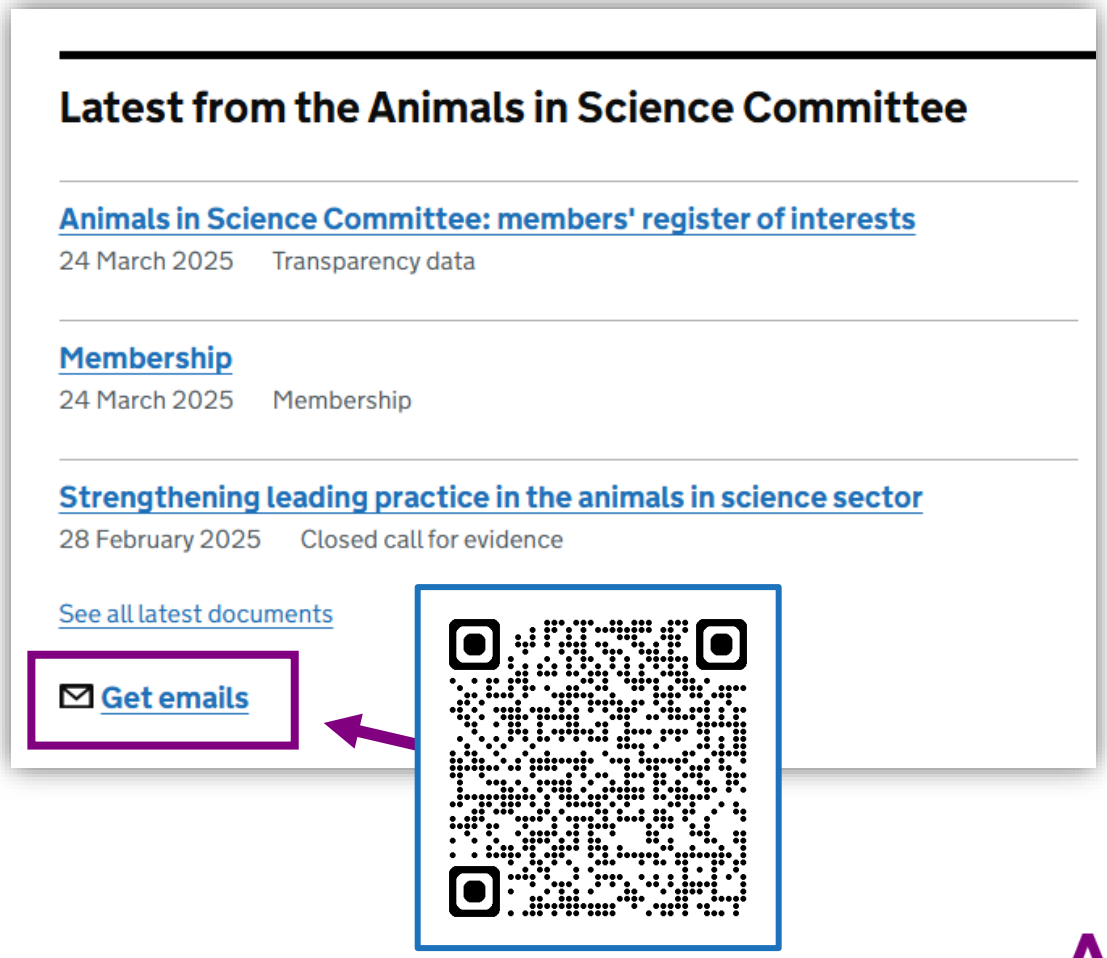
Wendy Jarrett, Understanding Animal Research

ASC Chair appointment

Professor David Main will finish his tenure as ASC Chair on 31 May 2025.

A new Chair has been appointed to begin their term on 1 June 2025.

The announcement will be published on the ASC website on **10 April 2025.**



The ASC
Animals in Science Committee

ASC AWERB Hub workshop report for October 2024

GOV.UK

Home > Business and industry > Science and innovation > Animal research and testing

Corporate report

ASC and AWERB Hub workshop report: October 2024

Report for the Animal Welfare Ethical Review Body (AWERB) subgroup of the Animals in Science Committee's (ASC) 11th workshop on 16 October 2024.

From: Animals in Science Committee

Published 9 January 2025

[ASC and AWERB Hub workshop report: October 2024 – GOV.UK]

The ASC
Animals in Science Committee

Hub Restructuring

- At the end of 2024, the Chair of the **Home Counties North West and Middlesex Hub** stepped down as Hub Chair.
- As there have been no volunteers for the Hub Chair role, the AWERBs within this Hub have now been reallocated, and the Home Counties North West and Middlesex Hub has closed.

- A volunteer has come forward from the previously inactive **East Anglia Hub** expressing interest in reactivating the Hub.
- Many of the AWERBs affected by Home Counties North West and Middlesex Hub closure have been reallocated to the newly reinstated East Anglia Hub.
- The paired ASC Member for the East Anglia Hub is Mrs Tina O'Mahony.

The updated list of AWERB Hubs:

Hub	Paired ASC Member
• Scotland	Dr Dharaminder Singh
• Northern Ireland	Mrs Wendy Jarrett
• Northern England	Dr Lucy Whitfield
• North-West England	Dr Lucy Whitfield
• Central England	Mrs Caroline Chadwick (Chair)
• Wales West and Southwest	Mrs Caroline Chadwick (Chair)
• East Anglia	Mrs Tina O'Mahony
• London	Mrs Wendy Jarrett
• South	Mrs Tina O'Mahony

Detailed Commissions Published

Correspondence

Commission on non-technical summaries and retrospective assessments

Published 18 December 2024

A commission for advice from the Home Office to the Animals in Science Committee (ASC) on improving non-technical summaries and retrospective assessments.

Correspondence

Commission on leading practice in the animals in science sector

Published 18 December 2024

A commission for advice from the Home Office to the Animals in Science Committee (ASC) on strengthening leading practice in the animals in science sector.

Correspondence

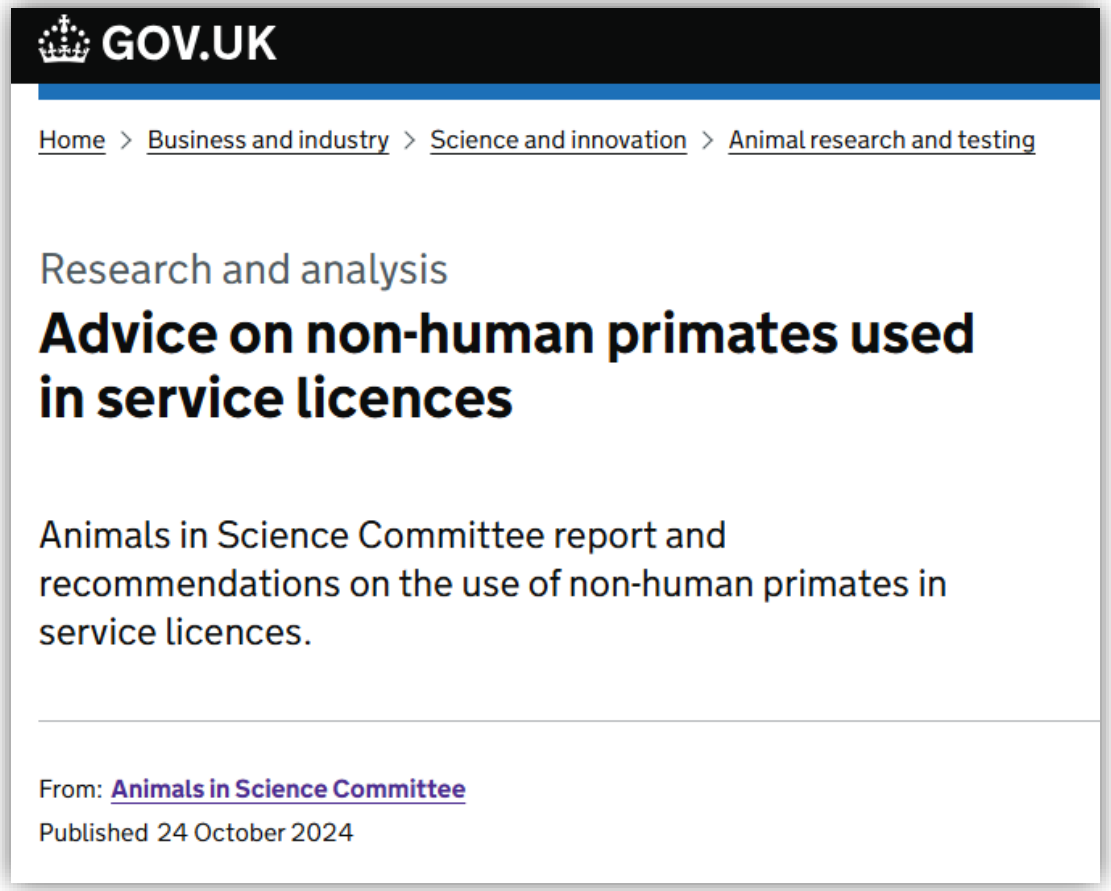
Commission on AWERBs and Named Information Officer

Published 12 February 2025

A commission for advice from the Home Office to the Animals in Science Committee (ASC) on strengthening the functioning of AWERBs and Named Information Officer.

The ASC
Animals in Science Committee

Non-human primates used in service licences report



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Home > Business and industry > Science and innovation > Animal research and testing

Research and analysis

Advice on non-human primates used in service licences

Animals in Science Committee report and recommendations on the use of non-human primates in service licences.

From: Animals in Science Committee

Published 24 October 2024

[Advice on non-human primates used in service licences - GOV.UK]

The ASC
Animals in Science Committee

AWERB-UK meeting

Strengthening AWERBs: Resource, Engagement, and Recognition

18 June 2025,
Central London,
Free to attend

How to ensure adequate resources for the AWERB, with respect for and engagement with it across the entire establishment.

Register here:
AWERB-UK - 18th June 2025, London

If you require any further information, please contact animalsinscience@rspca.org.uk.

The ASC
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Any Questions?

The ASC
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Update from the NC3Rs

Dr Nathalie Percie du Sert, NC3Rs

National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

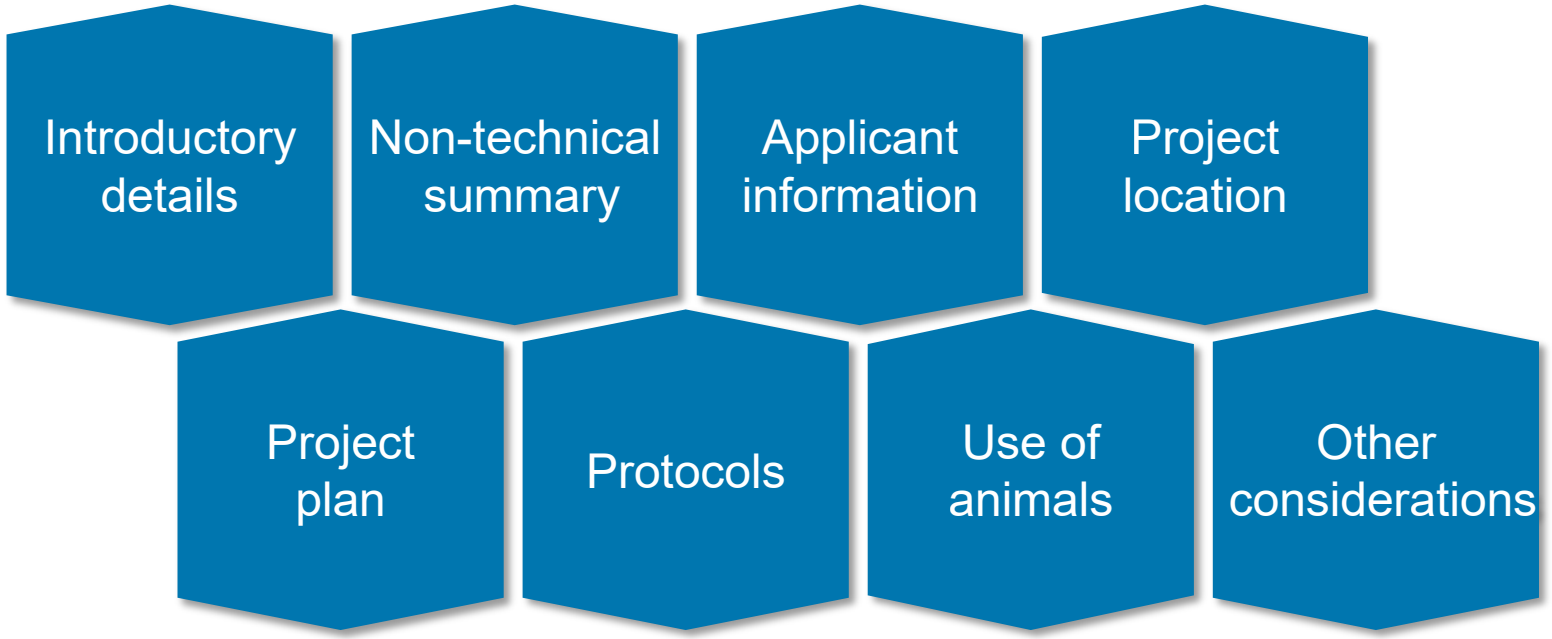
Update from the NC3Rs: Licence application review

Dr Nathalie Percie du Sert
Director of Research Practice

AWERB Hub Workshop
Wednesday 2 April

Pioneering Better Science

The current Project Licence form



Review process:

- Review by NC3Rs team – four staff from different teams across the organisation
- Consultations – interviews with selected stakeholders
- Recommendations to ASRU and ASRP (followed by further consultations)

The current Project Licence form – SWOT analysis

Strengths

- Detailed, all in one place
- Level of familiarity with existing process

Weaknesses

- Too long to review fully
- Repetitive – applicants miss the subtle differences between similar questions
- Repetition between licence and NTS
- Does not promote sharing of techniques – multiple groups doing same procedures in different ways
- 3Rs get lost in the current form

Opportunities

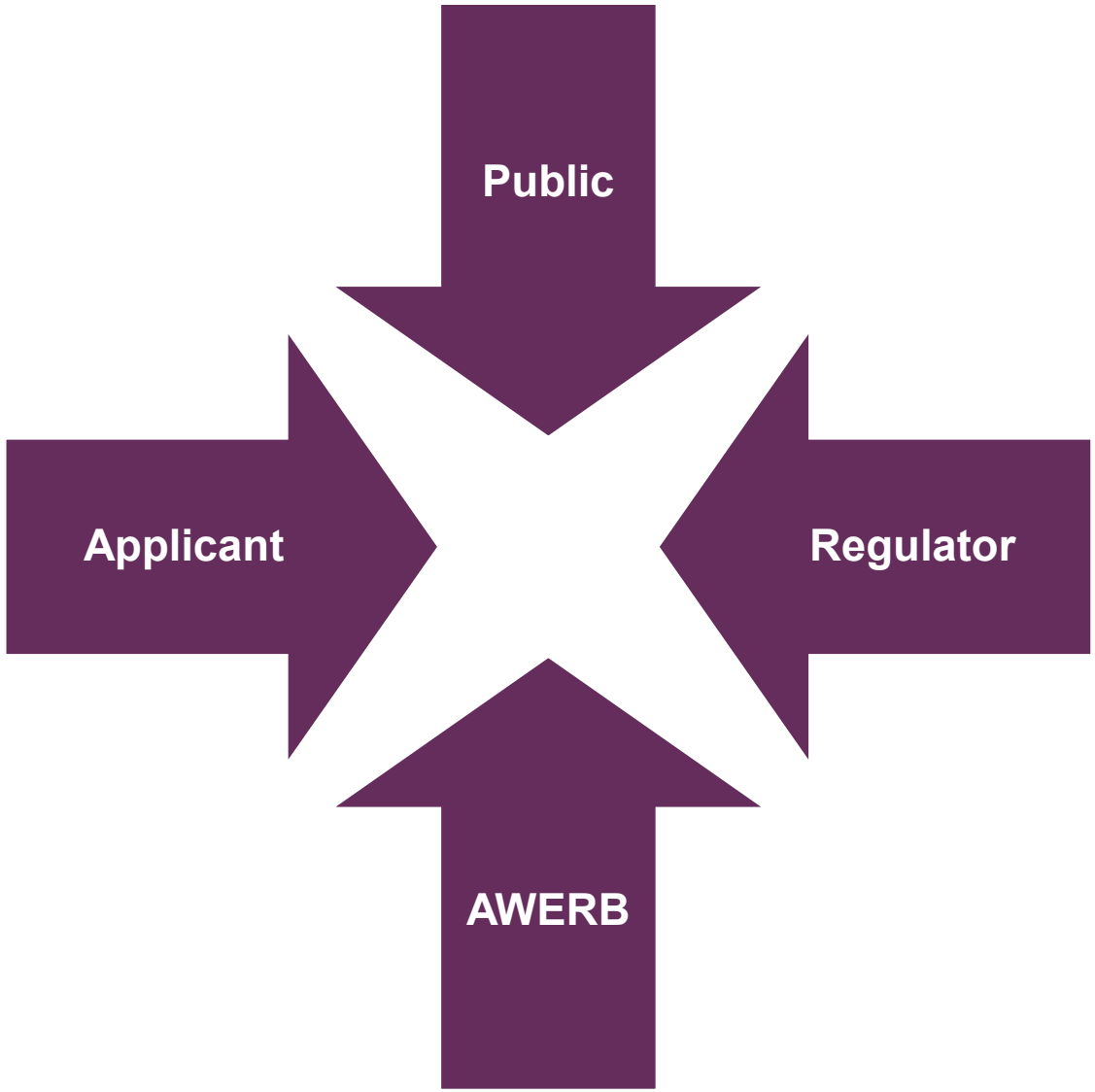
- AWERB to learn from HOI comments to a PPL application
- Use of study plans to audit training records and compliance

Threats

- Licence not reviewed appropriately because too long
- Copy and paste of answers between sections and during licence renewals obfuscate and stifle 3Rs progress

Options investigated

- **Consolidate the NTS and Licence questions**
- **Use Standard Operating Procedures (SOPs) outside of the licence to replace some question sets**
- **Greater use of study plans to monitor individual studies under a project licence**



Options investigated

- **Consolidate the NTS and Licence questions**
- **Use Standard Operating Procedures (SOPs) outside of the licence to replace some question sets**
- **Implement study plan documentation to monitor individual studies under a project licence**

Concepts covered in the NTS are duplicated in more nuanced ways in the Licence (e.g. protocols)

NTS	Licence
Which animal models and methods will you use during this project?	Why is each type of animal, experimental model, and/or method selected for this protocol a) the most appropriate scientific approach? b) the most refined for the purpose?
Why can't you use animals that are less sentient?	For each model and/or method, what is the scientific need for the expected clinical signs?
How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals?	Why scientifically do the animals need to suffer to this degree?
What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?	Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?
	How will you assess the suitability of these substances, and minimise the unnecessary harms arising from their administration given the particular strain or type of animal you will be using?

Options investigated

- **Consolidate the NTS and Licence questions**
- **Use Standard Operating Procedures (SOPs) outside of the licence to replace some question sets**
- **Implement study plan documentation to monitor individual studies under a project licence**

Concepts covered in the NTS are duplicated in more nuanced ways in the Licence (e.g. protocols)

NTS	Licence
How have you estimated the numbers of animals you will use?	How will you choose different experimental groups?
What steps did you take during the experimental design phase to reduce the number of animals being used in this project?	How will you choose control groups?
What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project?	How will you minimise variables to ensure reproducibility?
	How will you determine group sizes?
	How will you maximise the data output from the animals you use on this protocol?

Options investigated

- **Consolidate the NTS and Licence questions**
- **Use Standard Operating Procedures (SOPs) outside of the licence to replace some question sets**
- **Implement study plan documentation to monitor individual studies under a project licence**

Initial SWOT analysis

Strengths

- New format allows focus on HBA without diluting information between questions
- Removes repetition

Weaknesses

- Does not fit with current ASRU processes which split NTS from licence once approved.

Opportunities

- Saves time for researcher, AWERB and inspector
- Increased transparency to the public with greater detail
- More time can be allocated for audit and to focus on local best practice

Threats

- Applicants might be reluctant to disclose all information in the publicly available NTS
- Risk that language is either too lay or too technical for all audiences

Options investigated

- Consolidate the NTS and Licence questions
- **Use Standard Operating Procedures (SOPs) outside of the licence to replace some question sets**
- Implement study plan documentation to monitor individual studies under a project licence

Initial SWOT analysis

Strengths

- Allows focus on HBA, without dilution with extra info
- Shorter form reduces review fatigue
- Some SOPs/standard protocols already developed and used at facility level

Weaknesses

- Need to check SOPs to identify procedures not permissible/best practice

Opportunities

- Common local SOPs promote refinement – easier to identify opportunities
- Promote sharing of best practice e.g. via AWERB hubs
- SOPs support role of the NTCO
- Agility for minor changes to protocols
- Saves time for researcher, AWERB and inspector in the long run

Threats

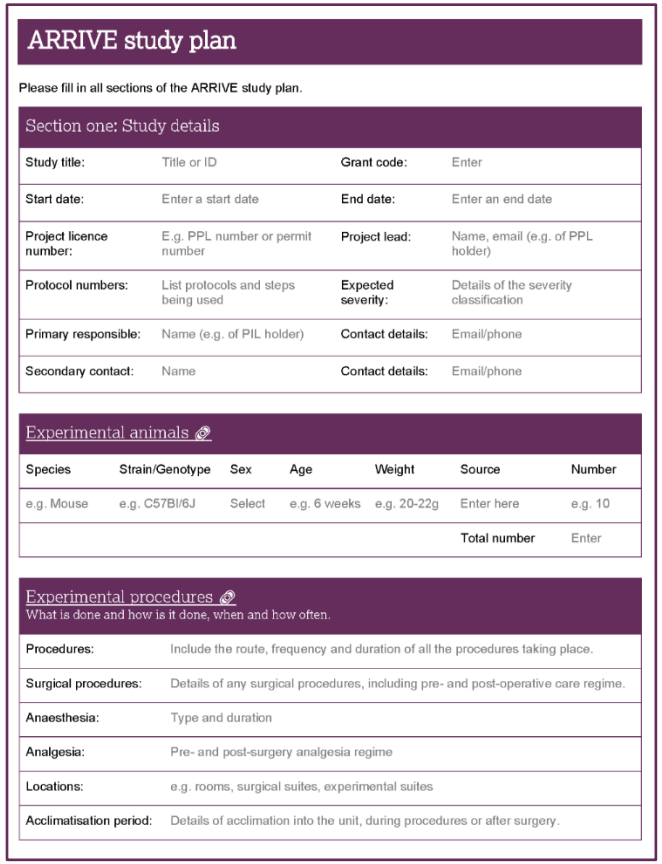
- May need standardised SOP templates
- Need to work at different levels (procedures and processes)
- Initial pressure on some AWERBs as SOPs are established
- Perceived accountability to the public
- Researchers reluctant to change individual practice

Options investigated

- Consolidate the NTS and Licence questions
- Use Standard Operating Procedures (SOPs) outside of the licence to replace some question sets
- **Implement study plan documentation to monitor individual studies under a project licence**

Capitalising on the use of study plans

- Details plan for an individual study
- Contain study-specific information:
  - Personnel involved
  - Animals
  - Monitoring and humane endpoints
  - Experimental design
- Study plans used by animal units for:
  - Record keeping
  - Compliance monitoring
  - HO audit
- Recently launched ARRIVE study plan
  - Template ensures all relevant information is included



ARRIVE study plan

Please fill in all sections of the ARRIVE study plan.

Section one: Study details

Study title:	Title or ID	Grant code:	Enter
Start date:	Enter a start date	End date:	Enter an end date
Project licence number:	E.g. PPL number or permit number	Project lead:	Name, email (e.g. of PPL holder)
Protocol numbers:	List protocols and steps being used	Expected severity:	Details of the severity classification
Primary responsible:	Name (e.g. of PIL holder)	Contact details:	Email/phone
Secondary contact:	Name	Contact details:	Email/phone

Experimental animals

Species	Strain/Genotype	Sex	Age	Weight	Source	Number
e.g. Mouse	e.g. C57Bl/6J	Select	e.g. 6 weeks	e.g. 20-22g	Enter here	e.g. 10
					Total number	Enter

Experimental procedures

What is done and how is it done, when and how often.

Procedures:	Include the route, frequency and duration of all the procedures taking place.
Surgical procedures:	Details of any surgical procedures, including pre- and post-operative care regime.
Anaesthesia:	Type and duration
Analgesia:	Pre- and post-surgery analgesia regime
Locations:	e.g. rooms, surgical suites, experimental suites
Acclimatisation period:	Details of acclimation into the unit, during procedures or after surgery.

arriveguidelines.org/resources/study-plan

National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

nathalie.perciedusert@nc3rs.org.uk
nc3rs.org.uk
linkedin.com/company/national-centre-3rs

Pioneering Better Science

Any Questions?

The ASC
Animals in Science Committee

The A S C
Animals in Science Committee

Introduction to alternative methods

Barney Reed, RSPCA

Dr Dharaminder Singh, CN Bio

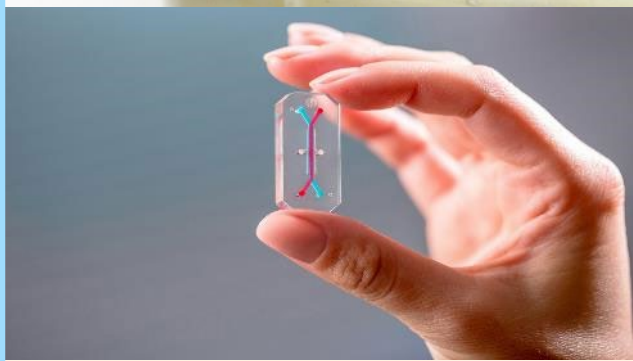
Prof Cathy Merry, The University of Nottingham

Poll

? How familiar are you with the field of alternative methods?

1. Not at all familiar
2. Slightly familiar
3. Neutral
4. Familiar
5. Very familiar

Accelerating the replacement of animals in science - initiatives and strategies



RSPCA ANIMALS IN SCIENCE

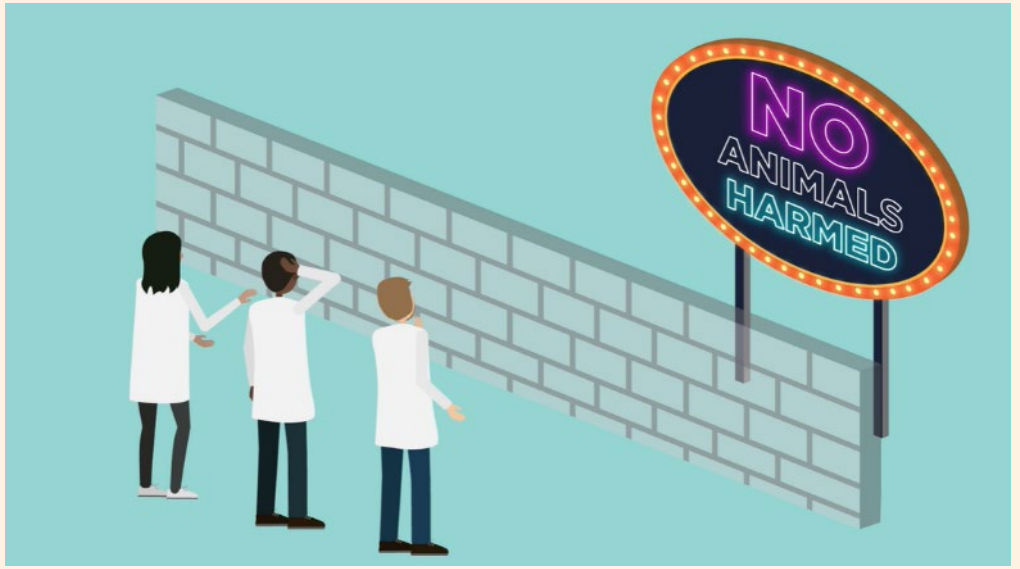
BARNEY REED

A shared ambition

To enable:

- high quality science to be undertaken
- important questions to be answered
- increased availability of safe and effective medicines etc.

- in scientific processes that do not involve causing harms to sentient animals



George Freeman,
Minister for Science,
Research & Innovation

25 October 2021

"…while I do not believe we are yet at the point where we can completely move away from reliance on animals, I make it very clear that ***we need to move faster.*** *We need to reiterate to the public that* ***that is our intent.***"

"We are seeking proper funding ***to move away from the use of animals.***"

Sarah Dines
Parliamentary Under Secretary of State
Home Office

16 January 2023

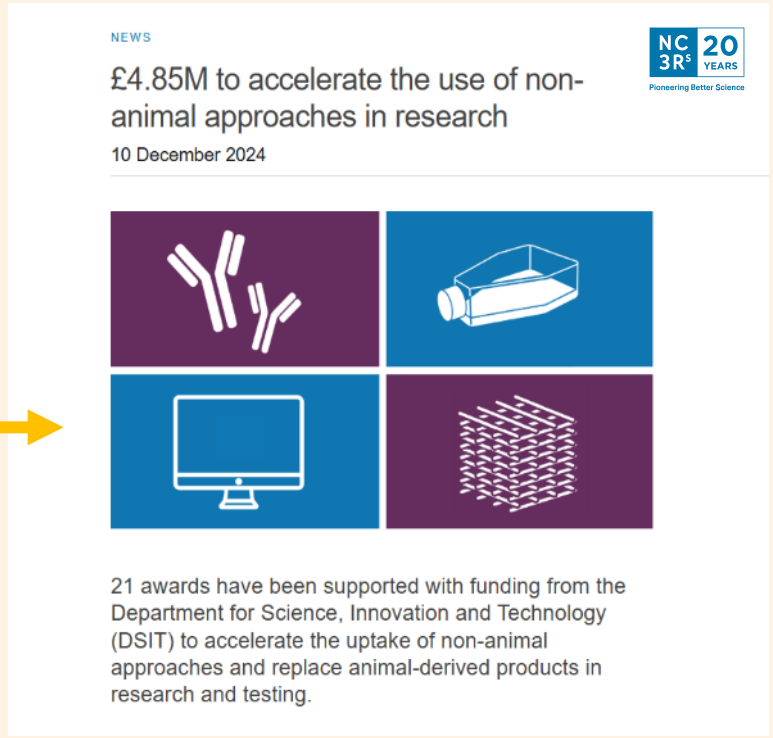
https://hansard.parliament.uk/commons/2021-10-25/debates/486708F3-E5DE-4121-B9E0-F146AFF73031/AnimalTesting
https://hansard.parliament.uk/commons/2023-01-16/debates/CE7E0DD2-CD4E-4C47-A58D-983D6E2BC128/CommercialBreedingForLaboratories

19 February 2024

Andrew Griffith MP
Minister for Science, Research & Innovation

*"I asked UKRI that we **double our investment** in research to achieve the three Rs and develop non-animal alternatives".*

"the Government will publish a plan to accelerate the development, validation and uptake of technologies and methods to reduce reliance on the use of animals in science".



NEWS

£4.85M to accelerate the use of non-animal approaches in research

10 December 2024

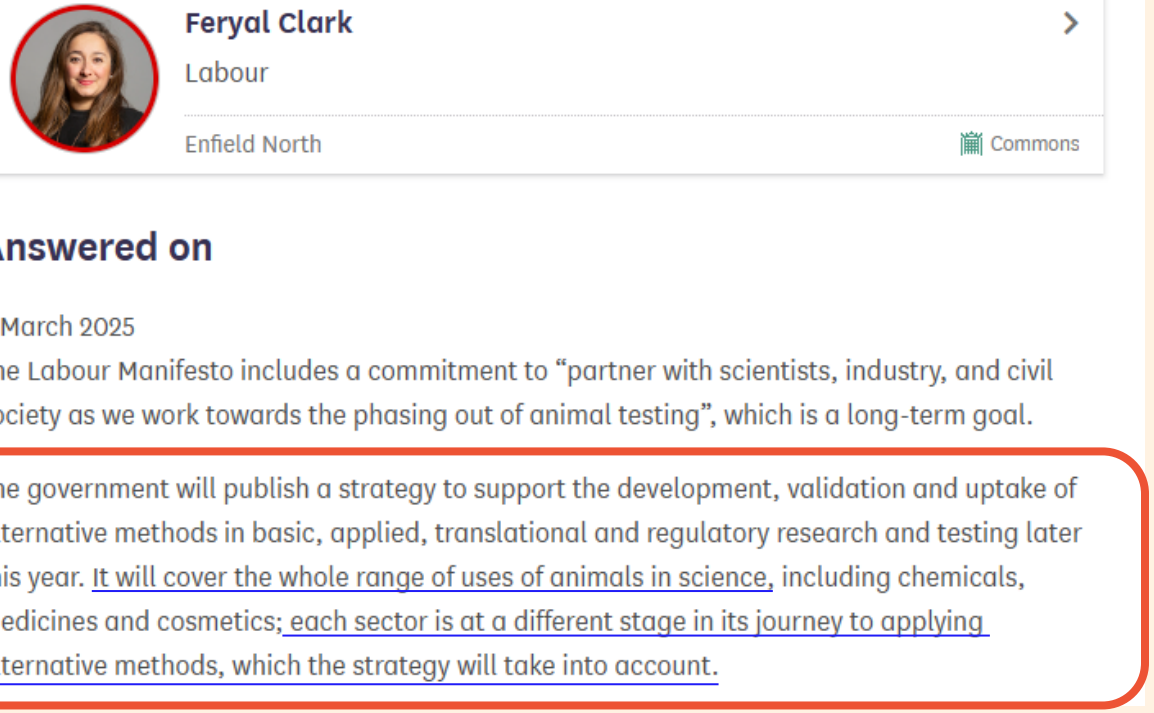
21 awards have been supported with funding from the Department for Science, Innovation and Technology (DSIT) to accelerate the uptake of non-animal approaches and replace animal-derived products in research and testing.

Support for infrastructure, and for the qualification of non-animal derived reagents for in vitro research.

https://hansard.parliament.uk/Commons/2024-02-19/debates/0C64E6BD-AE31-4DD7-80BB-3CEDC6272C2E/AnimalTesting

"We will partner with scientists, industry and civil society as we work towards the phasing out of animal testing"

https://labour.org.uk/change/my-plan-for-change



Feryal Clark
Labour
Enfield North
Commons

Answered on

4 March 2025

The Labour Manifesto includes a commitment to "partner with scientists, industry, and civil society as we work towards the phasing out of animal testing", which is a long-term goal.

The government will publish a strategy to support the development, validation and uptake of alternative methods in basic, applied, translational and regulatory research and testing later this year. It will cover the whole range of uses of animals in science, including chemicals, medicines and cosmetics; each sector is at a different stage in its journey to applying alternative methods, which the strategy will take into account.

4 March 2025

Petitions
UK Government and Parliament

"The manifesto committed the Government to partner with scientists, industry, and civil society as we work towards the phasing out of animal testing. This is ***a long-term goal,*** *and* ***it will need further scientific and technical advancement and validation*** *to reach this point* ***but we are determined to work towards it".***

"The Government will take steps to place the UK at the forefront of an alternative methods revolution *and* ***we believe that scientific advances make the prospects for change better than they have ever been"***

5 March 2025

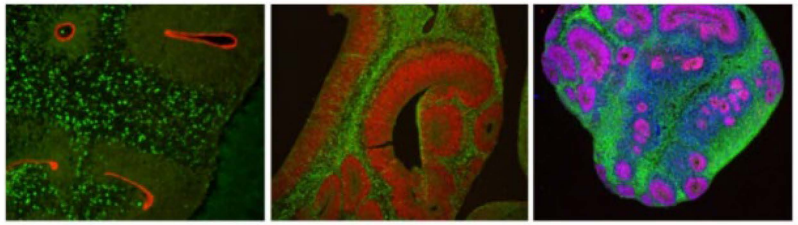
RSPCA ANIMALS IN SCIENCE

https://questions-statements.parliament.uk/written-questions/detail/2025-02-24/33012
https://petition.parliament.uk/petitions/705384?reveal_response=yes#response-threshold

IN THE LAB

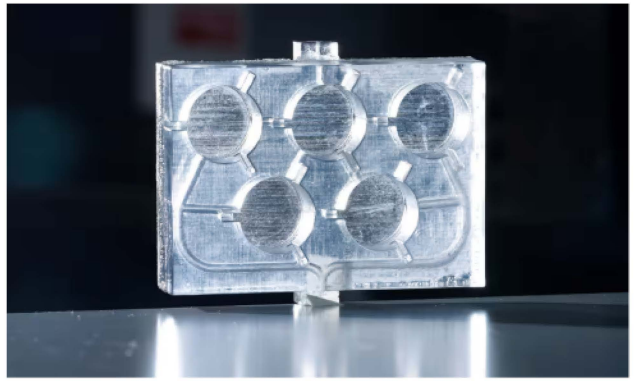
Research using brains-in-a-dish forces a radical rethinking of Huntington's disease

By Sharon Begley Dec. 10, 2019 Reprints



3D-printed chip showing body's reaction to drugs could end need for animal tests

Exclusive: Device with compartments replicating major organs could also speed up patients' access to new medicines



The plastic device uses positron emission tomography (PET) scanning to produce detailed 3D images showing what is going on inside the organs. Photograph: Murdo MacLeod/The Guardian

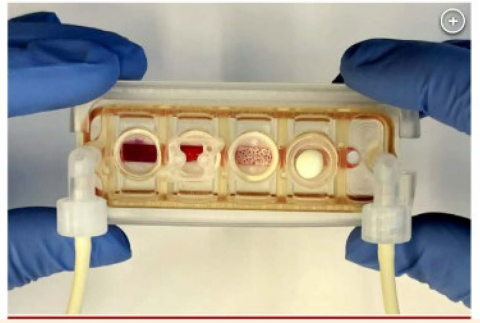
Scientists have developed a pioneering 3D-printed device that could speed up patient access to new medicines and eliminate the need for animal testing.

NEW YORK POST

LIVING

Tiny human organs cloned on chip to mimic patient's body for first time ever

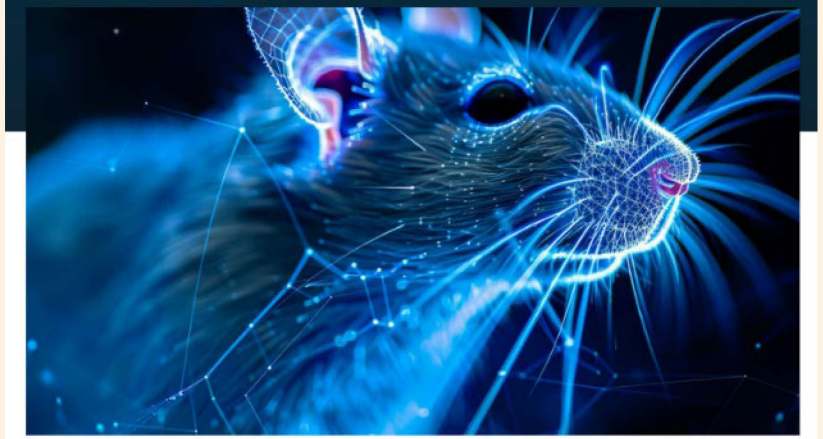
By Hannah Sparks April 27, 2022 | 5:38pm | Updated



Charles River and Sanofi collab to replace animals with virtual controls in preclinical research

By **Helen Floersh** · Jun 5, 2024 5:40pm

Sanofi | Charles River Laboratories | contract research organizations | animal testing



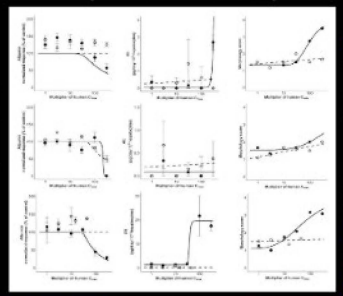
The idea behind virtual control groups is that because there are plenty of control data already from previous studies, data from treatment groups can simply be compared to that historical information. (Adobe Stock)

emulate GEN

WYSS INSTITUTE

Human Liver Chips are Better Predictors of Drug-Induced Liver Injury (DILI) than Animal Models

(Ewart et al. *bioRxiv* 2021; led by Emulate, Inc.)



- 780 Human Liver Chips analyzed (cells from 2 donors)
- Tested blinded set of 27 hepatotoxic and non-toxic drugs identified by pharma IQ Consortium
- Human toxicities of many drugs had been missed in animal models
- *Predicted human DILI with sensitivity = 87% and specificity = 100%*

European Directorate for the Quality of Medicines & HealthCare

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You are here: European Directorate for the Quality of Medicines & HealthCare | Newsroom | Ph. Eur. bids adieu to rabbit pyrogen test in its monographs

Newsroom

Ph. Eur. bids adieu to rabbit pyrogen test in its monographs

EDQM | STRASBOURG, FRANCE | 05/07/2024

EMA implements new measures to minimise animal testing during medicines development

Share

News 29/09/2021

EMA is putting in place special support to developers to replace, reduce and refine animal use for the development, manufacturing and testing of human and veterinary medicines. The Agency is promoting these three principles — replace, reduce and refine; commonly referred to as 3Rs — through EMA's Innovation Task Force (ITF). This action will facilitate the development and implementation of New Approach Methodologies (NAMs) that are in line with the European Union legislation on the protection of animals used for scientific purposes.

ITF is a dedicated forum for early dialogue between regulators and developers of medicines to discuss innovative aspects such as emerging therapies, methods and technologies. Set up to ensure coordination across the Agency, the ITF is a multidisciplinary group that includes scientific, regulatory and legal competences. It will provide an opportunity to discuss 3R-compliant methods and facilitate their integration into the development and evaluation of medicinal products.

The ITF's service is free of charge and any NAMs adhering to the 3Rs principles that can be used to fulfil testing requirements are eligible for consideration.

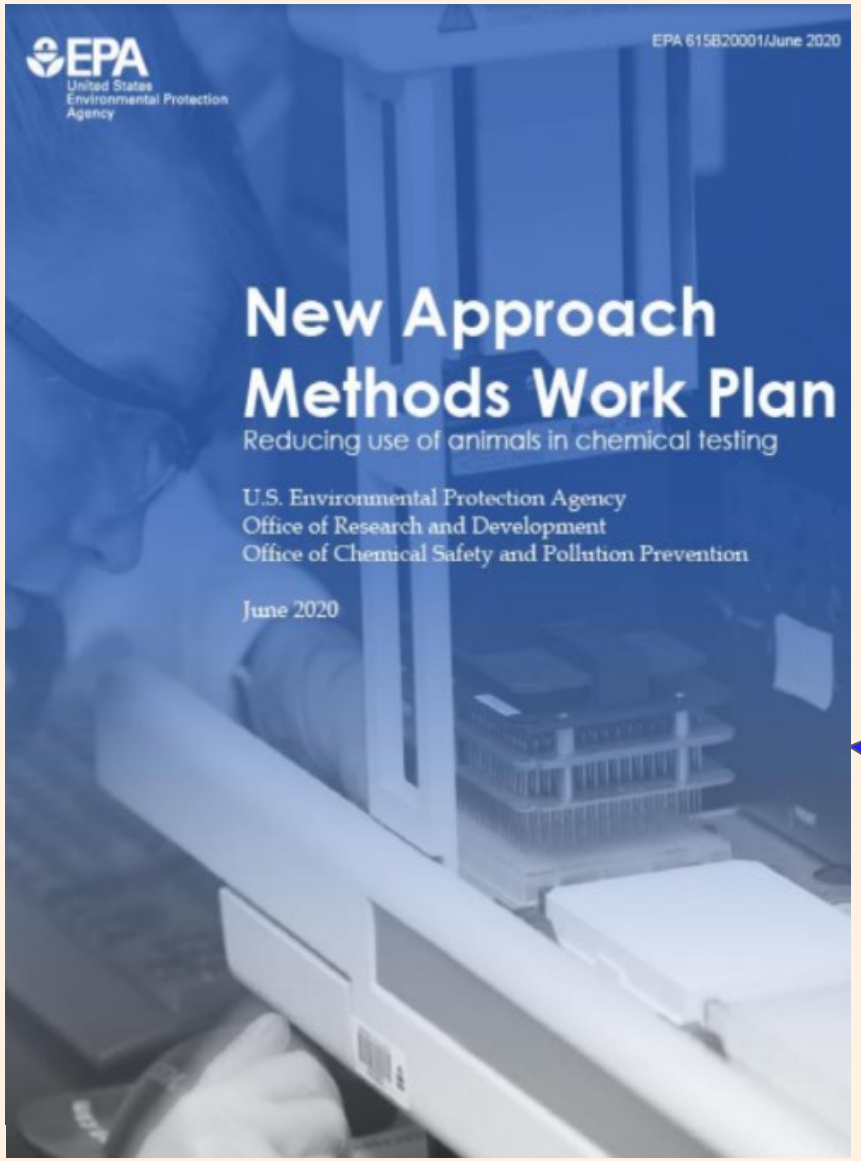
Alternative approaches to animal models, such as improved tests based on human and animal cells, organoids, organ-on-chips and in silico modelling, provide opportunities to develop better and more predictive scientific tools to protect human and animal health as well as the environment.

Opening the ITF platform to discussions of 3Rs-compliant methodologies is expected to encourage prioritising and speeding up the integration of alternative methods into the regulatory framework. This action supports the reduction of animal use and is in line with EMA's Regulatory Science Strategy to 2025 aiming to build a more adaptive regulatory system that will encourage innovation in human and veterinary medicine.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

*"**Alternative approaches to animal models**, such as improved tests based on human and animal cells, organoids, organ-on-chips and in silico modelling, **provide opportunities to develop better and more predictive scientific tools** to protect human and animal health as well as the environment."*

www.ema.europa.eu/en/news/ema-implements-new-measures-minimise-animal-testing-during-medicines-development



EPA United States Environmental Protection Agency

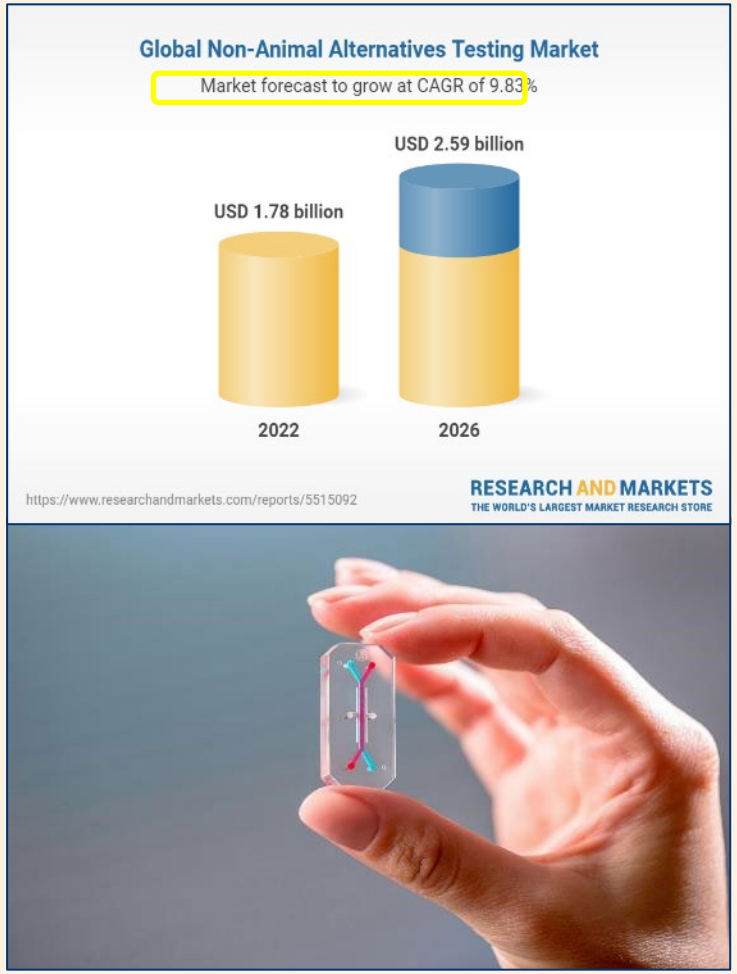
*"NAMs have the **potential to provide more rapid, cost-effective, and human-relevant information** on potential chemical risks compared with traditional animal testing."*

www.epa.gov/chemical-research/epa-new-approach-methods-work-plan-reducing-use-vertebrate-animals-chemical

"There is increasing recognition among companies and regulators of the limitations of preclinical models, including animal models, and the need for more predictive approaches…"

"Benefits [of NATs] go beyond replacing the use of animals e.g. increasing throughput, ***cutting development time and costs****, and* ***providing mechanistic insights that are not possible with in vivo research****."*

www.gov.uk/government/publications/non-animal-technologies-in-the-uk-a-roadmap-strategy-and-vision



Whole body-on-a-chip device

What is it? Multi-organ systems which can emulate human physiological responses to drugs. Have the potential to identify a drug's efficacy and its toxicity in other organs.

Why is it interesting? Offers a more accurate and cost-effective way of testing treatments before clinical trial. Body-on-a-chip devices could increase the success rates of clinical trials.

How could it change our lives? If successful, they could be used to develop or select therapeutics for individual patients. This could revolutionise clinical trial design and deliver a new wave of treatments and interventions, improving global health outcomes.

www.ukri.org/wp-content/uploads/2023/12/IUK-05122023-INO0617_Emerging-Tech-Report_AW2-final.pdf

*"**Advances in science and technology have brought our industry to an inflection point. Alternatives are the path to the next frontier of drug development**, allowing us to responsibly drive progress for the patients and animals that depend on our work"*

charles river

*"We will continue working… on the **phasing out of animal testing.**"*

cefic

*"**We support a roadmap to phase out animal testing by providing better solutions to guide science.**"*

MERCK

*"…is committed to the **science based phase-in of methods to replace the use of animals**"*

efpia

*"Society as a whole **should be committed to the ultimate goal of fully replacing animal use in science.**"*

IMPERIAL

3Rs Hub

P&G

*"We are **committed to make animal testing obsolete.**"*

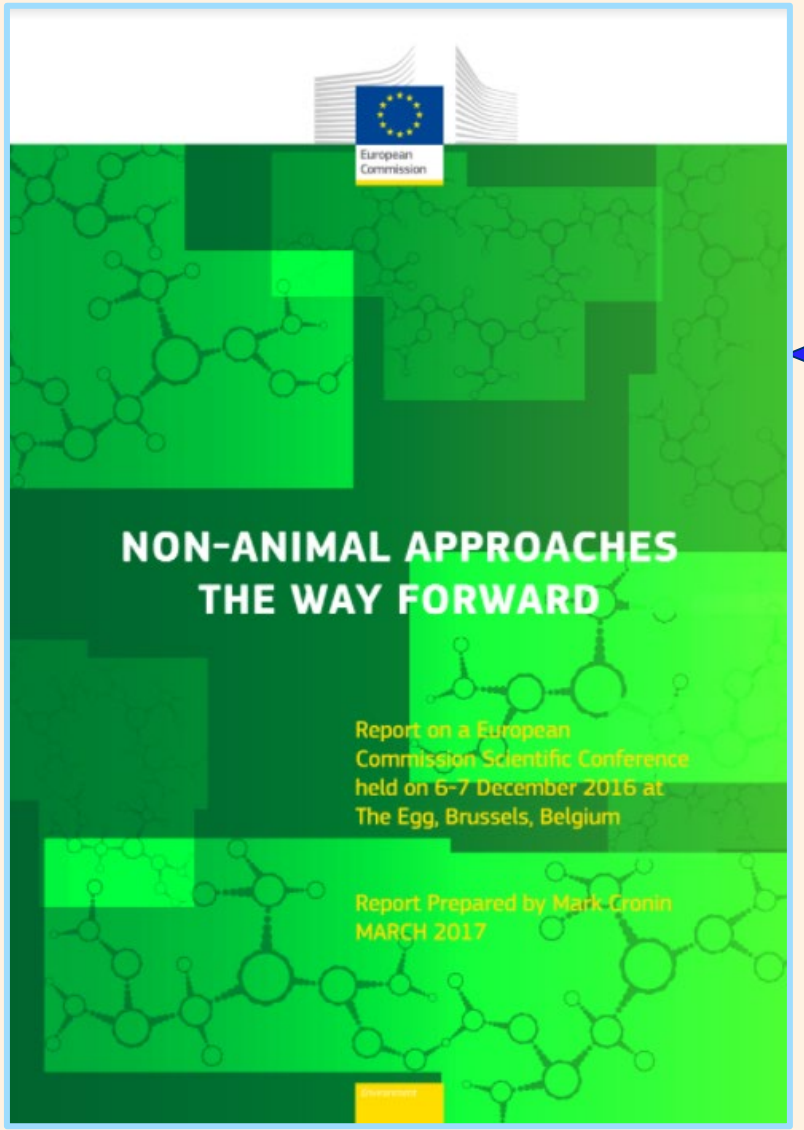
Barriers to replacing animals

Wider use of non-animal methodologies is currently limited by:

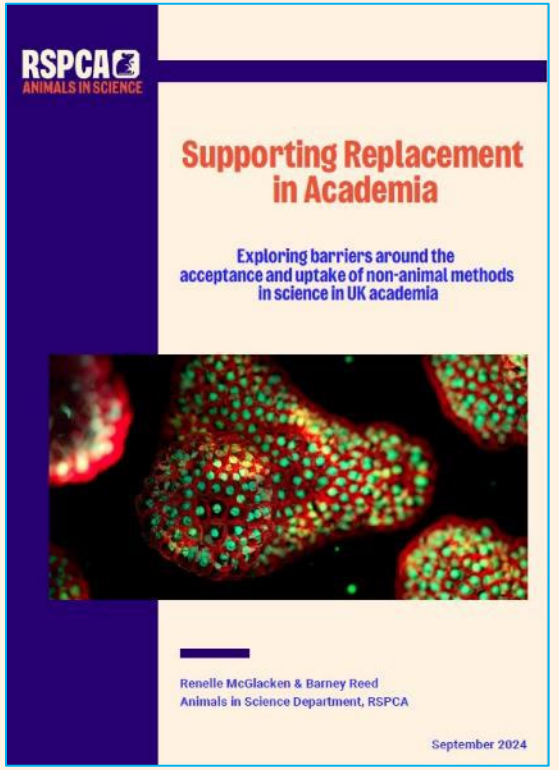
Development: overcoming scientific and technological challenges

Acceptance: recognition of and confidence in non-animal approaches by scientists, regulators of medicines, vaccines and chemicals etc, journal editors and reviewers

Uptake: awareness, knowledge and skills, willingness to move away from traditional approaches, access and availability

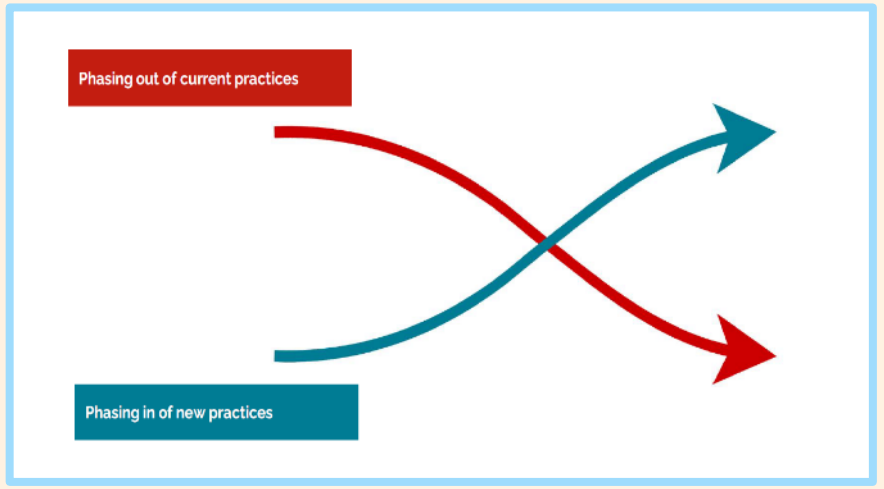


*"…**new technologies will not implement themselves**, neither will the obstacles to their implementation be resolved automatically."*



https://ec.europa.eu/environment/chemicals/lab_animals/3r/pdf/scientific_conference/non_animal_approaches_conference_report.pdf
https://science.rspca.org.uk/researchanimals/reportsandresources/animaluse

Key principles of a strategy



- **Prioritise** key areas where **resources** and **efforts** need to be **targeted**
  - potential for progress; number of animals and severity involved etc.
- Set out **action plans** - with the steps needed specific to each area of research and testing
- Provide **support** to stimulate change e.g. key **infrastructure**, **training** etc.
- Continued **critical review** of justification for, and impact of, **current animal use** - by funders, regulators, evaluators of project proposals etc.

"This Directive represents an important step towards achieving ***the final goal of full replacement of procedures on live animals*** *for scientific and educational purposes as soon as it is scientifically possible to do so."*

otection of Animals
r Scientific Purposes
Recital 10

https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32010L0063

European Parliament

2019-2024

TEXTS ADOPTED

P9_TA(2021)0387

Plans and actions to accelerate a transition to innovation without the use of animals in research, regulatory testing and education

European Parliament resolution of 16 September 2021 on plans and actions to accelerate the transition to innovation without the use of animals in research, regulatory testing and education (2021/2784(RSP))

Adopted 15 September 2021

31 August 2022

European Citizens' Initiative

1.4m signatures received

1. Protect and strengthen the cosmetics animal testing ban.
Initiate legislative change to achieve consumer, worker, and environmental protection for all cosmetics ingredients without testing on animals for any purpose at any time.

2. Transform EU chemicals regulation.
Ensure human health and the environment are protected by managing chemicals without the addition of new animal testing requirements.

3. Modernise science in the EU.
Commit to a legislative proposal plotting a roadmap to phase-out all animal testing in the EU before the end of the current legislative term.

www.europarl.europa.eu/doceo/document/TA-9-2021-0387_EN.pdf

https://eci.ec.europa.eu/019/public/#/screen/home/disabled

Press release | 25 July 2023 | Brussels

Commission acts to accelerate phasing out of animal testing in response to a European Citizens' Initiative

- *"…will **develop a roadmap** that will **outline milestones and specific actions…**"*
- *"**analyse and describe the necessary steps to replace animal testing…**"*
- *"**outline the path to expand and accelerate** the development, validation and implementation of non-animal methods"*

Joint Research Centre
JRC

PARC

€400m over 7 years
~200 partners

'Accelerating new approach methodologies to advance biomedical research and testing of medicinal products and medical devices'.

25 July 2023

https://ec.europa.eu/commission/presscorner/detail/en/ip_23_3993
https://european-research-area.ec.europa.eu/sites/default/files/documents/2025-02/COM_2025_62_F1_ANNEX_EN_V4_P1_3951029_3.PDF

Potential Approaches to Drive Future Integration of New Alternative Methods for Regulatory Decision-Making

A Report to the Science Board to the Food and Drug Administration from the New Alternative Methods Subcommittee

OCTOBER 2024

FDA

Paving the way for a UK Roadmap:

Development, Endorsement and Regulatory Acceptance of New Approach Methodologies (NAMs) in Chemical Risk Assessment and Beyond.

Committee on Toxicity

2023

Food Standards Agency

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Home > Events > 3Rs Working Party (3RsWP) plenary meeting - Public session on the 2025-2027 work plan

3Rs Working Party (3RsWP) plenary meeting - Public session on the 2025-2027 work plan

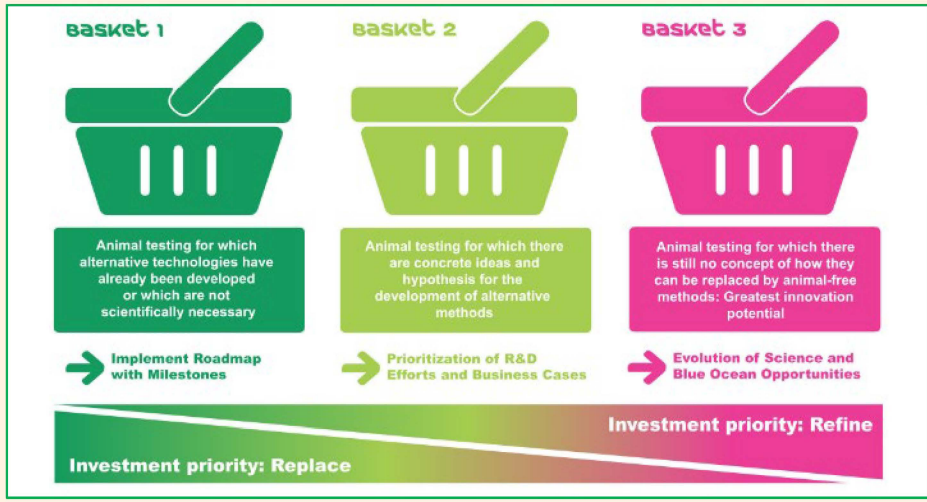
The 3RsWP is hosting this virtual public session to present the 3RsWP work plan and priorities for 2025-2027

Event | Human | Veterinary | Corporate

World Health Organization

WHO: DRAFT VERSION
ENGLISH ONLY

Guidelines on the phasing out of animal tests for the quality control of biological products



efpia

*"The Netherlands **aims to become an international frontrunner in creating innovations that make animal testing obsolete**".*

15 March 2024

Dutch National Growth Fund invests 124,5 million in transition to animal-free innovation

The Dutch National Growth Fund will invest €124,5 million in a new centre for animal-free biomedical testing. Of this investment, 55 million euros are awarded directly and 69.5 million euros are granted subject to conditions. Known as the Centre for Animal-Free Biomedical Translation, its aim is to generate safer, more effective treatments, while reducing animal suffering.

€124.5m over 10 years

The Centre for Animal-Free Biomedical Translation (CPBT) will use this funding from the National Growth Funds (NGF) to accelerate the transition to animal-free biomedical innovations. This will offer economic and social benefits with improved medicines and less animal testing.

tpi.

CSIRO — Australia's National Science Agency

Non-animal models

A strategy for maturing Australia's medical product development capabilities

Executive summary | 2023

*"Australia must **act now** to secure a key role in this **emerging capability**"*

NIH National Institutes of Health — *Turning Discovery Into Health*

$390m over 10 years

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THE NIH DIRECTOR

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- Advisory Groups
- NIH Leadership

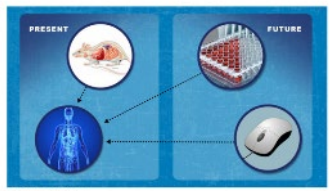
February 1, 2024

Statement on catalyzing the development of novel alternative methods

Major leaps in science are often driven by the invention of new technologies and approaches. For example, while genome editing technologies have been around for decades, the novel approach used by the CRISPR-CAS system transformed researchers' capabilities to solve previously intractable problems. By harnessing this new technological approach, we now have our first FDA-approved gene editing therapy for patients suffering from Sickle Cell Disease.

We also are seeing dramatic leaps in technologies that allow researchers to use complementary, non-animal-based approaches to study biological functions and human disease. These so called "novel alternative methods" or NAMs, which include computational modeling and predictive technologies, cell-free methods and assays and cell-based culture models, hold tremendous promise when applied to the appropriate scientific inquiry.

Advancing Alternative Methods at FDA



RÉPUBLIQUE FRANÇAISE — 20 ans anr — Submit a project — Press area

THE ANR | CALLS FOR PROJECTS | FUNDED PROJECTS AND IMPACT | FRANCE 2030

France 2030 / To consult

€48.4m over 6 years

Open – 2025

PEPR Exploratory "Organs and organoids on chips" MED-OOC - Call for projects - 2025

In recent years, animal models have demonstrated significant limitations in exploring the mechanisms of onset and progression of human diseases. This partly explains the high failure rate (90%) of clinical trials of new drugs that have proven effective in animals. Moreover, in a context that aims to reduce animal experimentation to comply with the "3R" policy (Reduce, Replace, Refine), current in vitro cell culture models have certain limitations in their ability to reproduce in vivo mechanisms and do not easily address variability between patients, a key issue in the rapidly expanding field of personalized medicine.

FRANCE 2030

India takes first step to remove animals from drug-testing process PREMIUM

A new Rule authorises researchers to use non-animal methods to test new drugs.

June 29, 2023 10:30 am | Updated July 02, 2023 01:32 pm IST - Hyderabad

SURAT PARVATAM

COMMENTS SHARE READ LATER

A file photo of mice held by a hand. An amendment to the New Drugs and Clinical Trial Rules (2023), recently passed by the Government of India, aims to replace the use of animals in research, especially in drug testing. Image for representational purposes only. | Photo Credit: AFP

An amendment to the New Drugs and Clinical Trial Rules (2023), recently passed by the Government of India, aims to replace the use of animals in research, especially in drug testing. The amendment authorises researchers to instead use non-animal and human-relevant methods, including technologies like 3D organoids, organs-on-chip, and advanced computational methods, to test the safety and efficacy of new drugs.

Government of Canada Gouvernement du Canada

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› Share your thoughts: Strategy to replace, reduce or refine vertebrate animal testing

Notice of intent on the development of a strategy to guide the replacement, reduction, or refinement of vertebrate animal testing under the Canadian Environmental Protection Act, 1999 (CEPA)

Purpose

This notice is to inform people living in Canada that the Government of Canada intends to commence work on the development of a strategy to guide continued efforts to replace, reduce or refine the use of vertebrate animals when addressing chemical 1 assessment data needs under the Canadian Environmental Protection Act, 1999 (CEPA).

Planned actions

While vertebrate animal testing provides essential information for regulatory programs that aim to protect people living in Canada and their environment, the Government of Canada is committed to advancing efforts to replace, reduce, or refine the use of vertebrate animals in toxicity testing where possible.

In line with this, the Government of Canada introduced amendments to CEPA under Bill S-5 (*Strengthening Environmental Protection for a Healthier Canada Act*) that recognize the need to replace, reduce or refine the use of vertebrate animal testing when assessing the risks that substances may pose to human health and the environment. These amendments, which received Royal Assent in June 2023, support Health Canada (HC) and Environment and Climate Change Canada (ECCC) in their efforts to promote the development and timely incorporation of alternative methods and strategies, as science permits.

LAW No. 15,022, OF NOVEMBER 13, 2024

It establishes the National Inventory of Chemical Substances and the assessment and risk control of chemical substances used, produced or imported in the national territory, with the aim of minimizing adverse impacts on health and the environment; and provides other measures .

Art. 18. Testing on animals should be the last resort to determine the danger of a chemical substance and may only be used if all alternative methods have been exhausted.

§ 1º The alternative methods to animal experimentation referred to in the *caput* of this article must be scientifically recognized and present a degree of reliability considered adequate for decision-making by the Technical Committee for the Evaluation of Chemical Substances.

§ 2 The public authority will designate a supervisory body, so that, in consultation with the institutions concerned, it can establish a strategic plan to promote the use of alternative methods to animal experimentation.

What AWERBs can do

- Have ‘supporting replacement’ as a **strategic ambition** and AWERB objective - and be able to demonstrate actions you are taking.
- Think about how you can **support your scientists to transition to non-animal methods** in your establishment (facilitate collaborations, increase access to training opportunities, infrastructure etc).
- Ensure the **Named Information Officer is supported** - time, resource, status.
- **Stay up-to-date with developments** - both at a macro level, and in the specific areas of research or testing relevant to the establishment.
- Challenge the status quo - what questions do you ask as **reassurance that all replacement options have been fully explored**?
- Look for opportunities to input into **external initiatives**.

Additional info of interest

- **Reviewing Current Guidance for the ‘R’ of Replacement and Rethinking it with the ‘Replacement Checklist’** [Replacing Animal Research] https://journals.sagepub.com/doi/10.1177/02611929251319265

- **Care-Full Stories - Talking about Replacement** [AnNex/RSPCA] https://www.geog.ox.ac.uk/sites/default/files/2023-11/Story8-talking-about-replacement-v4.pdf

- **How AWERBs can support Named Persons** [RSPCA] https://science.rspca.org.uk/documents/d/science/how-awerbs-can-support-named-persons

Alternative methods

AN INDUSTRY PERSPECTIVE

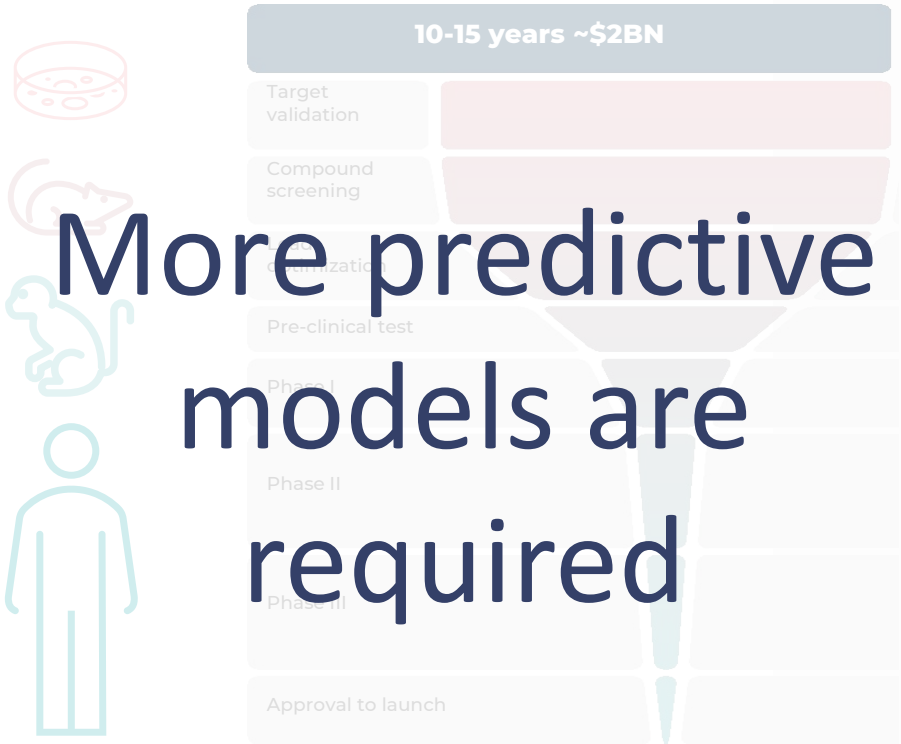
Dharaminder Singh

Agenda

Alternative methods

- Why focus on Alternative methods/MPS?
- Comparison to current methods?
- Example models and applications
- Are the technologies ready?

Why the focus on Alternative methods?



More predictive models are required

Technology is now ready to be utilized

Sun D, Gao W, Hu H, Zhou S. Why 90% of clinical drug development fails and how to improve it? Acta Pharm Sin B. 2022 Jul;12(7):3049-3062. doi: 10.1016/j.apsb.2022.02.002. Epub 2022 Feb 11. PMID: 35865092; PMCID: PMC9293739.

What is OOC / MPS?

Microphysiological systems (MPS) come in many shapes and sizes but have some common features

Human cells and tissue

Human cells typically grown in 3D and with geometrical confinement or patterning

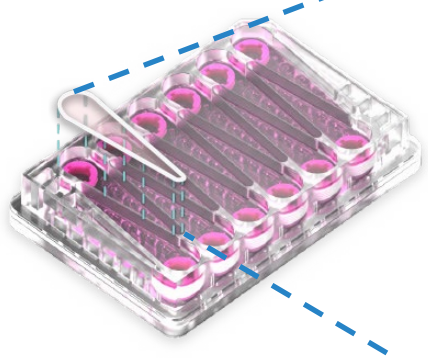
Fluidic flow

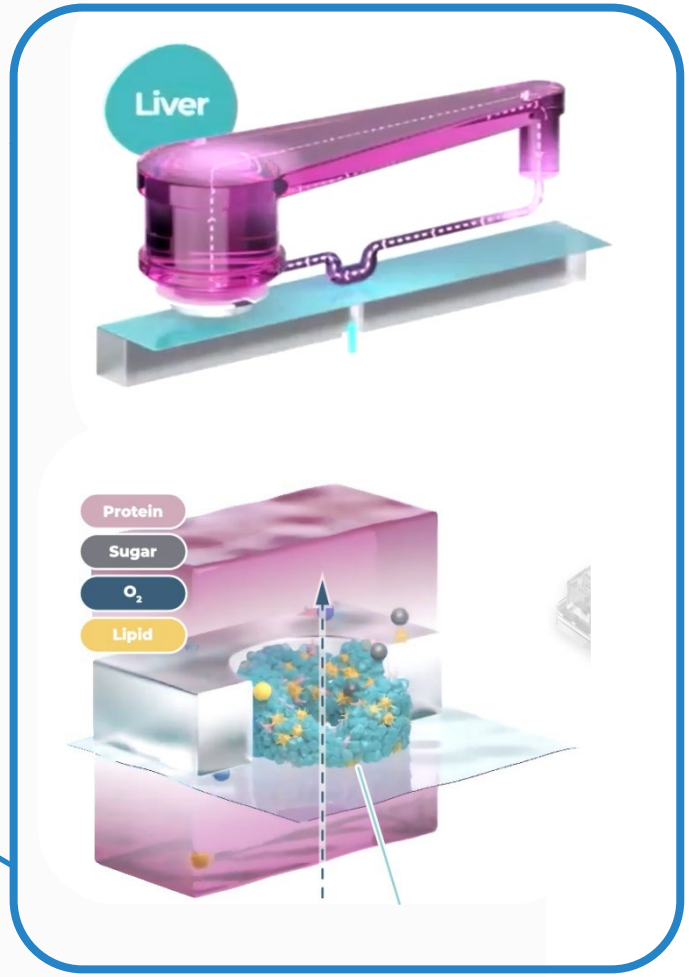
Mimic flow of blood, provide O_2 and nutrient supply and provide biomechanical stimuli, control of gas exchange and growth factors

Human-relevant endpoints

Enable the investigation of mechanisms of action and pathways, using relevant endpoints for clinical translatability

Example of an MPS model





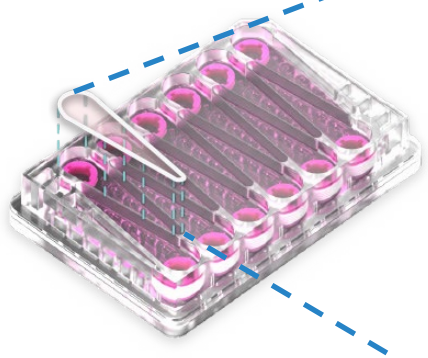
Human cells and tissue
- 3D with geometric patterning

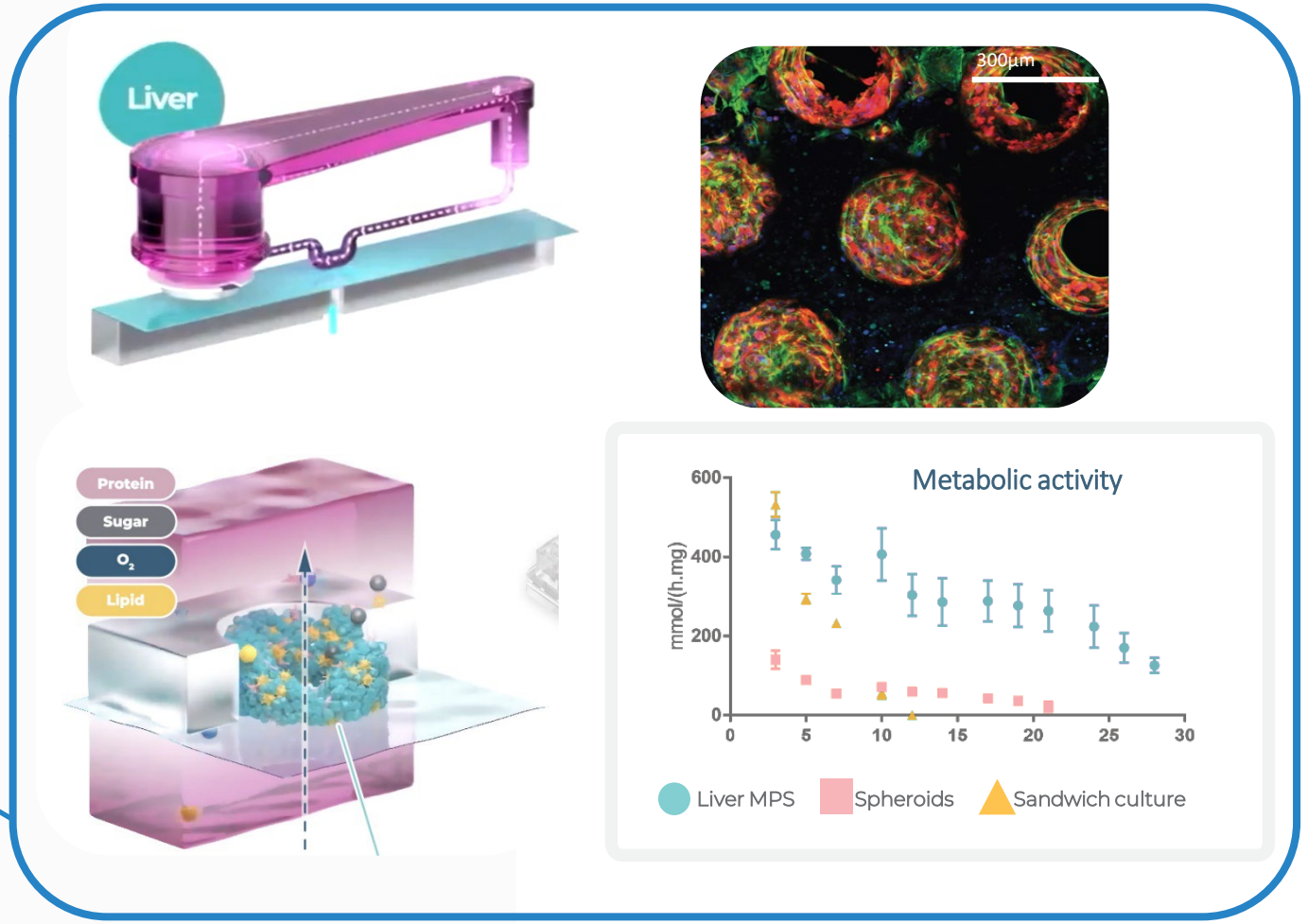
Fluidic flow
- Mimic blood flow
- O2 and nutrient supply
- Mechanical stimuli

Environmental control
- Mechanical actuation
- Control of gas/media/growth factors

Drug dosing and/or sensors
- Control of exposure
- Various readouts

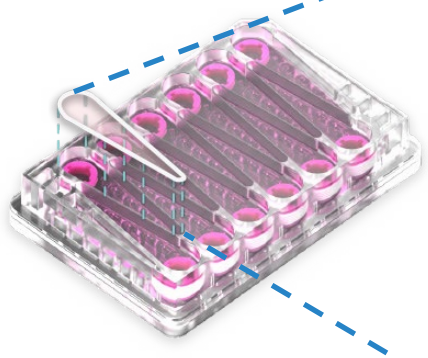
Comparison to traditional *in vitro?*

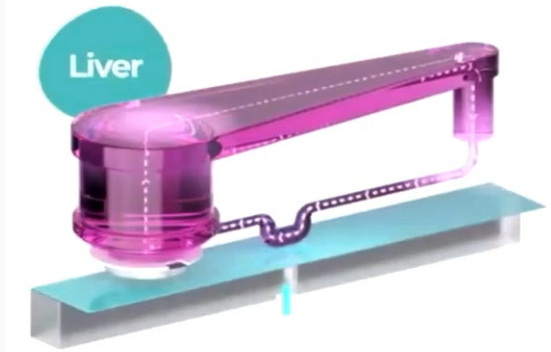


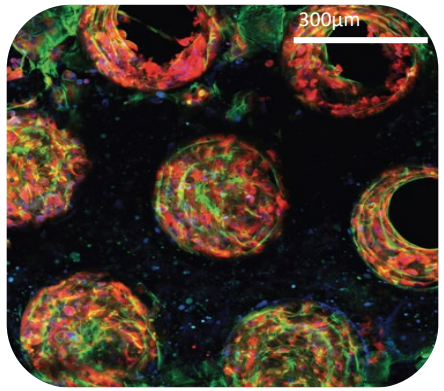


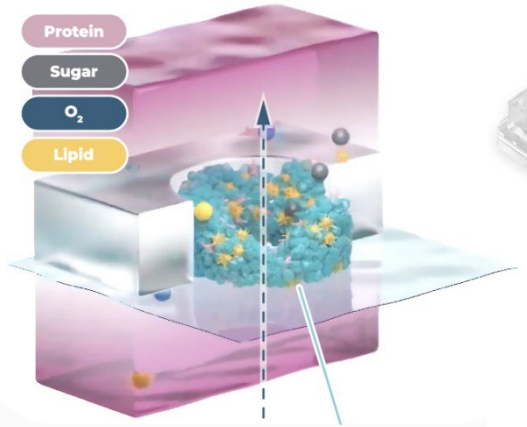
Rubiano A,. Characterizing the reproducibility in using a liver microphysiological system for assaying drug toxicity, metabolism.... Clin Transl Sci. 2021 May;14(3):1049-1061.

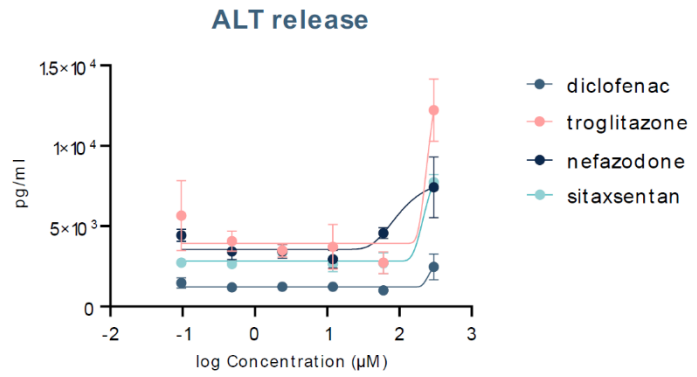
Comparison to traditional *in vivo?*









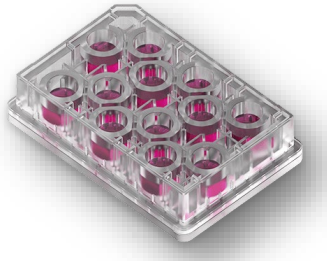


Poster: Bridging the gap, Christiana S., Emily R, Tomasz K.

PhysioMimix® Multi-chip plates

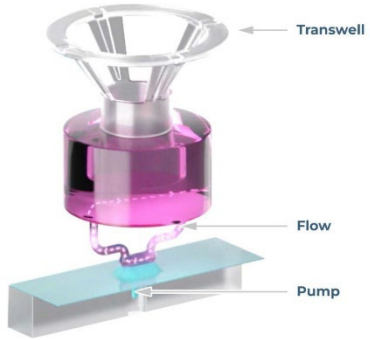
Barrier model

Basolateral flow



GUT

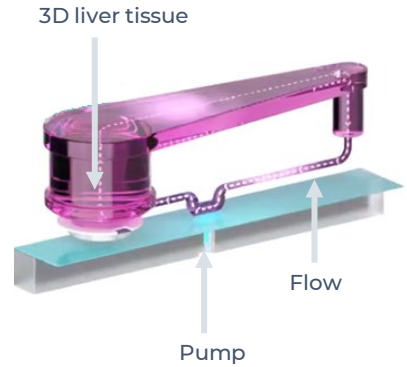
LUNG



Liver model

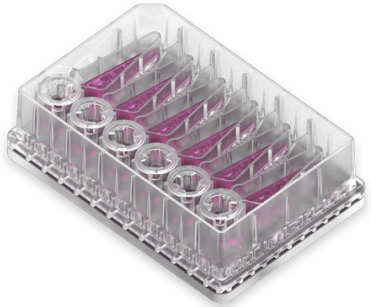
Individual well/microtissue perfusion

LIVER



Dual-organ model

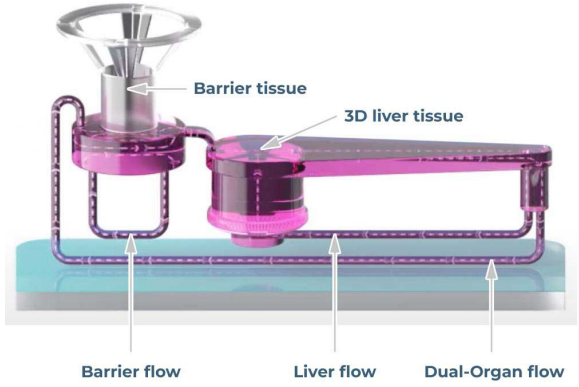
Interconnected flow

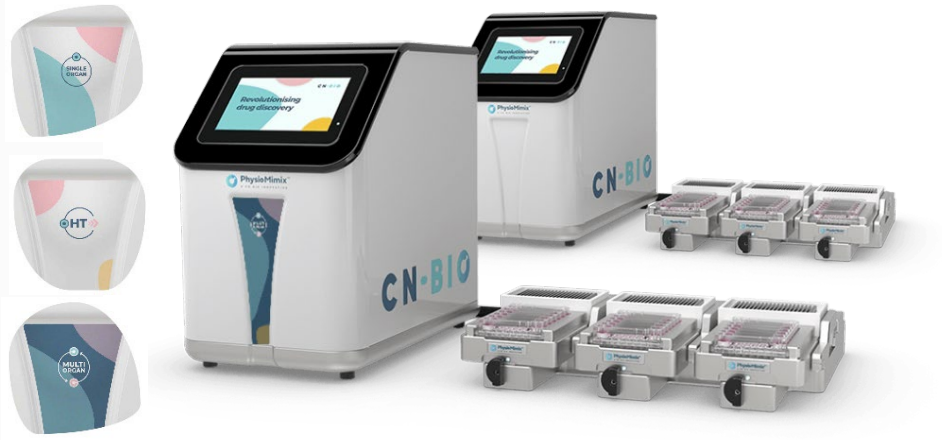


LUNG

GUT

LIVER

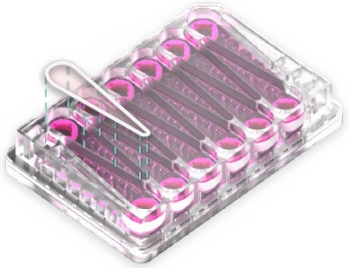




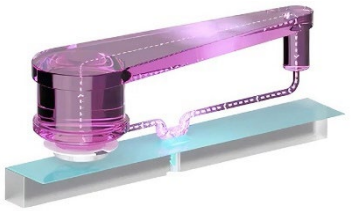
Three examples of OOC/MPS models

LIVER

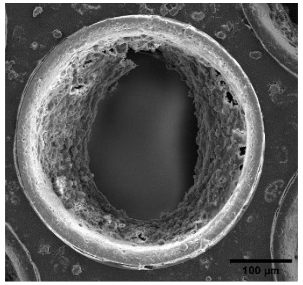
Consumable plate



Individual well



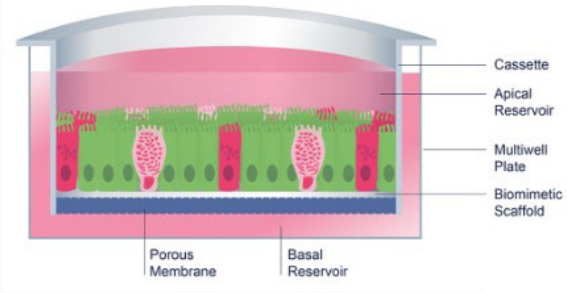
Individual microtissue



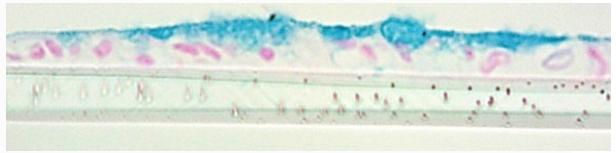
GUT

Gut

RepliGut®



RepliGut®

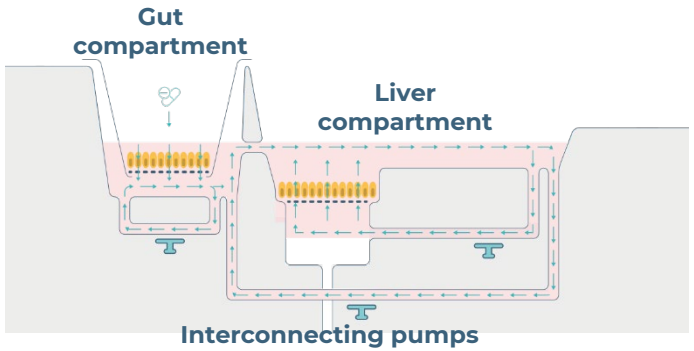


Caco-2

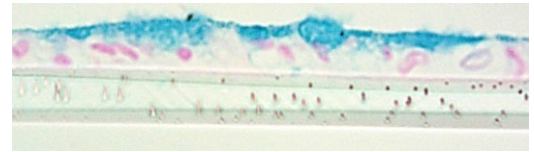
GUT

LIVER

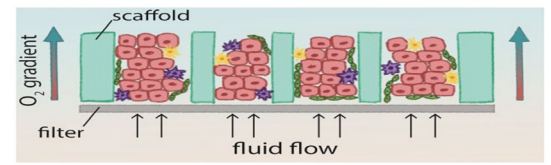
Gut/Liver



Gut - RepliGut®



Liver



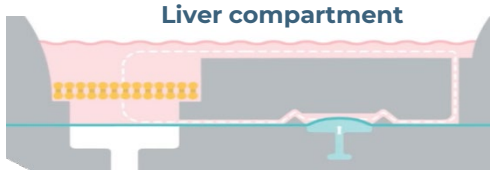
Three example applications

Safety Toxicology

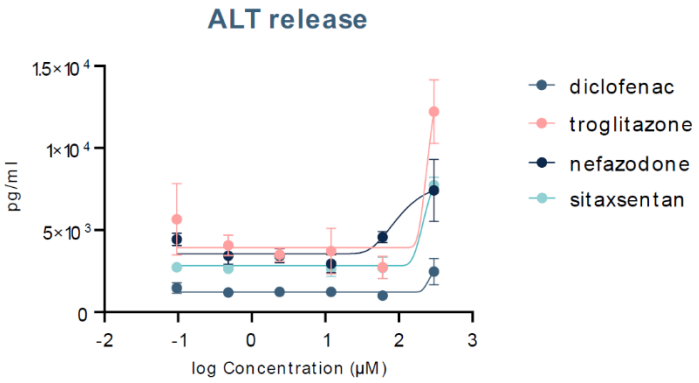
LIVER

Drug Induced Liver Injury: a leading cause of attrition of compounds in drug development

Liver well



DILI compounds



Poster: Bridging the gap, Christiana S., Emily R, Tomasz K.

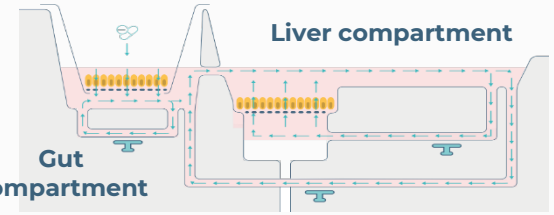
ADME

GUT

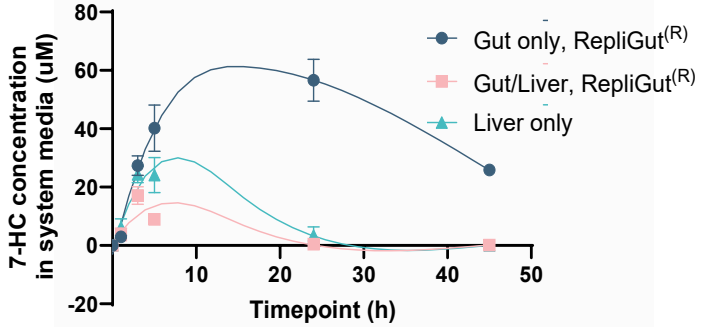
LIVER

Absorption, Distribution, Metabolism and Excretion: key criteria for drug dose setting

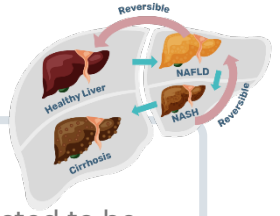
Gut/Liver well



Metabolism of 7-hydroxycoumarin



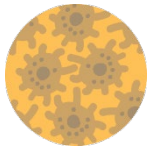
Disease modelling



Non-alcoholic Steatohepatitis: expected to be leading cause of Liver transplantation by 2025 in US

NASH model

Primary Human Hepatocytes

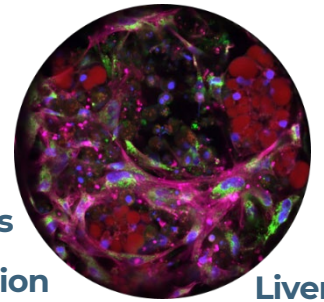


Human Hepatic Stellate cells

Human Kupffer cells

Dietary fat medium

14-day Exp



Steatosis

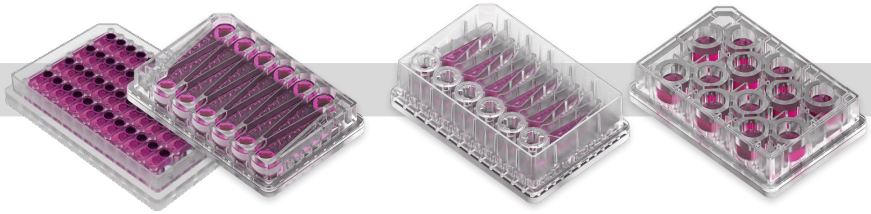
Inflammation

Fibrosis

Liver functionality

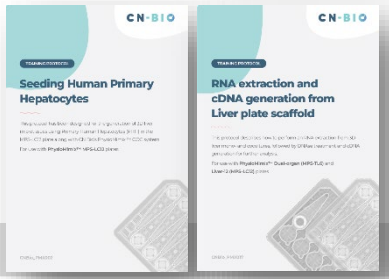
Full solution for easy adoption

Multi-chip consumable plates

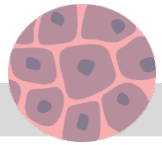


Liver | Dual-organ | Barrier

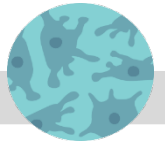
Validated SOPs



PhysioMimix 3D validated cells



Primary Human Hepatocytes



Human Kupffer cells

Human Hepatic Stellate cells

IN-A-BOX

Assay kit solutions

How has MPS been used to date?

CN Bio PhysioMimix® Organ-on-a-Chip data supports Inipharm's INI-822 for metabolic liver disease treatment now in clinical testing.

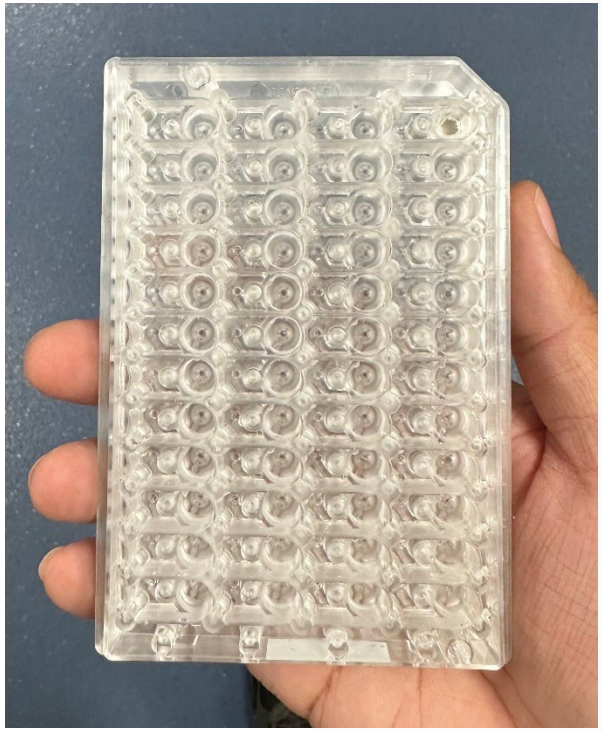
- PhysioMimix NASH assay used to provide human-relevant data on compound efficacy for Inipharm's lead candidate, INI-822
- Submission represents first example of an OOC provider's data supporting clinical progression of a drug for metabolic, fibrotic liver disease

Mimetas…

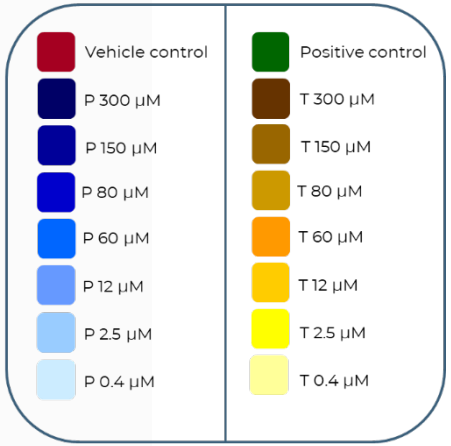
Hesperos…

Are these technologies ready?

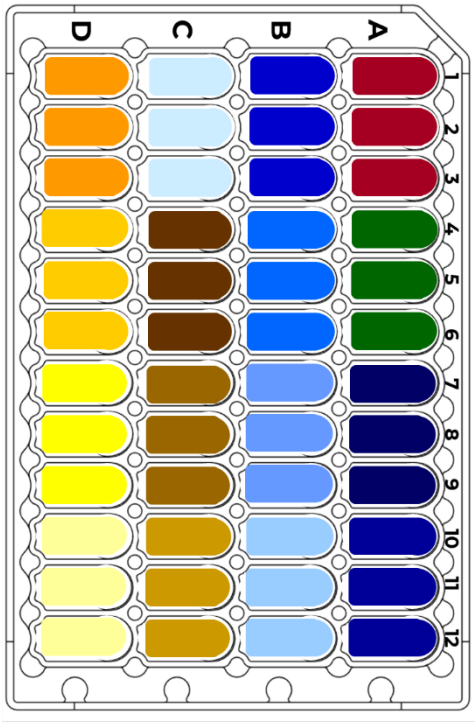
Technology readiness



Example plate plan,
(compounds “P” & “T”)

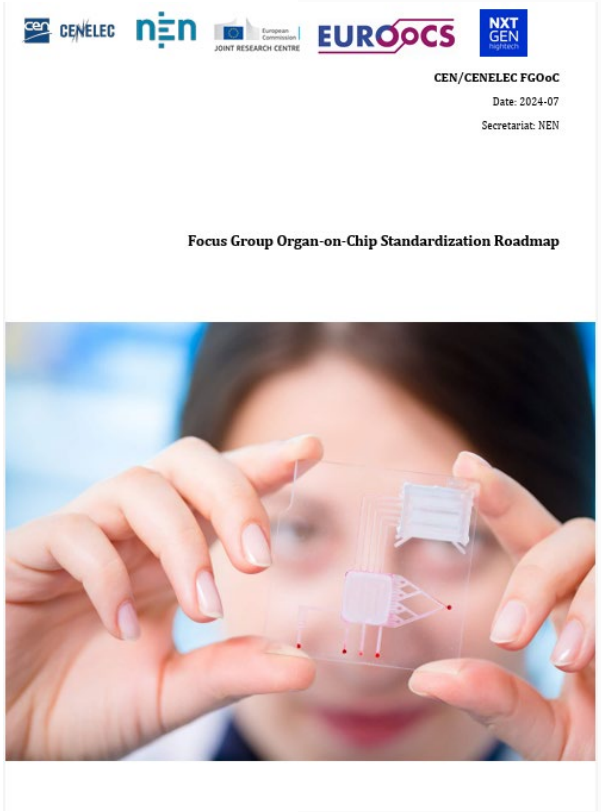


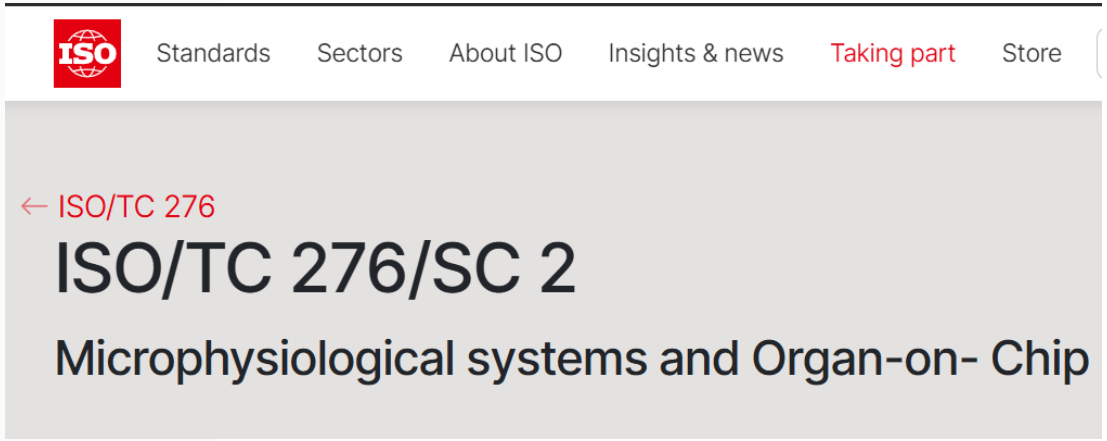
2 compounds, 7 concentrations,
positive and negative control



Are these technologies ready?

Developer Standards





Are these technologies ready?

Regulators & frameworks

CRITICAL PATH INSTITUTE

be EU

famhp

2024 COMPLEX IN VITRO MODEL (CIVM)
QUALIFICATION FRAMEWORK PUBLIC WORKSHOP

Final Agenda Multistakeholder Kick-off Workshop:

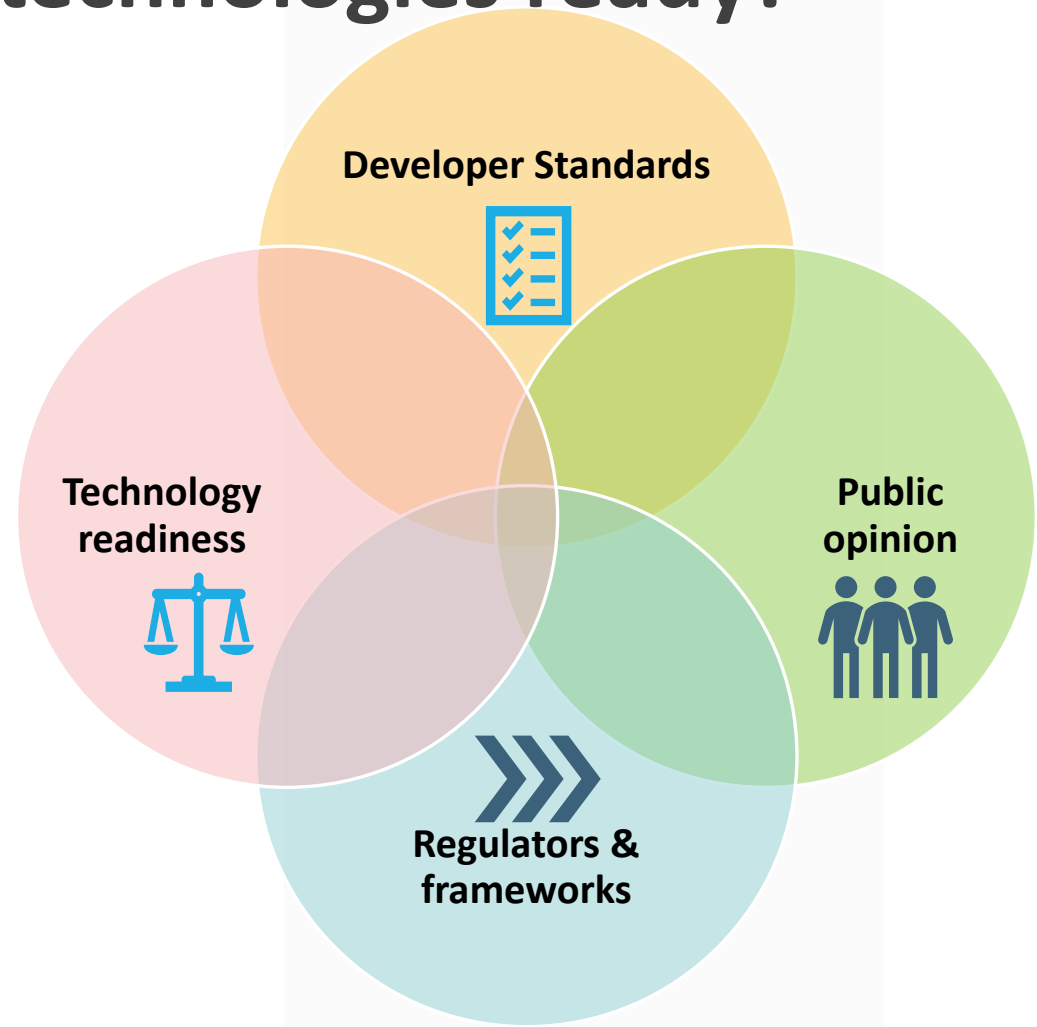
Towards Qualification of MicroPhysiological Systems including Organ-on-Chip Models for Specific Contexts of Use to be Applied in the Pharmaceutical Area

Brussels, 30th January 2024

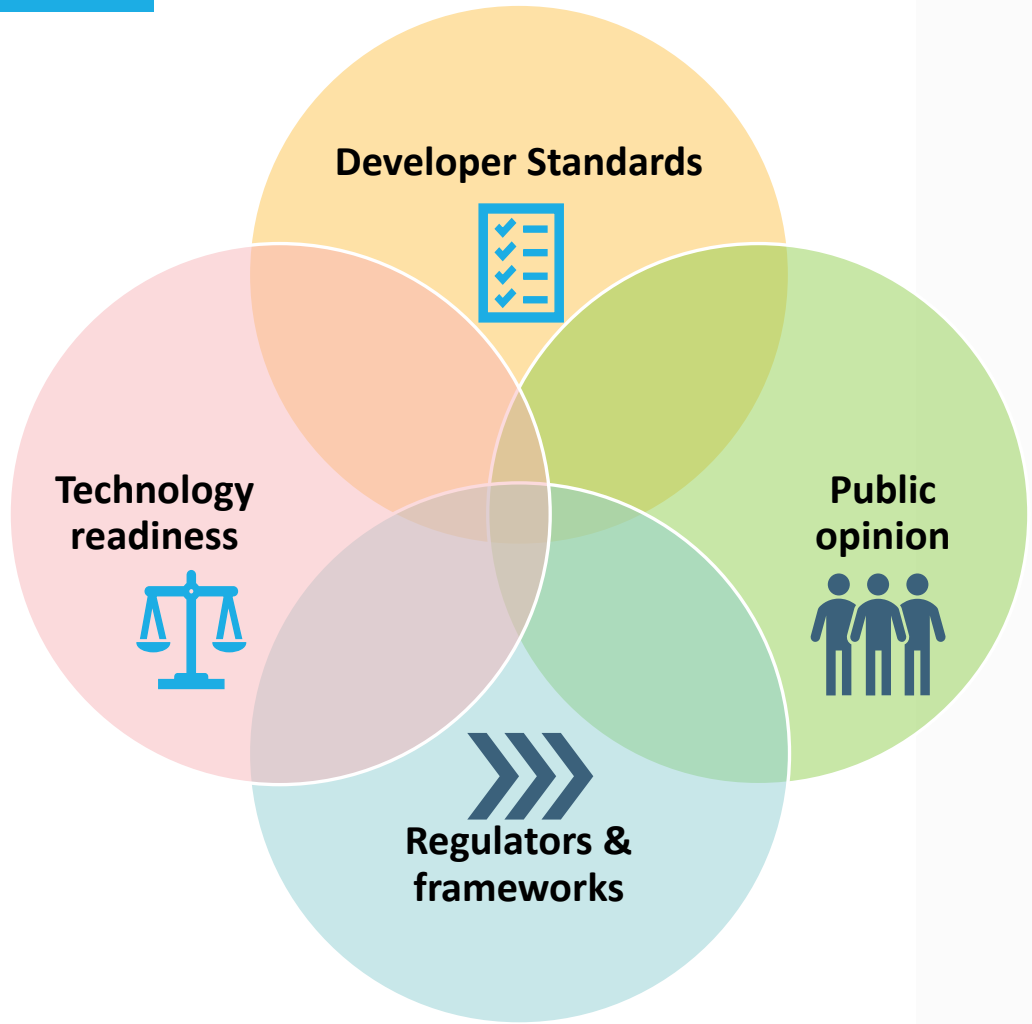
Are these technologies ready?

Public opinion

Are these technologies ready?

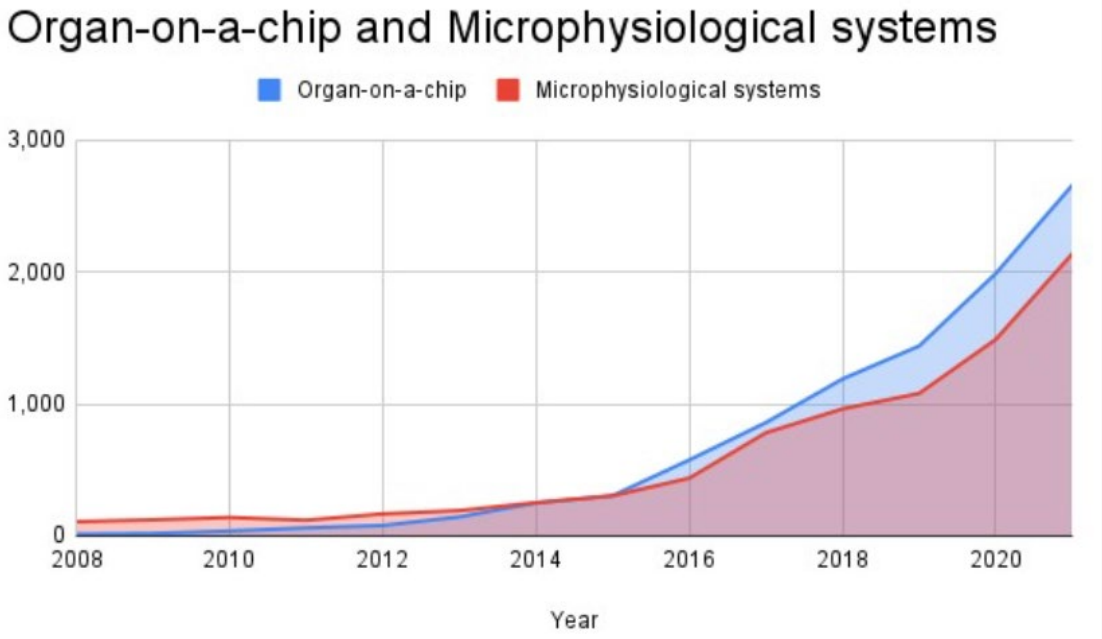


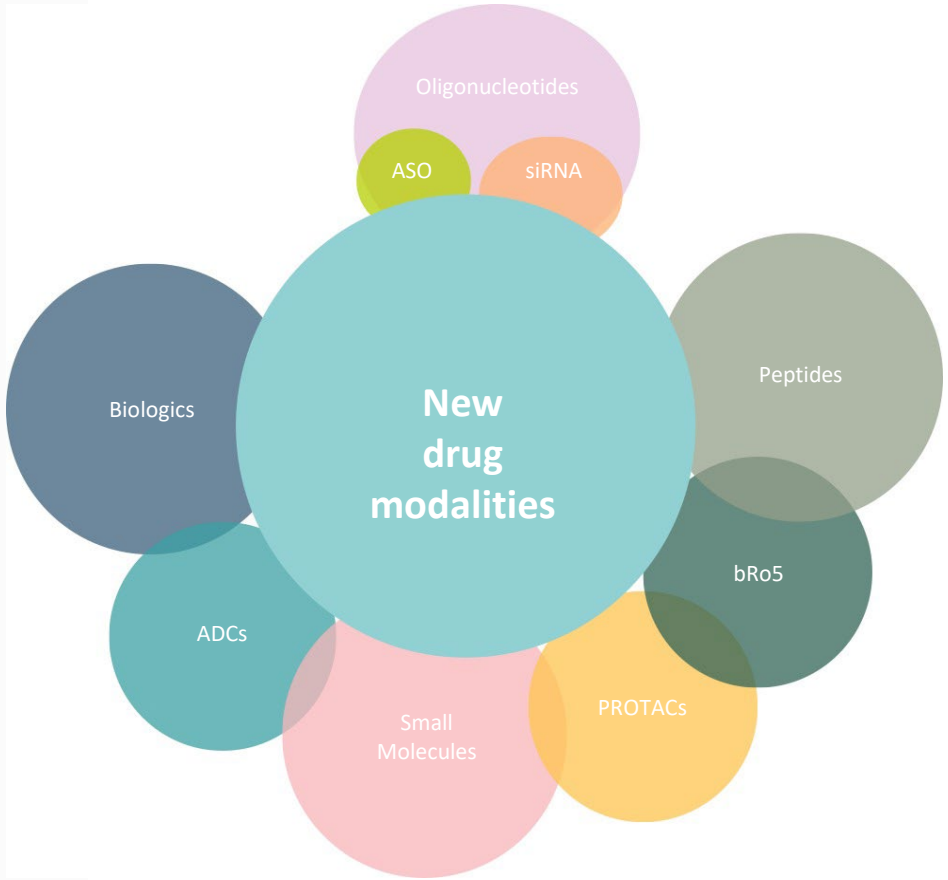
Available resources?



- https://nc3rs.org.uk/3rs-resource-library/nams-network
- https://3rc.org/microphysiological-systems-companies/
- https://impss.org/
- https://www.iqmps.org/

Future of Alternative methods?





https://www.whatisbiotechnology.org/index.php/science/summary/organchip/organs-on-a-chip-provide-valuable-insights-into-organ

Thank you

Dharaminder Singh

Dharaminder.singh@gmail.com

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Animal welfare value of synthetic matrices replacing animal tissue-based Matrigel

Cathy Merry

Stem Cell Glycobiology Group
Biodiscovery Institute
University of Nottingham
and Biomedical Centre, Uppsala University, Sweden

NC 3Rs 20 YEARS
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The challenge of *in vitro* models

Humans are complex and variable

Human disease is complex and multifactorial

New treatment options and improved detection are driving a move towards personalised medicine

However, cost is always a factor in drug development

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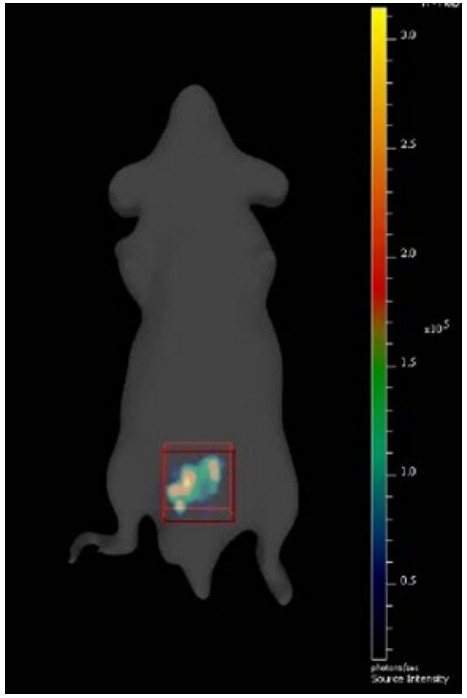
The challenge of *in vitro* models

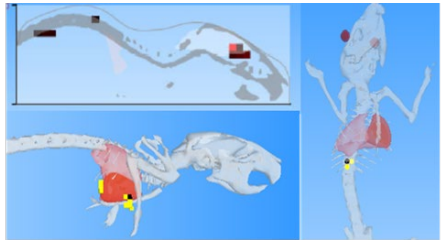
Rodents are often used to model human disease

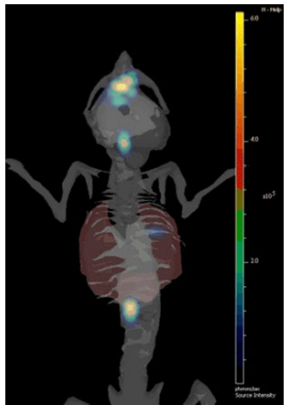
Some models e.g. cancer are well–developed and take advantage of modern imaging methods

Genetic engineering can create models of disorders such as diabetes / heart disease / neurodegenerative disorders



Bioluminescently-labelled orthotopic prostate tumour





Experimental model of metastasis with colonisation of brain and spine

The challenge of *in vitro* models

Many models fail to recapitulate human disease well

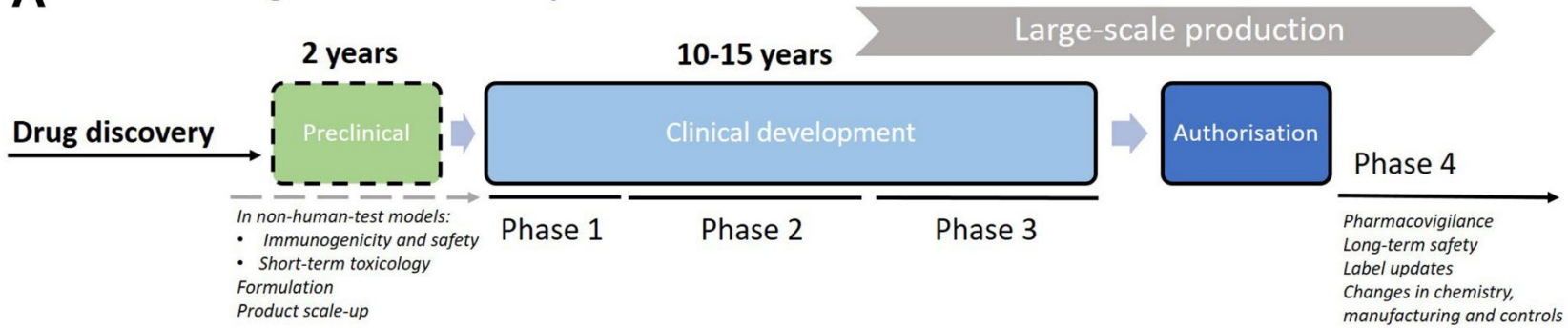
Particularly true for diseases of ageing (different life spans) or tied to human physiology (brain architecture is very different in rodents)

To date, very few drugs have been successfully transferred to humans directly from work in animal models

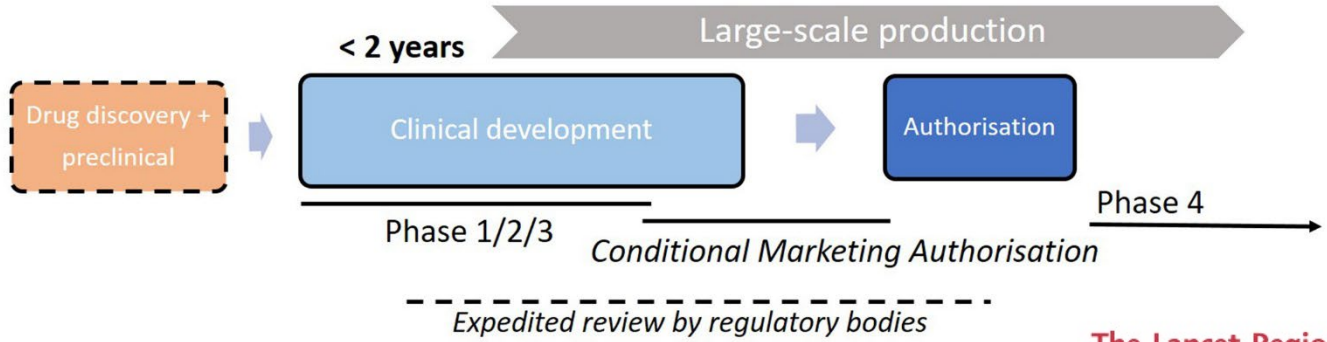
Factors associated with acceleration of clinical development for infectious diseases: a cross-sectional analysis of 10-year EMA registration data

Hanna K. de Jong,[a,*] Sabine M. Hermans,[a,b] Sophie M. Schuitenmaker,[a] Maya Oli,[a] Mariëtte A. van den Hoven,[c] and Martin P. Grobusch[a,d,e,f,g,*]

A Traditional drug and vaccine development model



B Emergency outbreak drug and vaccine development model (i.e. COVID-19 pandemic)



The Lancet Regional Health - Europe 2024;43: 100983

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Alternative approaches to animal use: Sanctioned in FDA modernization act 2.0 in 2022

NEWS

Recommendations to integrate 3Rs approaches in WHO guidance for biological products

09 November 2023

NC 3Rs 20 YEARS
Pioneering Better Science

- Each product-specific guideline should be updated to include the new 3Rs text where animal tests are currently recommended.
- The WHO should draft a position statement and guidance on the incorporation of 3Rs practices into quality control and batch release testing.
- A separate manual should be drafted to support the adoption of 3Rs approaches specifically for endotoxin and pyrogenicity testing.
- Changes should be made to the way WHO guidance documents are updated to improve their accessibility and utility.

New approach methodologies (NAMs) – for safety and toxicology testing

NC 3Rs National Centre for the Replacement Refinement & Reduction of Animals in Research

Unilever

Workshop report:

Opportunities for the UK to develop world-leading chemicals regulation

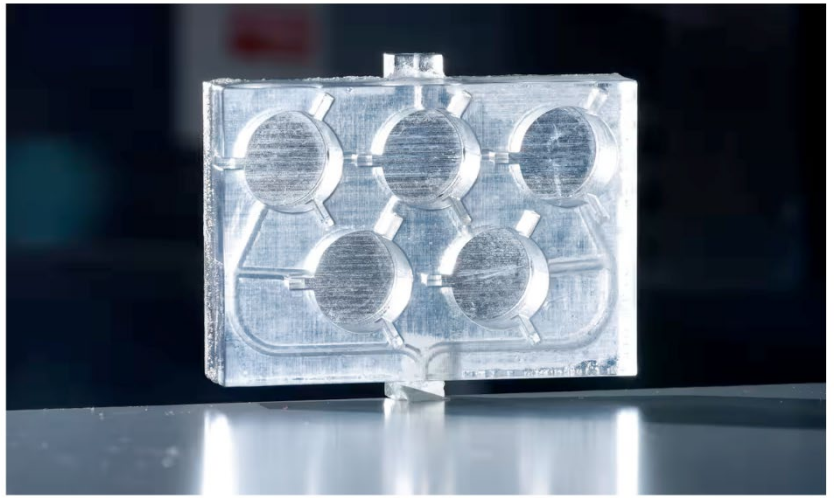
Workshop: 11 May 2023
Report published: 23 October 2023

Dr Natalie Burden, NC3Rs
Dr Carl Westmoreland, Unilever
Dr Andrew Scott, Unilever
Professor Ian Kimber, University of Manchester

The Guardian UK

3D-printed chip showing body's reaction to drugs could end need for animal tests

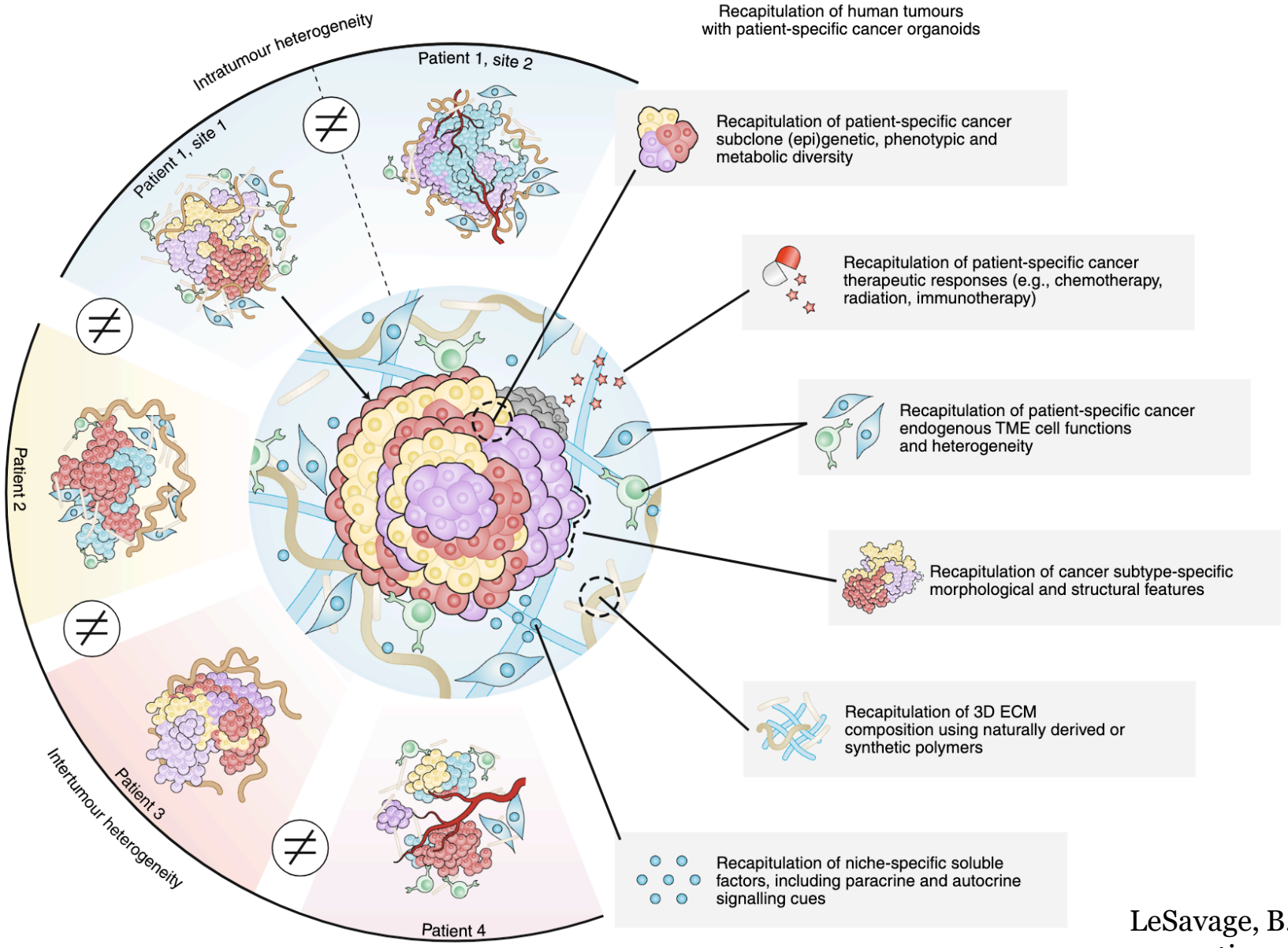
Exclusive: Device with compartments replicating major organs could also speed up patients' access to new medicines



The plastic device uses positron emission tomography (PET) scanning to produce detailed 3D images showing what is going on inside the organs. Photograph: Murdo MacLeod/The Guardian

Scientists have developed a pioneering 3D-printed device that could speed up patient access to new medicines and eliminate the need for animal testing.

What are the alternatives?

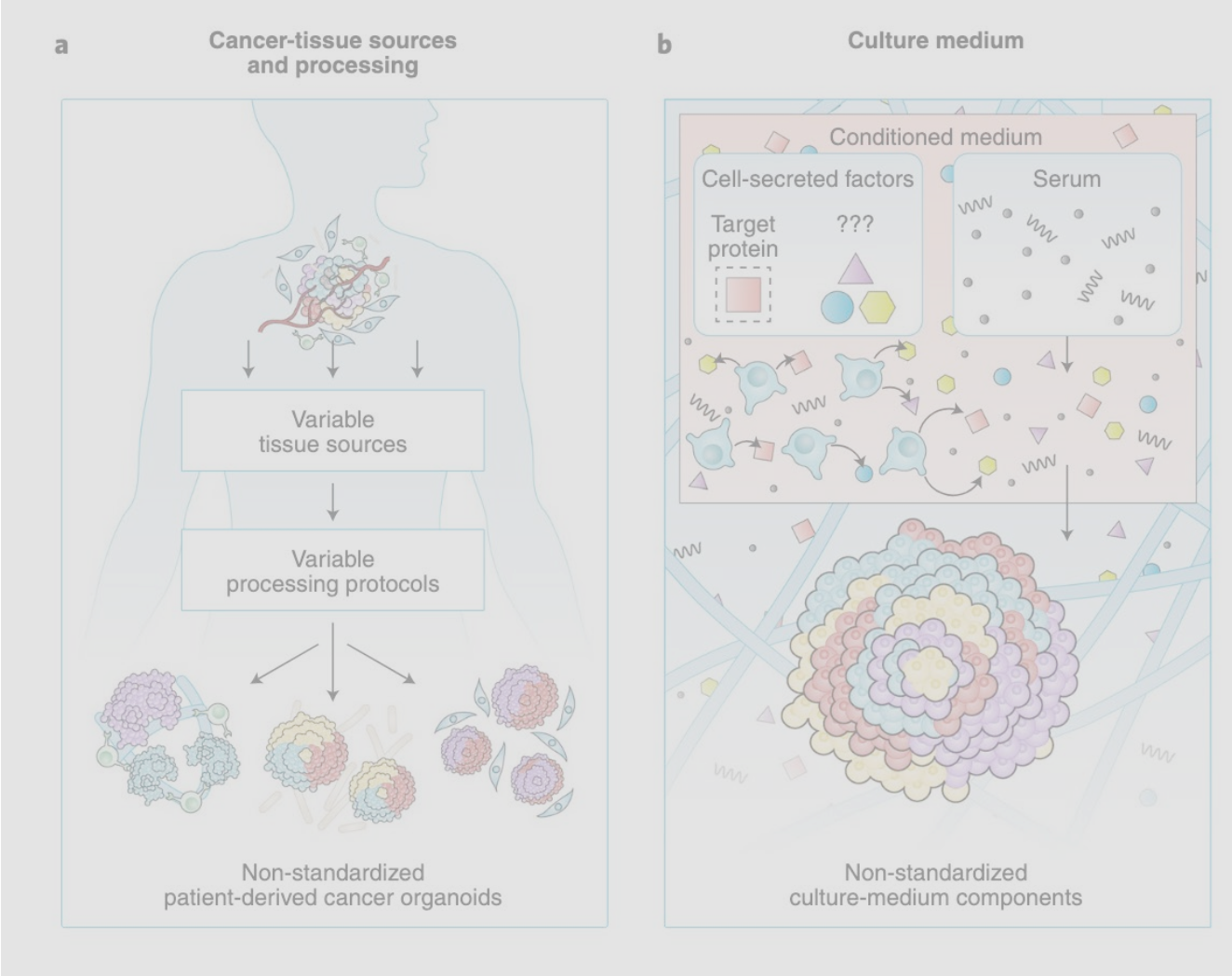


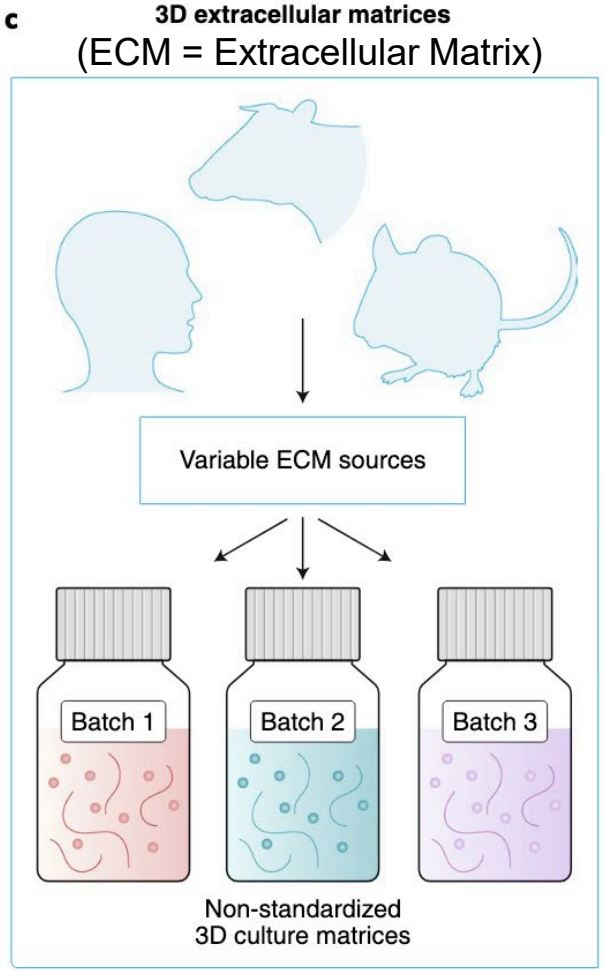
Organoids
(Cancer organoids shown here)

1. Recapitulate multiple patient characteristics
2. Allow rapid personalization of treatment options
3. Enable drug screening at an early stage against a large population

LeSavage, B.L., Suhar, R.A., Broguiere, N. *et al.* Next-generation cancer organoids. *Nat. Mater.* **21**, 143–159 (2022)

Limitations of current organoid technologies

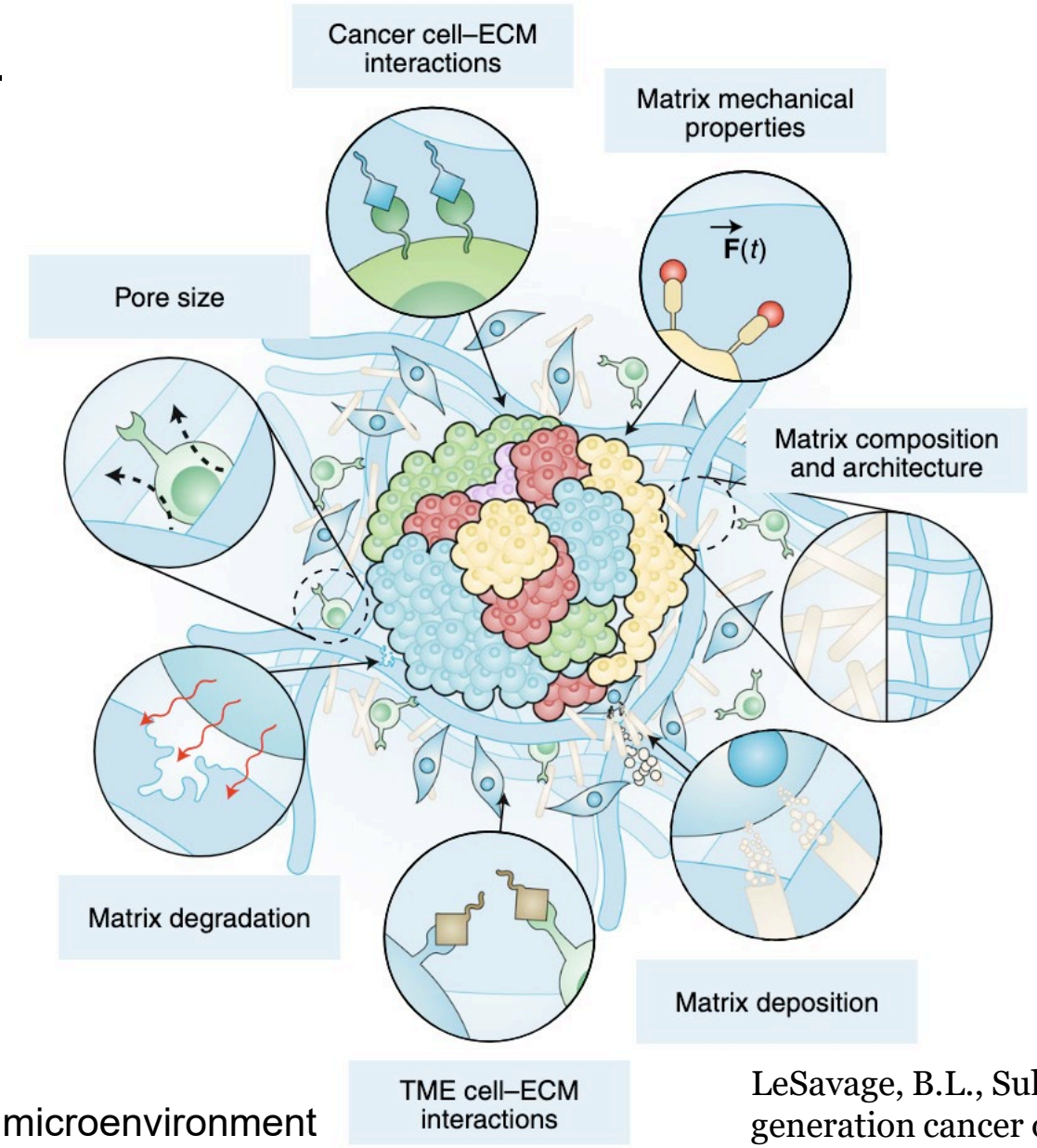




LeSavage, B.L., Suhar, R.A., Broguiere, N. *et al.* Next-generation cancer organoids. *Nat. Mater.* **21**, 143–159 (2022)

The extracellular matrix (ECM) controls cell behavior in multiple diseases

The ECM is an under-developed space in drug targeting for therapeutics

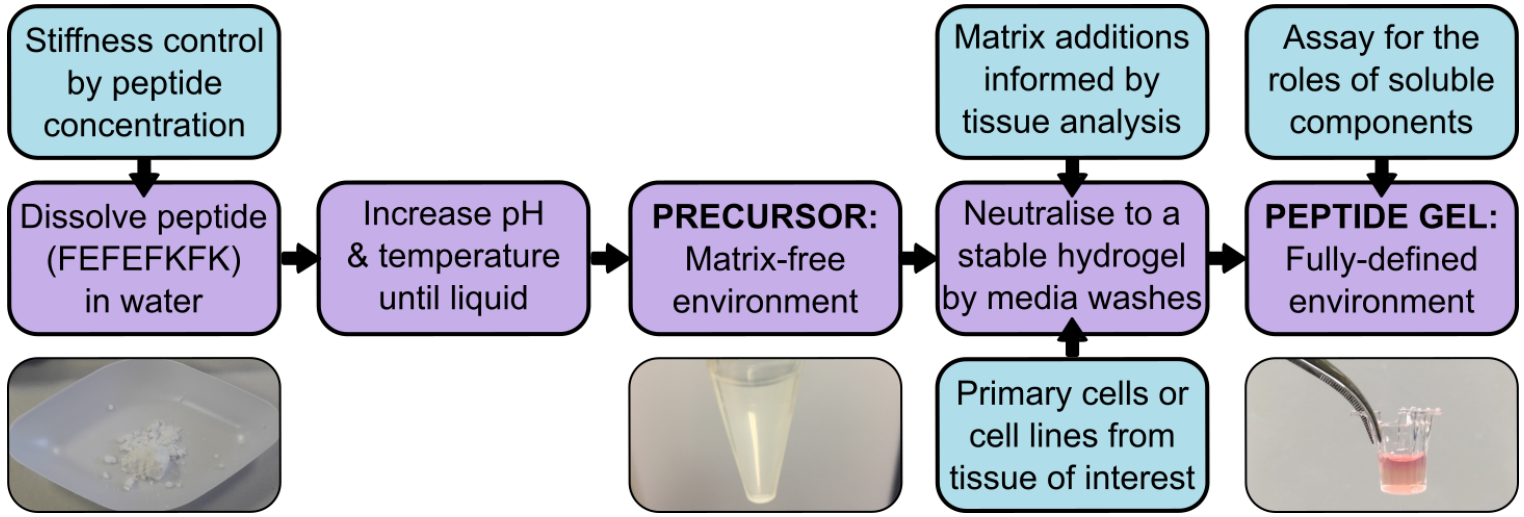


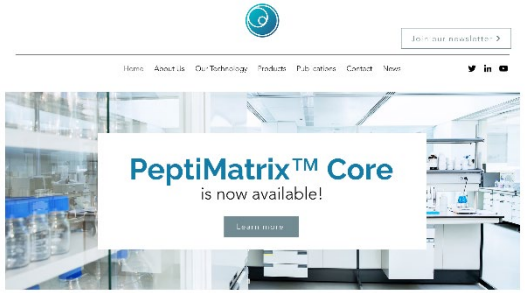
Changes in matrix properties are often part of diagnosis and likely should influence treatment

TME = Tumour microenvironment

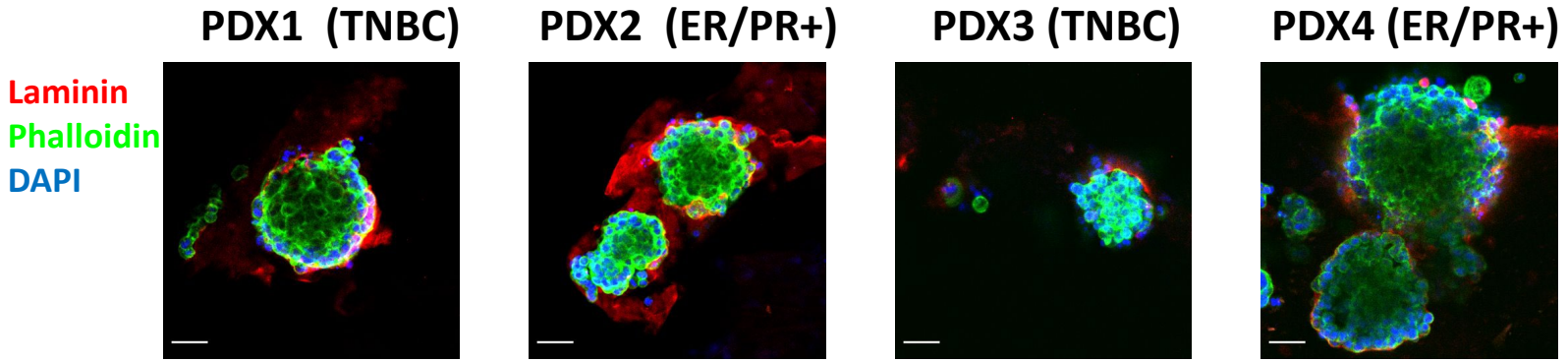
LeSavage, B.L., Suhar, R.A., Broguiere, N. *et al.* Next-generation cancer organoids. *Nat. Mater.* **21**, 143–159 (2022)

Fully-defined, synthetic alternatives to animal-derived matrices





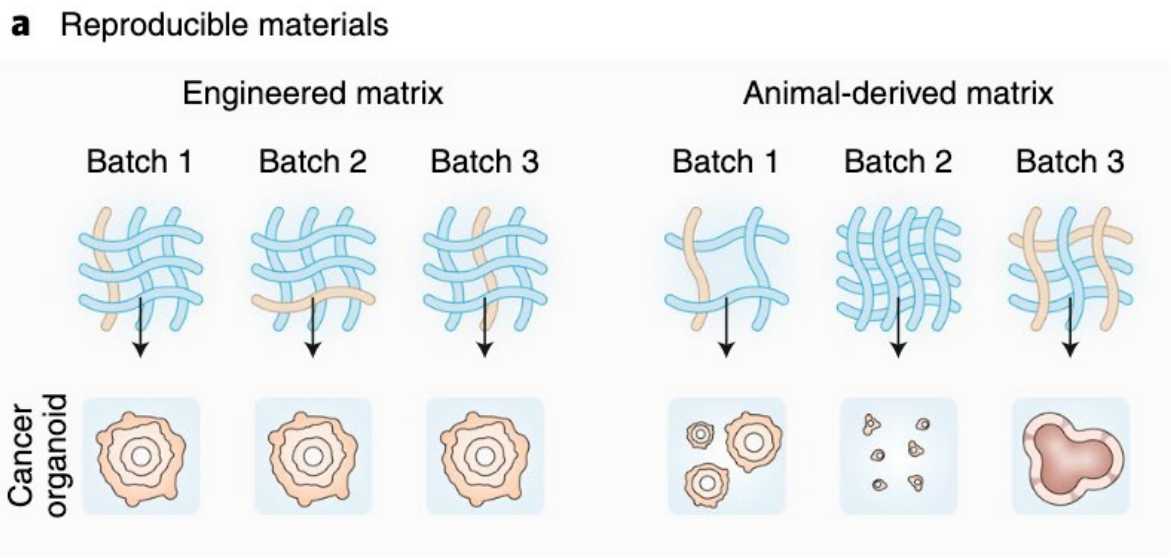
Jenny Ashworth

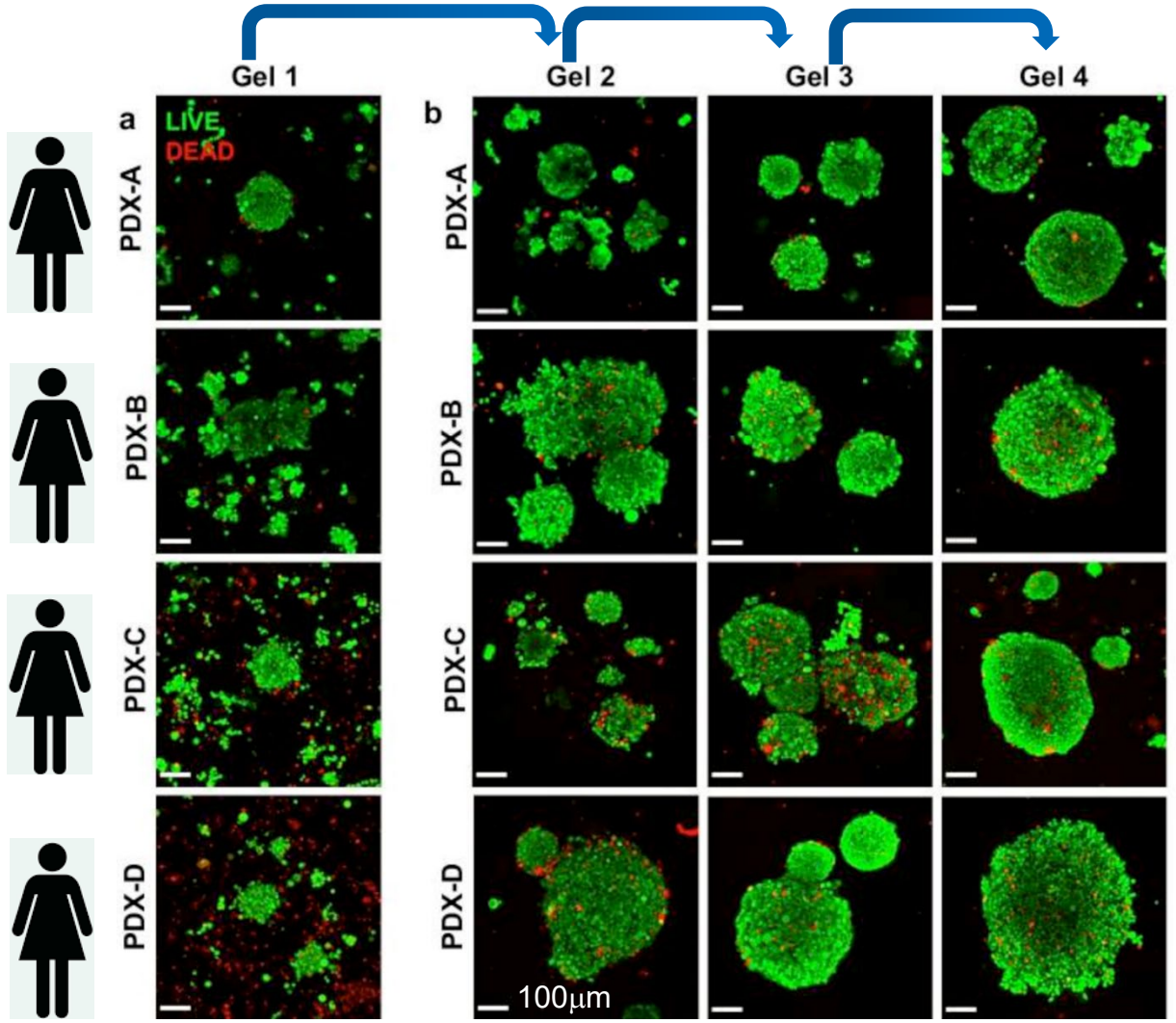


Sal Jones

JC Ashworth, JL Thompson et al. (2020) *Matrix Biology*, JC Ashworth et al. (2020) *JOVE*

Engineered (non-animal) matrices provide major benefits (e.g. over patient derived xenografts/PDXs)





Patient derived cells can be expanded *in vitro*

LeSavage, B.L., Suhar, R.A., Broguiere, N. *et al.* Next-generation cancer organoids. *Nat. Mater.* **21**, 143–159 (2022)

Jones S *et al.* Application of a 3D hydrogel-based model to replace use of animals for passaging patient-derived xenografts. In Vitro Model. 2023;2(3-4):99-111.

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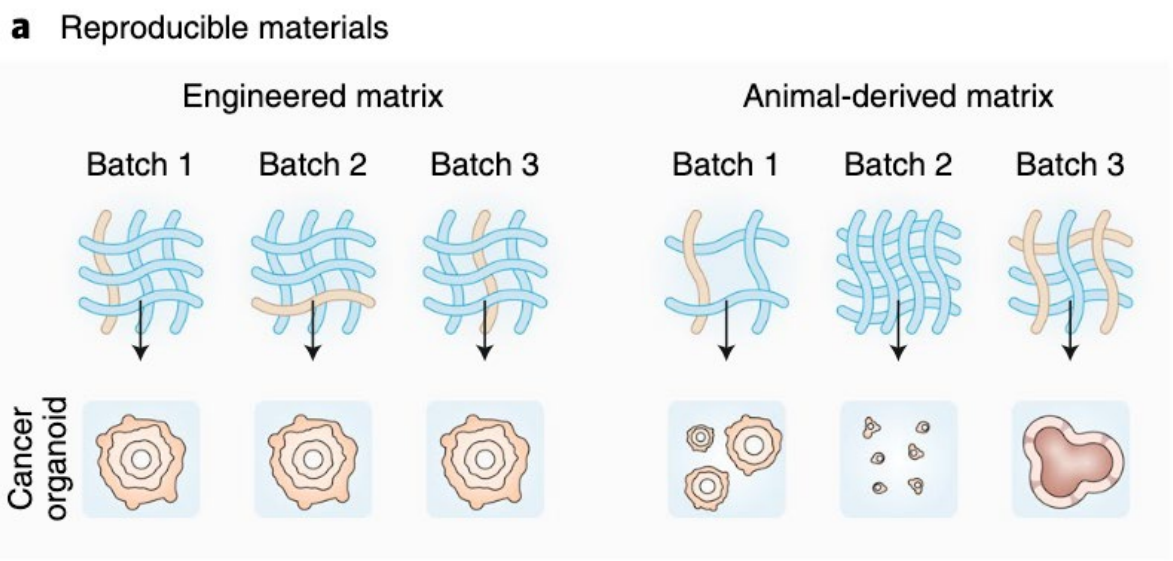

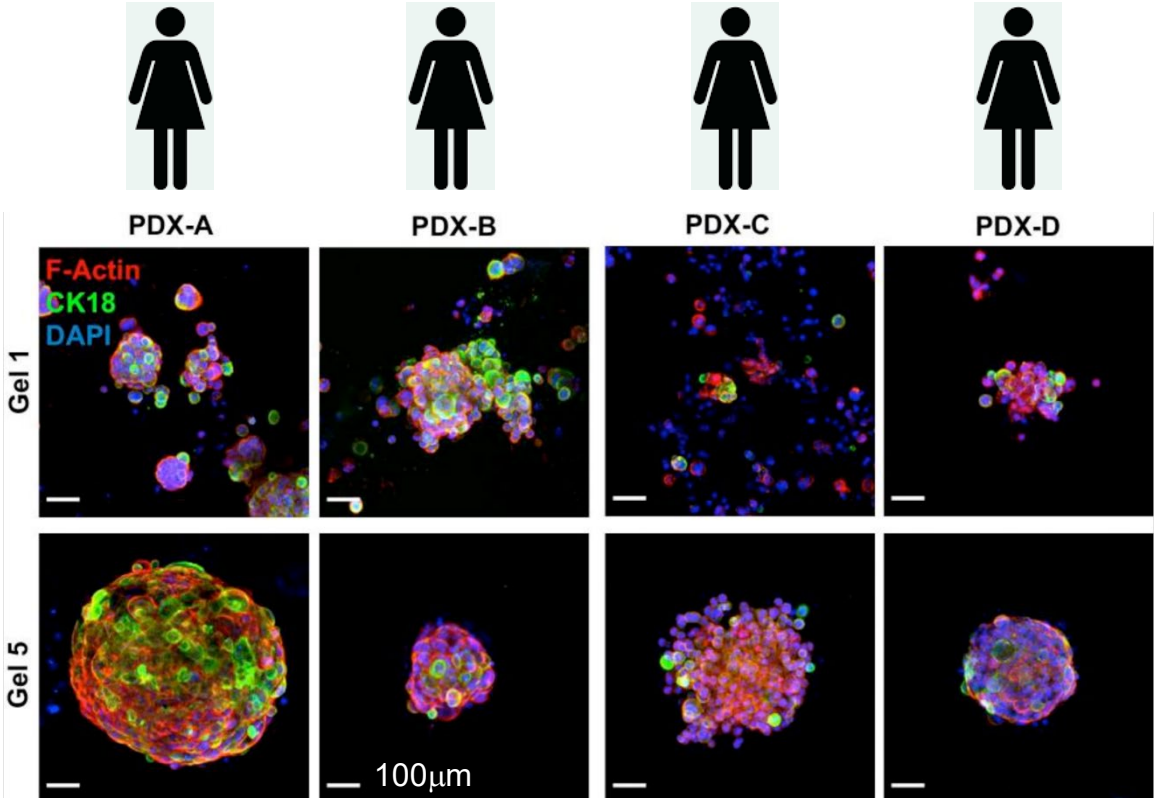

Patient-specific differences are maintained

LeSavage, B.L., Suhar, R.A., Broguiere, N. *et al.* Next-generation cancer organoids. *Nat. Mater.* **21**, 143–159 (2022)

Jones S *et al.* Application of a 3D hydrogel-based model to replace use of animals for passaging patient-derived xenografts. In Vitro Model. 2023;2(3-4):99-111.

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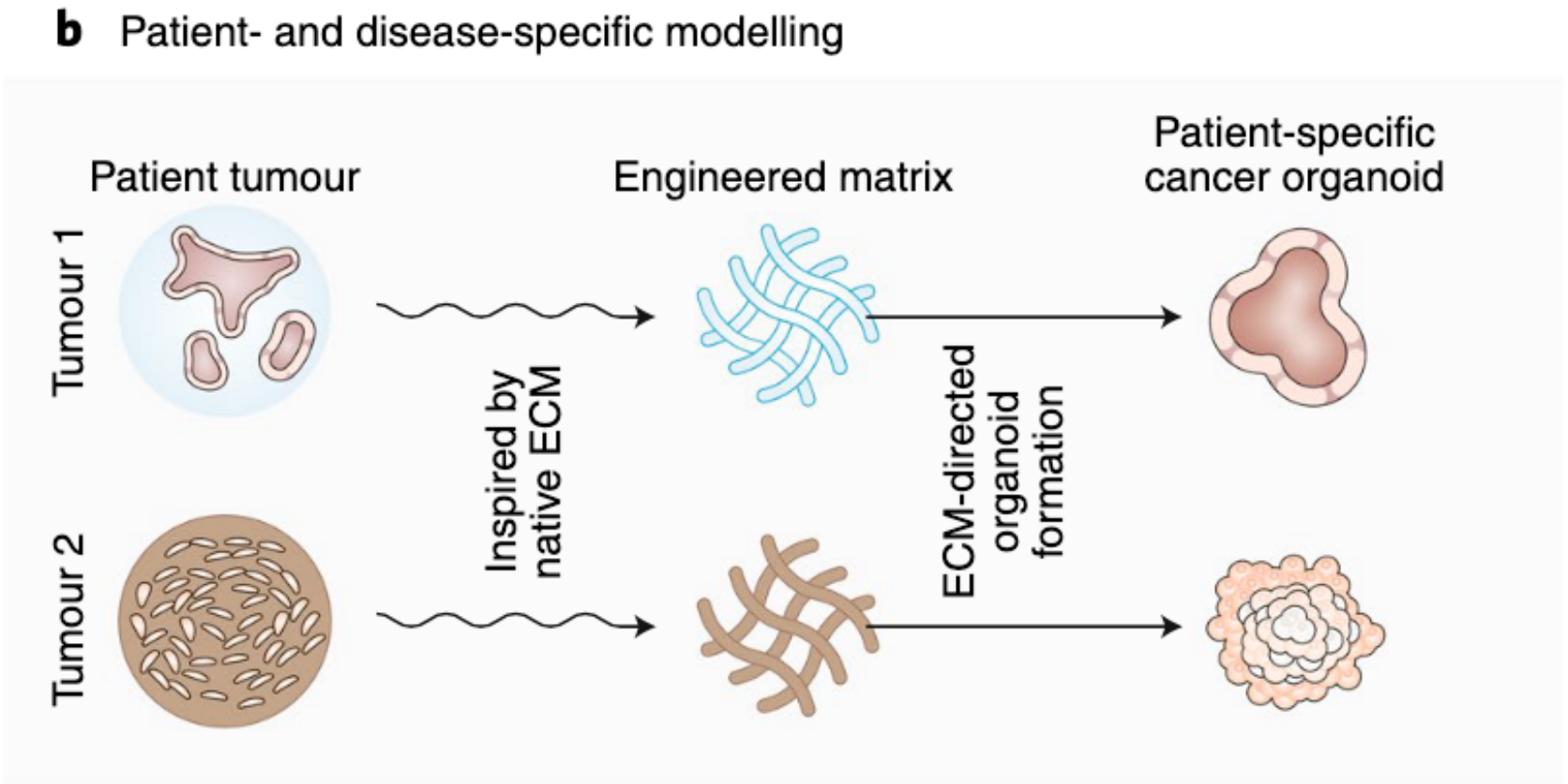

LeSavage, B.L., Suhar, R.A., Broguiere, N. *et al.* Next-generation cancer organoids. *Nat. Mater.* **21**, 143–159 (2022)

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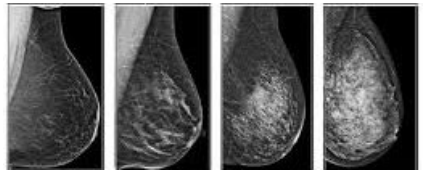
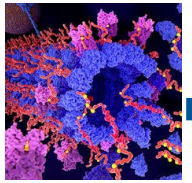
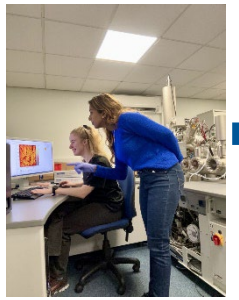


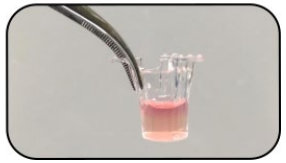
Matrix Proteomics



Matrix glycan analysis

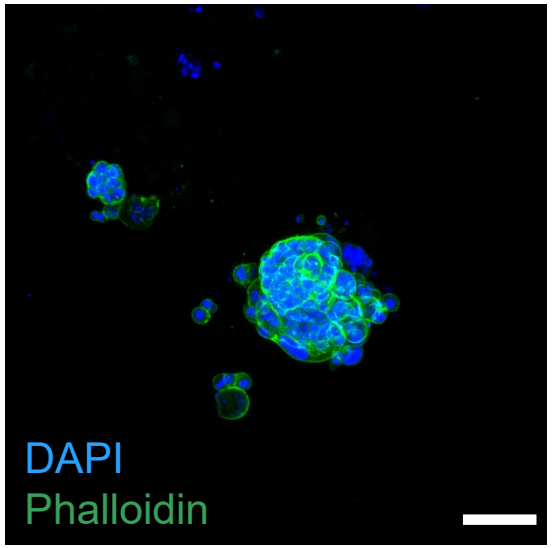


Select gel components

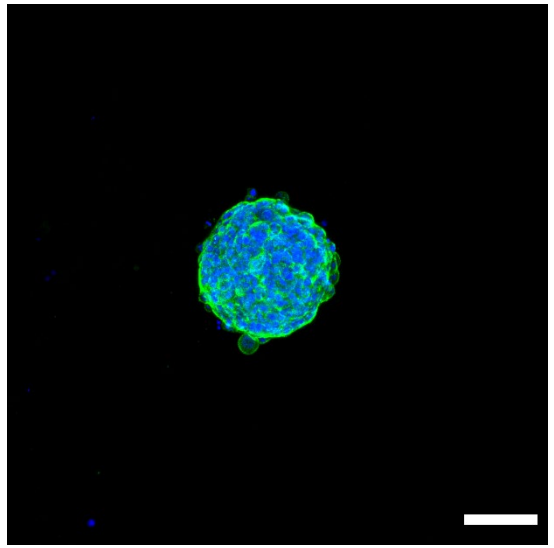


Normal Breast Matrix Model

Patient 1

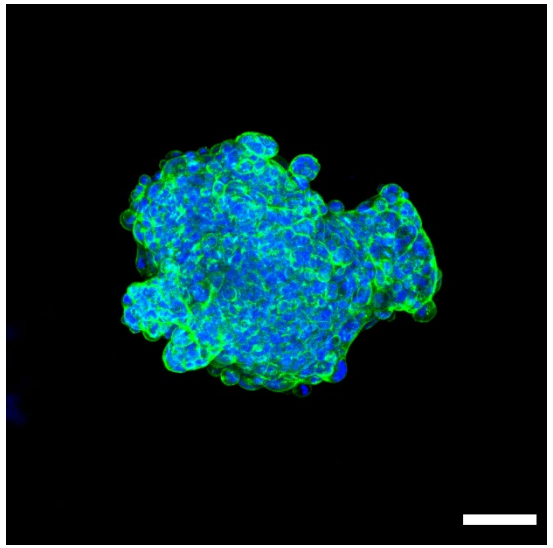


Patient 2

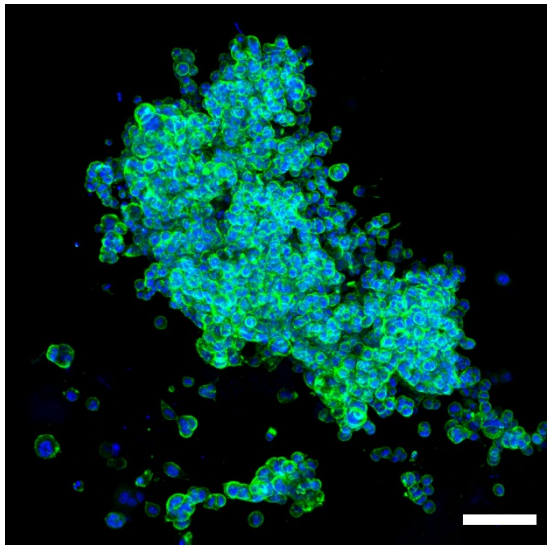


Invasive Matrix Model

Patient 1



Patient 2



Scale bar 100 μm

Unpublished data, Ashworth et al.

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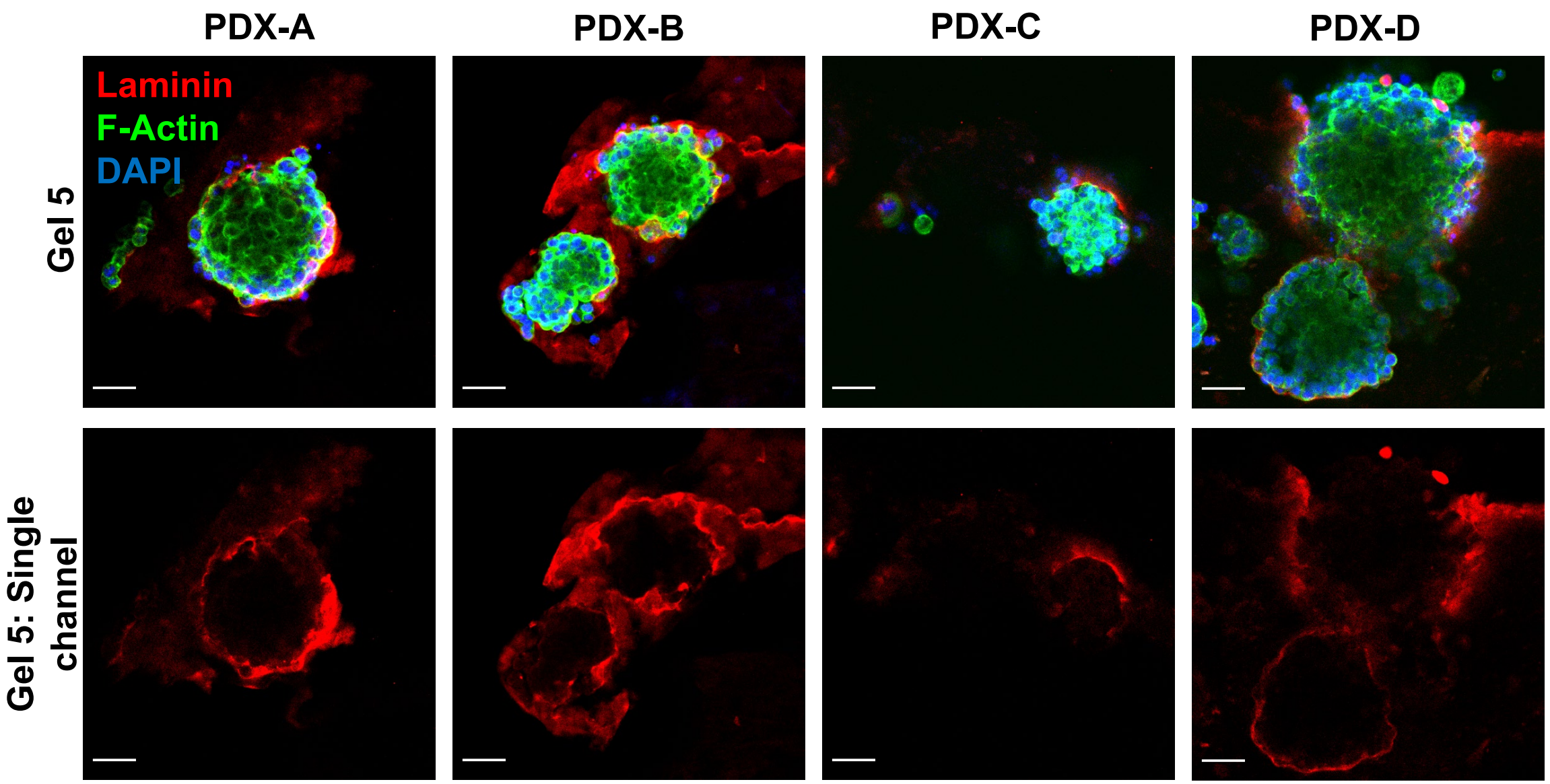
Patient derived xenografts (PDXs) or embedded cells re-model the matrix environment



Scale bar 100 µm

Jones S et al. In Vitro Model. 2023

University of Nottingham
UK | CHINA | MALAYSIA

Summary

Good alternatives to the use of animal models or models using animal-derived materials now exist

These need to be carefully validated against patient outcomes

Legislation is changing rapidly, allowing the use of these non-animal models

Switching away from animal models has the potential to save time and money in research and drug development as well as environmental and animal welfare benefits

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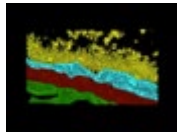

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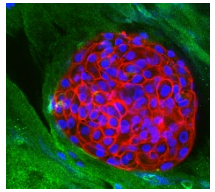

Funding

NC 3Rs National Centre for the Replacement Refinement & Reduction of Animals in Research

UKRI Biotechnology and Biological Sciences Research Council

UKRI Engineering and Physical Sciences Research Council

Collaborators

CHO library
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Mouse model of stroke
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Septic mouse tissue (Brain, Kidney, Blood & Urine)
Joseph Hippensteel, University of Colorado Hospital.

PeptiMatrix™ Next generation peptide hydrogels

GLYCOWEB

University of Nottingham
University of Liverpool
University of Manchester
The Crick Institute
with
University of Georgia
University of Copenhagen

Any Questions?

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Break

Please be back promptly at 14:40

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Practical advice for AWERBs on assessing replacement

Prof Adrian Smith, Norecopa

Elaine Blair, University of Strathclyde

Resources for AWERBs on assessing replacement available on the Norecopa website

Adrian Smith

adrian.smith@norecopa.no
linkedin.com/in/adrian-smith-bb567b5a
@adrian_3r

norecopa.no/ASC

Practical advice on literature searching on alternatives for AWERBs and applicants

Elaine Blair, Science Faculty Librarian

Session Aims

To conduct an online literature search:

- Construct strategies to search databases
- Identify the main bibliographic databases
- Manage your results

Literature searching

- A literature search is likely to be a requirement for any AWERB application
- Needs to be completed in a thorough and organised manner using recognised literature sources and appropriate keywords
- Ensures that replication of experiments are kept to a minimum
- Identifies the 3Rs linked to the research
  - Reduction
  - Refinement
  - Replacement

Choosing keywords

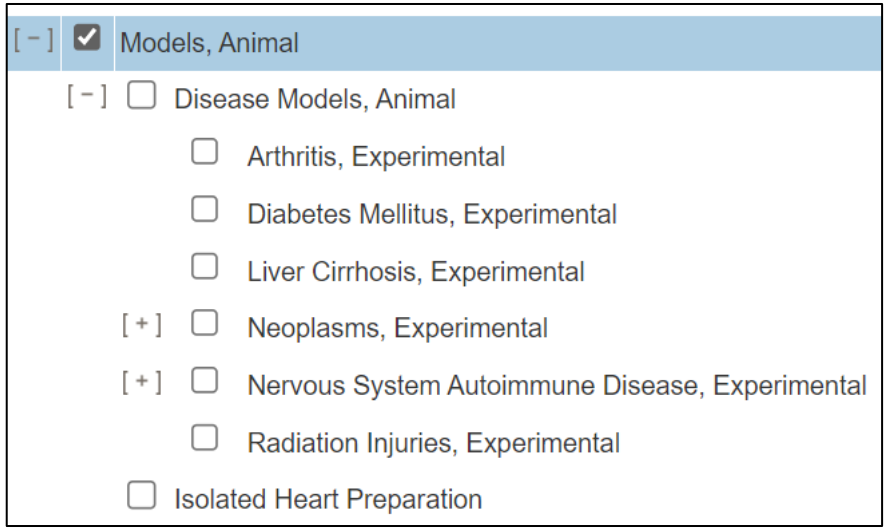
- List keywords relevant to the research protocol
  - E.g. name of the animal or species, name of the disease or condition, drugs and compounds, procedures and methods especially painful or distresssing
- List keywords for the reduction, refinement, or replacement of animal research subjects
- Reduction
  - For example: animal reduction, animal model, repurposing animals
- Refinement
  - For example: handling, husbandry, caging, enclosure, educate, train, analgesia, pain management
- Replacement
  - For example: animal testing alternatives, animal use alternatives, artificial intelligence, computer simulation
- Think about synonyms and acronyms

Subject searching (thesaurus)

- Subject headings are assigned to papers from a predefined list
- They describe the content of the paper
- You only search in the subject field - less flexible
- Subject terms are consistent – no matter what term author uses
- They are found in the database thesaurus – not all database have a thesaurus
- Different databases may use different subject headings – e.g. Embase uses Emtree, PubMed/MEDLINE use MeSH

MeSH Subject Headings

- MeSH (Medical Subject Headings) are used by PubMed, MEDLINE, Cochrane Library, PsycINFO
- Tree structure
  - Main heading, subheadings
  - Broader, narrower and related terms
  - Explode to include all the narrower terms
  - Focus where the subject is the main focus of paper



- Example from MEDLINE (Ovid): animal models maps to the MeSH heading models, animal

Search hedges

- Ready made searches that can be copied and pasted into a database
- AWIC Search hedges – Animal Welfare Information Center search hedges in collaboration with AVIS.

Example:

- AVIS Search Strategies Working Group. 2024. Non-Animal Model Search Hedges. AVIS Search Strategies Working Group Hedges. Open Science Foundation.
  DOI 10.17605/OSF.IO/JY2HB https://osf.io/jy2hb/

Example PubMed Non-animal model search hedge

("Animal Testing Alternatives"[MeSH Terms] OR "Animal Use Alternatives"[MeSH Terms] OR 3Rs[Title/Abstract] OR "3 Rs"[Title/Abstract] OR "alternative to animal model*"[Title/Abstract] OR "alternatives to animal model*"[Title/Abstract] OR "alternatives animal"[Title/Abstract:~2] OR "alternative animal"[Title/Abstract:~2] OR ex-vivo[Title/Abstract] OR "new approach method*"[Title/Abstract] OR in-chemico[Title/Abstract] OR in-vitro-model*[Title/Abstract] OR in-silico[Title/Abstract] OR in-vitro-method*[Title/Abstract] OR in-vitro-stud*[Title/Abstract] OR new-alternative-method*[Title/Abstract] OR nonanimal-method*[Title/Abstract] OR non-animal-model*[Title/Abstract] OR non-animal-stud*[Title/Abstract] OR three-rs[Title/Abstract] OR "reduction refinement replacement"[Title/Abstract:~2] OR "reduce refine replace"[Title/Abstract:~2] OR "Animal replacing"[Title/Abstract:~2] OR "Animals replacing"[Title/Abstract:~2] OR "Animal replacement"[Title/Abstract:~2] OR "Animals replacement"[Title/Abstract:~2] OR "Animal replacements"[Title/Abstract:~2] OR "Animals replacements"[Title/Abstract:~2] OR "Animals replace"[Title/Abstract:~2] OR "Animal replace"[Title/Abstract:~2] OR "Animals replaces"[Title/Abstract:~2] OR "Animal replaces"[Title/Abstract:~2] OR "Animal replaced"[Title/Abstract:~2] OR "Animals replaced"[Title/Abstract:~2])

Construct your search

- Boolean – AND, OR, NOT
- Truncation – finds words with the same root. Usually * or ? E.g. behav* finds behaviour, behaviours, behave, behaves etc.
- Phrase searching – exact terms. Usually”” E.g. “animal model”
- Proximity operators– find words near to each other. ADJ, NEAR, ~, W, N, E.g. alternative* NEAR/2 animal
- Check the database help for search syntax
- Join your search terms to make a search string
- Search history can be helpful for complex searches
  - Can construct the search in parts then join together

Select databases

- Always search more than one database
- PubMed/MEDLINE
- Another biomedical database (EMBASE, BIOSIS Citation Index/Previews, Biological Abstracts)
- Web of Science or SCOPUS – multidisciplinary databases
- Database related to an aspect of the protocol design
- Find other funded research projects – e.g. UKRI gateway
- GoogleScholar and AI tools are not suitable as alternative databases

Modify your search

- Too many results?
  - Limit by field (e.g. title only search), limit by article type, limit by year, limit by language, add additional terms (AND), use an exact phrase, use proximity operators, more specific terms, search another database
- Too few results?
  - Add alternative terms (OR), use more general terms, use truncation to find all words with same root, check spellings, check limits, search another database

Record and Manage results

- Record details of your search
  - Keywords, search strategy, databases searched, years covered, date of search
- Reference management tools
  - EndNote, Zotero, RefWorks, Mendeley

Checklist

- Databases searched >1
- Don’t use Google Scholar or AI tools
- Keywords and subject terms used - protocol specific and 3Rs, multiple keywords, use of search hedges
- Search strategy – check Boolean and other search operators
- Time period – at least five years
- Date searched

Resources

- Animal Welfare Information Center (2022) Alternatives Literature Searching worksheet
- National Agricultural Library Literature Searching: How to Find Animal Use Alternatives

Poll

How confident do you feel in assessing the implementation of replacement in a project licence application?

1. Not at all confident
2. Slightly confident
3. Neutral
4. Confident
5. Very confident

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Breakout rooms

1. What do you find to be the difficulties with assessing replacement?
2. What are some of the more general questions that you find particularly helpful in assessing replacement?
3. What might you look for in an application to determine whether the applicant has adequately considered replacement?
4. What resources do you currently use to assess replacement?
5. How might you stay on top of future developments in non-animal alternatives?
6. How might you work with other AWERBs or other stakeholders to share knowledge on replacement?

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Final thoughts and feedback

Poll

On a scale of 1-5, how useful did you find this workshop?

1 Not at all useful

5 Very useful

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Thank you!

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Useful links:

ASC website – Animals in Science Committee - GOV.UK (www.gov.uk)

ASC and AWERB Hub workshop report: October 2024 – GOV.UK

Commission on non-technical summaries and retrospective assessments - GOV.UK

Commission on AWERBs and Named Information Officer - GOV.UK

Commission on leading practice in the animals in science sector - GOV.UK

AWERB-UK Registration - 18th June 2025, London

AWERB Knowledge Hub – Welcome - Knowledge Hub (khub.net) [khub.net]
(please email asc.secretariat@homeoffice.gov.uk to join)