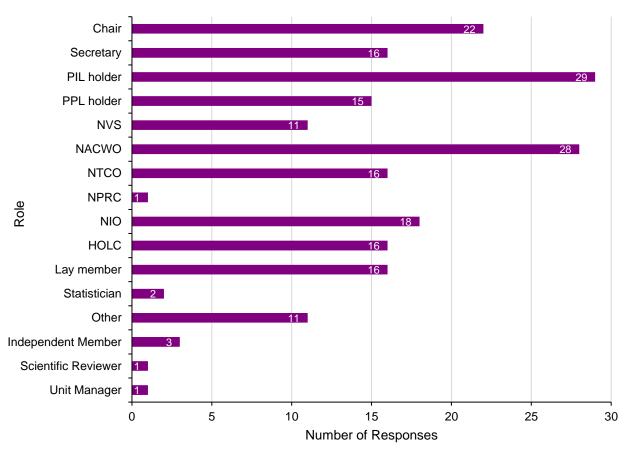
Animals in Science Committee and Animal Welfare Ethical Review Body Hub Workshop: 2 April 2025

The AWERB Hub workshop was convened and held under the aegis of the ASC's AWERB Subgroup. The views summarised in this report are those expressed by attendees of the workshop, and do not necessarily represent the views of the ASC. This report is not intended to be, and should not be interpreted as, a policy statement or a work plan.

Introduction

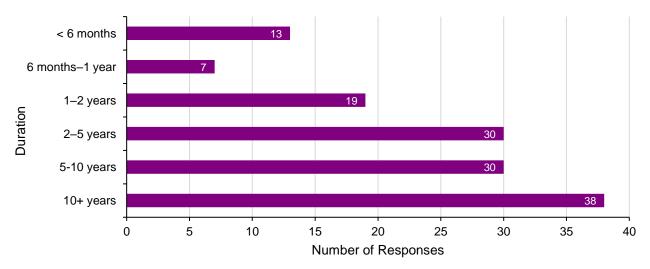
- 1. The twelfth Animals in Science Committee (ASC) and Animal Welfare Ethical Review Body (AWERB) Hub workshop was convened on 2 April 2025 via a virtual platform.
- 2. The aim of the event was to enable attendees to share and discuss:
 - a. An update on the work of the Animals in Science Committee
 - b. An update from the National Centre for the Replacement, Refinement, & Reduction of Animals in Research (NC3Rs)
 - c. An introduction to alternative methods
 - d. Practical advice for AWERBs on assessing replacement
- 3. More than 180 individuals attended the workshop. Attendees included AWERB Chairs and/or their nominated representatives, and AWERB members from a variety of roles and backgrounds. The event was organised and facilitated by members of the ASC AWERB Subgroup, the ASC Secretariat and presenters, who were all also in attendance. The workshop was chaired by Mrs Caroline Chadwick (Chair of the ASC AWERB Subgroup).

4. The workshop began with two polls to gauge the composition of the audience. The first poll question was, "What is your role within your AWERB?". Respondents were able to select more than one response. 133 attendees responded to the poll.



What is your role within your AWERB?

5. The second poll question was, "How long have you been a member of your AWERB?". Respondents were asked to select one response. 137 attendees responded to the poll.



How long have you been a member of your AWERB?

- 6. The agenda for the workshop can be found at Annex A. Presentations were delivered by:
 - a. Update on the work of the Animals in Science Committee: Mrs Wendy Jarrett (ASC AWERB Subgroup)
 - b. Update from the NC3Rs: Dr Nathalie Percie du Sert (N3CRs)
 - c. Introduction to alternative methods: Mr Barney Reed (RSPCA), Dr Dharaminder Singh (CN Bio) and Prof Cathy Merry (The University of Nottingham)
 - d. Practical advice for AWERBs on assessing replacement: Prof Adrian Smith (Norecopa) and Ms Elaine Blair (University of Strathclyde)
- 7. This report outlines the key points and findings from the event. Presentations during the workshop have been made available to attendees to circulate within their AWERBs.

Update on the work of the Animals in Science Committee

- 8. Mrs Wendy Jarrett delivered the first presentation, which aimed to provide an update on the work of the ASC since the last ASC AWERB Hub workshop in October 2024.
- 9. The format of the session was a presentation followed by time for Q&A.
- 10. The key points covered by the presentation were:
 - a. Professor David Main will finish his tenure as ASC Chair on 31 May 2025 and a new Chair had been appointed to begin their term on 1 June 2025. The <u>announcement</u> will be published on the ASC website on 10 April 2025.
 - b. The ASC had recently published the <u>ASC and AWERB Hub workshop</u> report: October 2024.
 - c. At the end of 2024, the Home Counties North West and Middlesex AWERB Hub closed. The AWERBs within the affected Hub have been reallocated. The East Anglia AWERB Hub had been reactivated.
 - d. Detailed commissions have been published:
 - i <u>A commission on improving non-technical summaries and</u> <u>retrospective assessments.</u>
 - ii. <u>A commission on strengthening leading practice in the animals in</u> <u>science sector.</u>
 - iii. A commission on strengthening the functioning of AWERBs and Named Information Officer.
 - e. The ASC report on <u>non-human primates used in service licences</u> had been published.
 - f. The AWERB-UK meeting, hosted by RSPCA and titled *Strengthening AWERBs: Resource, Engagement, and Recognition*, would be held on 18 June 2025 in Central London and is free to attend.
- 11. At the end of the presentation, attendees were invited to ask any questions, but none were raised.

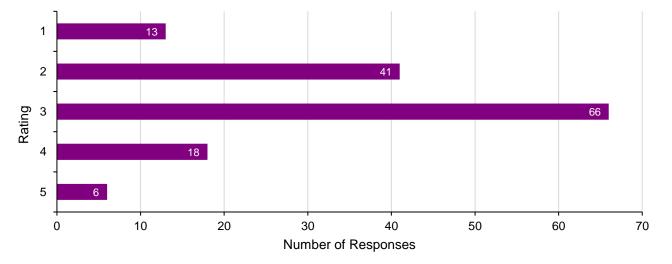
Update from the NC3Rs

- 12. The Chair then welcomed the speaker for the next item, Dr Nathalie Percie du Sert, who delivered an overview of the progress of the ongoing NC3Rs review of the project licence (PPL) application questions, focusing specifically on the 3Rs.
- 13. The format of the session was a presentation followed by time for Q&A.
- 14. The key points covered by the presentation were:
 - a. An NC3Rs team will review the project licence application form, conduct consultations, then draft recommendations to the Animals in Science Regulatory Unit (ASRU) and Animals in Science Regulation Policy Unit (ASRPU). An analysis of the current project licence form was presented.
 - b. Three options were presented as initial investigation targets:
 - i. Consolidate the NTS and licence questions.
 - ii. Use Standard Operating Procedures (SOPs) outside of the licence to replace some question sets.
 - iii. Use study plan documentation to monitor the implementation of the 3Rs in individual studies under a project licence.
- 15. At the end of the presentation, attendees were invited to ask any questions. The following points were raised:
 - a. One organisation raised that they already assess study plans via their AWERB, and another mentioned that their study plans are reviewed by NACWOs.
 - b. The projected timelines were for the NC3Rs to feed back to ASRU and ASRPU by the end of summer 2025. ASRU will have to provide any further timelines on advice uptake.
 - c. Best practice would suggest that SOPs should include a review date.

Introduction to alternative methods

- 16. The Chair then welcomed the three speakers for the next item, Mr Barney Reed, Dr Dharaminder Singh, and Prof Cathy Merry.
- 17. The format of the session was the delivery of all three presentations in succession, followed by a Q&A session. The aim of the session was to facilitate discussion around the barriers, opportunities, and development of alternatives to animal systems.

18. The session began with the following poll question: "How familiar are you with the field of alternative methods?", where "1" was "not at all familiar" and "5" was "very familiar". 144 attendees responded to the poll. The average score was 2.7.



How familiar are you with the field of alternative methods?

- 19. Following the poll, the Chair introduced Mr Barney Reed, who delivered an overview of initiatives and strategies to accelerate the replacement of animals in science. The key points were:
 - a. As well as scientific and technological challenges associated with the faster and wider development and uptake of non-animal approaches, there are also significant socio-cultural factors linked to 'how science is done' (e.g. funded, incentivised, published) which can act as barriers to people's awareness of, access to, enthusiasm for, and confidence in new models and approaches.
 - b. Strategies for promoting replacement generally include activities for reviewing the current situation, prioritisation of efforts and resources, developing clear action plans for specific areas of research or testing, and providing practical support for implementation.
 - c. Governments and industry in a number of countries are seeking to leverage the significant scientific, economic and ethical benefits increasingly on offer from the exploitation of new technologies and new approach methodologies.
 - d. Individual AWERBs can contribute by establishing replacement as a strategic ambition and objective; facilitating collaborations between researchers within the institution; supporting access to training; supporting the Named Information Officer role; staying up to date with developments in replacement technologies; challenging the status quo; and looking for opportunities to contribute their expertise to external initiatives.
- 20. The Chair thanked Mr Barney Reed and passed onto Dr Dharaminder Singh, who delivered an overview on industry perspective on alternative methods. The key points were:

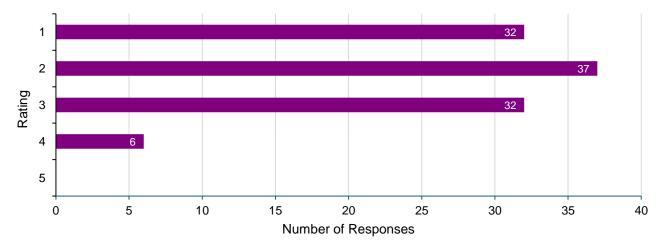
- a. Overview of Microphysiological Systems (MPS) and how they share common features such as human cells and tissues, fluidic flow, and endpoints relevant to human biology.
- b. Examination of the setup and functionality of a liver MPS, and its comparisons against traditional *in vitro* and *in vivo* approaches.
- c. Description of the types of multi-chip plates: barrier model, dual-organ model, and liver model with three examples of their applications: safety toxicology, Absorption, Distribution, Metabolism and Excretion (ADME) in a dual organ setup, and disease modelling.
- d. A description of a recent case study of alternative methods supporting a Clinical Trial Authorisation submission.
- e. Summary of key areas for alternative method implementation: technology readiness, developer standards, regulators and frameworks, and public opinion.
- 21. The Chair thanked Dr Dharaminder Singh and passed onto Prof Cathy Merry, who delivered an overview on the animal welfare value of synthetic matrices replacing animal tissue-based Matrigel. The key points were:
 - a. Overview of the challenges in developing alternatives to animal use, including cost and established expertise in using rodents to model human diseases. Many *in vitro* models do not accurately represent human diseases, especially those associated with aging.
 - b. Summary of the strengths and limitations of organoid technologies, highlighting their ability to provide better and more rapid representation of population variability, against a lack of standardisation and serum-based media producing variability.
 - c. Overview of systems that mimic extracellular matrices being an underdeveloped area in drug targeting therapeutics where changes in matrix properties should likely inform treatment. Current solutions have similar issues to organoids and are known to include animal derived products in large quantities.
 - d. Overview of a fully defined, synthetic alternative to animal-derived matrices, and a summary of benefits over patient-derived xenografts. Patient-specific differences are maintained, and matrix models derived from patient proteomics can more accurately represent diseases.
 - e. Summary of the benefits of alternative methods, emphasising the need for careful validation against patient outcomes. Legislation is changing rapidly, and switching away from animals can save time and money in drug development while providing environmental and animal welfare benefits.
- 22. At the end of the presentations, attendees were invited to ask any questions. The following points were raised:
 - a. On the topic of future possibilities to have a whole-body multi-organ system, Dr Singh summarised the current approach of a dual-organ system in tandem with modelling to consider other elements, referenced <u>a</u> <u>grant to integrate multiple organ-on-chip systems to mimic the whole</u> <u>human body</u> and that a whole-body system should be conceptually

possible, but reiterated that the systems used would vary depending on what scientific questions needed to be answered.

- b. On the topic of balancing new technologies against validation, Dr Singh explained that one difficulty was that there was no validation or qualification frameworks that existed currently, so getting consensus across the field was difficult. They mentioned that there were multiple teams working on this, with the most advanced developing context-of-use specific qualification frameworks.
- c. On the topic of how changes to PPL applications, specifically with the use of SOPs replacing some questions, could work if a licence is covering multiple establishments, Dr Percie du Sert flagged that, while this had not been formally considered, these circumstances would need to be checked.

Practical advice for AWERBs on assessing replacement

- 23. The Chair then welcomed the two speakers for the next item: Prof Adrian Smith and Ms Elaine Blair.
- 24. The format of the session was the delivery of both presentations in succession, followed by a Q&A session. The objective of the session was to facilitate discussion around the resources available for assessing replacement. The



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

attendees were then assigned to break-out groups to discuss an allocated question, before feeding back to the full group in a plenary session. Each break-out group was facilitated by an ASC AWERB Subgroup member or one of the presenters.

- 25. The session began with the following poll question: "How confident do you feel in assessing the implementation of replacement in a project licence application?", where "1" was "not at all confident" and "5" was "very confident". 107 attendees responded to the poll. The average score was 2.1.
- 26. Following the poll, the Chair introduced Prof Adrian Smith, who delivered an overview of resources for AWERBs on assessing replacement available on the Norecopa website. The key points were:

- a. The website to access the slides containing the links from Norecopa was: <u>https://norecopa.no/ASC</u>. The main Norecopa website was <u>https://norecopa.no/</u>.
- b. An overview of Norecopa: a national consensus platform for the 3Rs with the major four stakeholders in their governing body: research, government, industry, and animal welfare, with a website that aims to be the most comprehensive for global 3R resources.
- c. The Norecopa website hosts resources such as an upcoming and recorded meetings calendar, refinement wiki, alternative databases, the International Culture of Care Network, and the website of the European Network of National Networks of Animal Welfare Bodies: <u>https://norecopa.no/ENAWB</u>
- d. Overview of the Planning Research and Experimental Procedures on Animals: Recommendations for Excellence (PREPARE) guidelines that covered topics on planning and collaboration. Animal Research: Reporting of In Vivo Experiments (ARRIVE) and PREPARE were cited in over 50% of non-technical summaries published in 2024. Norecopa hosted a website the accompanies the PREPARE guidelines with publications and resources on relevant topics which are constantly refined and updated.
- 27. The Chair thanked Prof Adrian Smith and passed onto Ms Elaine Blair, who delivered an overview on literature searching on alternatives for AWERBs and applicants. The key points were:

a. Overview of how to choose relevant keywords and subject searching using Medical Subject Headings.

b. Explanation of search hedges with ready-made searches, and constructing searches using Booleans, truncations, phrase searching, and proximity operators.

c. Emphasis on selecting multiple databases, while avoiding Google Scholar or AI tools, and modifying your search to achieve desired result numbers before recording and managing results.

- 28. At the end of the presentation, attendees were invited to ask any questions, but none were raised.
- 29. Attendees were then randomly assigned to break-out groups to discuss one of five questions posed by the ASC AWERB Subgroup. Following this session, attendees returned to the plenary meeting to present the key points and feedback from their discussion. Comments are presented as unattributed quotes; these may not be verbatim, but express the point that was made.

What do you find to be the difficulties with assessing replacement?

"As an AWERB member, there is discussion on whether the assessment of replacement is made by the applicant prior to the project licence application, specifically in any prior discussions within the lab and plan of work that came to the conclusion that the use of animals was necessary."

"AWERB members should be reassured that replacement has been considered with all due diligence, without needing to be experts in replacement models themselves, in a non-confrontational manner with applicants."

"There are some successful examples of replacement methods, such as using human skin models, artificial blood for feeding mosquitoes, organ-on-a-chip technology, and appointing a replacement expert to an AWERB."

What are some of the more general questions that you find particularly helpful in assessing replacement?

"It is challenging to know where to start asking questions about replacement and the non-animal technologies available, especially as science moves quickly."

"Having a crib sheet with good questions to ask and guidance about what NAMs are available and what has been considered in a project would be very helpful for AWERB members, especially for lay members and the Named Information Officer (NIO) who have a role to challenge."

"The ASC could provide guidance and questions to ask about replacement methods, as it is difficult to know what questions to ask at the start of the journey."

What might you look for in an application to determine whether the applicant has adequately considered replacement?

"There is variability in how different AWERBs ask about replacement in applications, and whether the question has been adequately addressed."

"Applicants are often experts in their field, but it is important for them to document how thoroughly they have searched for replacement methods to confirm their expertise."

"AWERBs should have members with expertise in replacement or the 3Rs to support applicants in their searches and ensure thorough consideration of alternatives."

"There is a discussion on whether the current project licence application forms ask sufficient questions to assist AWERBs in making informed decisions about replacement."

What resources do you currently use to assess replacement?

"The NC3Rs are working on providing a checklist or decision tree to help assess replacement, which could be sent to applicants."

"Discussion on the role of funders in promoting replacement, suggesting that animal replacement should also be considered at the funding application stage rather than just at the project licence stage."

"Lay members need more support, such as symposia and centralised resources with perhaps a national resource to keep all relevant information in one place, to help them assess replacement effectively."

How might you stay on top of future developments in non-animal alternatives?

"Staying up to date by attending relevant conferences, meetings, and events like today's workshop, which provide valuable information and resources."

"Involvement with local AWERB Hub, subscribing to newsletters, and engaging with networks such as Norecopa, NC3Rs, and the Concordat for Openness."

"We should encourage researchers to attend relevant meetings and conferences to foster collaboration."

"There should be a culture of challenging yourself even when you think replacement may not be possible, and there is work to be done regarding getting the message across to everyone involved."

How might you work with other AWERBs or other stakeholders to share knowledge on replacement?

"Utilising AWERB hubs and proposing a freely available AWERB/NIO forum dedicated to sharing information on replacement methods, including effective resources used by NIOs and AWERB members."

"Creating a central repository of shared NIO newsletters and resources to make information easily accessible."

"Encouraging AWERBs to better promote the replacement methods used within their own establishments to wider AWERBs and other forums."

"Developing a mechanism to capture and share information about replacement methods used at early stages of research programme discussion, which may not progress to using animals, ensuring AWERBs are aware of these alternatives."

Final thoughts and feedback

- 30. The Chair thanked everyone for joining and sharing their contributions throughout the workshop. Attendees were invited to submit feedback to the ASC Secretariat or to the Chair directly, specifically on:
 - a. How participants found the workshop format.
 - b. Suggestions for future workshop topics.
- 31. Participants were informed that the slides from the day would be shared, and a report on the Animals in Science Committee website and the AWERB Knowledge Hub.

Annex A – AWERB Hub Workshop (April 2025) Agenda
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Time	Торіс	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	Dr Nathalie Percie du Sert
13:40 – 14:30	Introduction to alternative methods	Mr Barney Reed Dr Dharaminder Singh Prof Cathy Merry
14:30 – 14:40	Break	
14:40- 15:55	Practical advice for AWERBs on assessing replacement	Prof Adrian Smith Ms Elaine Blair
15:55 – 16:00	Final thoughts and feedback	Caroline Chadwick