The role of review and regulatory approvals processes in supporting the implementation of the 3Rs: the role of AWERBs

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ASC AWERB Hubs Workshop

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Background and Context

- Adoption of 3Rs advances into routine practice can be quite slow
- Academic research usually reviewed 3 times – (Funders, AWERBs & ASRU).

In 2022:

- ASRU change programme
- Independent Review of Research Bureaucracy – may lead to changes in funders' grant processes

Project aims

Focussing on academic-led research involving animals in the UK:

1. To map in detail what the various regulatory and review processes and bodies currently do to ensure compliance with 3Rs principles and to promote adoption of 3Rs advances
2. To identify any current variations in review processes, any gaps (or overlaps) in coverage and any lessons to be learned from examples of particularly effective practice
3. To explore opportunities for adjusting current processes and responsibilities so as to cover any gaps, remove unnecessary duplication and more effectively promote adoption of 3Rs advances

Project Approach

Online semi-structured interviews with ~40 stakeholders, including:

- AWERB chairs, members & secretariat staff
- Current & former ASRU inspectors
- Establishment, Project and Personal Licence Holders
- NACWOs, NVSs, NIOs & facility managers
- Funders (2 Research Councils and 7 charities)
- ASC members
- Senior scientists with experience of peer review

Written input from ASRU & discussions with the Heads of ASRU and the new Animals in Science Policy Unit

Observation of 3 AWERB meetings at which PPL applications and amendments were discussed

Findings

Replacement

The “R” least well covered by review processes.

- AWERBs & ASRU rarely suggest replacements – 'too late' by the time a project comes to them
- AWERBs, NVSs and HO Inspectors don't usually have the in-depth scientific expertise to know if replacements are available and/or suitable
- Funders have access to specialist scientific expertise in peer review, but the focus is not explicitly on possibilities for replacement. The extent to which the need to use animals is challenged varies between funders.
- ASRU audits will check local processes for supporting applicants to find and implement replacements
- Legal responsibility to consider possible replacements sits with the PPL holder

Reduction

- All report paying much closer attention to experimental design and statistics in recent years.
- There is a shortage of experimental design and statistics expertise for reviews and to support researchers
- The NC3Rs Experimental Design Assistant is not yet widely used in PPL or grant applications
- Breeding and colony management are rarely covered in grant or PPL review. Funders think this is, or should be covered locally, but not all AWERBs have processes in place to oversee efficient colony management.
- Some AWERBs have oversight of local systems to make best use of tissues from culled animals.
- Neither AWERBs nor funders reported much discussion of the potential to use methodological advances (eg in-cage monitoring, micro-sampling, or imaging) to enable more information to be obtained from fewer animals.

Refinement

- AWERBs, NACWOs, NVSs are all confident to challenge plans for refinement to experimental protocols and that their input – at the application stage and as the research progresses - adds value.
- Funders only consider refinement in specific cases – eg for specially protected species or severe protocols (usually via NC3Rs review).
- Housing and Husbandry is rarely covered in project review unless it is critical to the experimental design
- Refinement of housing and husbandry are overseen by NACWOs, NVSs and sometimes AWERB subcommittees.
- ASRU expects to ensure compliance via facility audits.
- Difficult to share information on advances and things that didn't work

Barriers to adoption of 3Rs advances

- Lack of expertise, and the time and cost involved in setting up new techniques in a lab.
- Lack of validation of replacement technologies
- Concerns about acceptance for publication (or by the regulator)
- Lack of compatibility with earlier data
- Lack of access to information on 3Rs advances

Other Points

- The heavy workload of PPL review often means AWERBs do not have enough time to focus on other functions that are important in promoting the 3Rs
- Assumptions about peer review do affect AWERB and ASRU decision making – peer reviewed and funded work is assumed to be of high scientific quality which affects the harm/benefit analysis and the judgement on whether objectives are likely to be achieved.
- Several establishments find it useful to review individual study plans before each new study starts, to:
  - check refinements,
  - check licence compliance,
  - check resources and trained staff are available, and/or
  - check experimental design (in one case using a template based on ARRIVE)
- The role of NIO is often poorly defined and under resourced. NIOs need good training in how to search for information effectively.

Recommendations

Recommendations (1)

1. Funders should make best use of their access to highly specialist scientific peer reviewers to ensure that possibilities for use of replacements or new approaches to obtain more information from fewer animals are identified and implemented where appropriate. …
2. Funders could introduce more targeted questions for applicants to elicit information on replacement and reduction, and guidance for applicants on expectations, with the assumption that in most cases optimising refinement will be ensured by ASRU and AWERB oversight.
3. Funders should be prepared to provide additional funding to allow grant holders to explore and validate the use of new alternatives alongside their established models, and to facilitate dissemination of new methods....
4. It should be made clear in a PPL application what parts of the work have already been funded and by whom, so that AWERBs and ASRU are clear what has been externally peer-reviewed and what has not...

Recommendations (2)

5. Establishments should ensure that their processes allow the use of animals to be challenged early in the research planning process. AWERBs should ask questions about whether/how an applicant has searched for information on possible replacements or reduction strategies. They should expect a clear explanation of what replacements have been considered and why they are not suitable, and whether approaches to get more information from a group of animals have been considered. This could be facilitated by guidance to AWERBs on questions to ask and what should reasonably be expected of applicants.
6. Best practice for induction for AWERB members should include training in the 3Rs and the principles of experimental design. The introduction of audit process in ASRU's new ways of working provides an opportunity to clarify expectations for training of AWERB members and to confirm via audit that these are being followed. In the longer term the requirement for CPD for all AWERB members should be considered by the sector, in line with the Research Ethics Committees which cover projects involving human participants.
7. AWERBs should be clear on the expectations for their role in promoting the 3Rs on a facility-wide basis outside the process of PPL review, including the importance of spending enough time and attention on this part of their role and what constitutes good practice. Areas to cover include refinement of housing and husbandry, efficient colony management and breeding, good experimental design, tissue sharing and sharing of 3Rs advances.

Recommendations (3)

8. The expectations of the NIO role should be set out clearly at each Establishment in line with ASPA and LASA/IAT guidance. Establishments must ensure that NIOs have the expertise, time and appropriate resources and training to effectively support researchers, AWERB members and animal facility staff in accessing information on 3Rs advances....
9. To facilitate access to information about 3Rs advances, the NC3Rs, scientific or learned societies and/or funders should convene expert groups to review information on 3Rs advances ….., to produce authoritative, up-to-date and easily accessible information for researchers, peer reviewers and AWERBs....

Recommendations (4)

10. All AWERBs and funder review panels should have access to expertise in statistics and experimental design. Inventive solutions may be necessary to make best use of available expertise for reviewing given the shortage. The NC3Rs Experimental Design Assistant (EDA) should be more widely used in applications; this may require further development to make it more accessible....
11. ASRU and AWERBs should ensure that information on 3Rs advances obtained from retrospective reviews and retrospective assessments of PPLs is available to the research community, whether via publication or some other means.
12. To reduce unnecessary bureaucracy funders can rely on AWERBs and ASRU for checking implementation of refinement and on ASRU to monitor compliance with ASPA ……However, it remains important for funders to check that AWERBs have reviewed any animal research that falls outside of the ASPA, such as work taking place overseas.

Good Practices?

- Applicant to present to AWERB before starting a new licence application
- Applicant **required** to meet with NVS, NACWO, NIO and facility manager at the drafting stage for all licence applications and significant amendments
- Applicant **required** to attend AWERB meeting for discussion of PPL or major amendment
- Applicants get to see comments on PPL in advance and respond (online)
- Use subcommittees as necessary to ensure AWERB has time to cover its full remit
- Review of study plans before each study starts, with study plan templates based on ARRIVE2
- Standard housing and husbandry protocols for the establishment developed by a 3Rs subcommittee, reviewed annually, approved by AWERB.

Q & A and Discussion

- What should initial training and CPD requirements for AWERB members be?
- AWERB role in promoting the 3Rs outside PPL review – are expectations clear?
- Can you access experimental design and statistical expertise? Is support available for researchers?
- How could information from retrospective reviews and retrospective assessments be shared?

Thank You

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