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4th March 2025

Dear Animals in Science Committee,

Licence Report Recommendations

We are writing to acknowledge and thank you for your 2020 report and recommendations on the sample of licenses considered by the Licence Analysis subgroup. We appreciate the time taken by the group to consider these licences and make appropriate recommendations. We acknowledge that there has been a delay in responding to this report, for which we apologise. However, we can confirm (as below) that work on many of the recommendations is either in train or completed.

From our (Animals in Science Regulation Policy Unit (ASRP)) analysis and categorisation of all the recommendations we considered many of the recommendations could be incorporated into licensing work via changes to both the guidance on the use of the Animals in Science Regulation Unit's (ASRU) e-licensing system, ASPeL, and the prompt text in ASPeL. As part of the ongoing reform programme, ASRU is taking forward work to improve the licensing journey, working with developers on ASPeL.

Below we provide information on actions ASRP, ASRU or wider stakeholders have taken in relation to recommendations set out in the ASC's licensing report. Information has sometimes been grouped for related recommendations. Some recommendations are for the applicant but have been included here for reference.

1.1. The applicant should ensure that project titles should be descriptive or specific enough to summarise the work proposed briefly and clearly.

New project licence (PPL) application guidance, published in February 2024, now includes advice on the content and language to be used in project titles (page 4). A link to this guidance is presented at the top of every ASPeL page.

2.1. ASRU should consider whether the new licence application form should include a question that specifically asks for the scientific rationale.

2.2. The applicant should ensure that the scientific rationale underpinning the projects is clear.

2.3. In licences where the use of genetically altered animals is stated, applicants must provide the rationale for the use of the particular lines and modifications, and ASRU should ensure that this has been done.

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) has been commissioned and is presently undertaking a review of the licensing application form to enhance the clarity of questions, reduce potential duplication,

and ensure that the most meaningful information is effectively elicited.
In 2018, ASRU published the Assessment Framework for the Efficient Breeding of Genetically Altered Animals, which can be referred to by establishments when considering the efficiency with which they breed genetically altered (GA) animals.
In 2022, updated Guidance on the Use of Standard Genetically Altered Animal Protocols was also published, covering the routine breeding of GA mice and fish to create new lines.
ASRU will continue to carry out their duties to ensure applicants have supplied enough information and the programme of work is appropriately governed and justified via a Harm-Benefit Analysis (HBA).

3.1. In line with the guidance given in the annotated project licence, applicants should provide clear project plans with descriptions of decision points for the overall project including in vitro and pilot steps.

Application guidance was updated in February 2024 to include more guidance on providing clear project plans (page 22). Furthermore, as aforementioned, NC3Rs and ASRU is undertaking a review of ASRU's licence application form to help ensure that all the required information is elicited in a robust and efficient way.

3.2. ASRU could consider whether including a descriptive figure within the NTS would be beneficial.

A review of NTSs has been commissioned, from the Minister to the ASC, and the NC3Rs review of the application form will also consider the NTS. The NC3Rs intend to collaborate with the ASC on this.

4.1. Typical experiments should be described including the number (or range) of animals to be used.

In the non-technical summary section, applicants provide an estimate of the total numbers of each type of animal that will be used in the project. In the protocol section the applicant has to provide the maximum numbers of animals that will be used in that protocol and the maximum number of uses per animal. This is not per experiment but for that protocol over the 5 years. Animals may be used in one protocol and re-used in this protocol or in other protocols or projects. Animals may also be continually used on other protocols of this project or other projects.

4.2. The licence should include an experimental (and where possible statistical) justification for the numbers of animals to be used, and a description of how this figure was determined.

4.3. Where genetically altered (GA) animals are included, an explanation and breakdown of the number of GA versus non-GA animals should be provided. Where the breeding of GA animals is required, these numbers should also include an estimation of how many non-GA animals will simultaneously be produced.

In the non-technical summary section, ASRU asks the applicant to explain how they have estimated the numbers of animals that they will use, what steps they will take to reduce the numbers of animals being used and what measures apart from good experimental design they will use to optimise the number of animals used. If a protocol generates quantitative data and the experimental design is not determined by a regulatory guideline ASRU requests more detailed experimental design information as follows:

- How and when pilot studies are used

- How different experimental groups are chosen
- How control groups are chosen
- How experiments and data analysis are randomised and blinded
- How variables minimised to ensure reproducibility.

The NC3Rs experimental design assistant is referenced in both the application form and ASRU's guidance for applicants.

5.1. In order to improve the consistency of severity classification across licences, more refined definitions are required of the durations envisaged by 'short' and 'long-term' harms, and of the distinction between 'likely' and 'expected' experiences of the animals.

ASRU published guidance in 2014 on severity classifications, and work is ongoing in this area as part of continuous improvement. The recommendation has been noted as part of the review of ASRU's licence application form.

6.1. The applicant should make clear, both in the licence and the NTS, what is the step change in knowledge to be expected from this specific programme of work, and why this particular increment in knowledge constitutes an important benefit.

Please see 3.2.

6.2. The ASC should monitor a range of licences prepared under the new system, to assess whether the benefits section (and the NTS) is improving as a result of the new guidance, or whether more consideration could be given to describing what is required from this section.

This is for the ASC to consider.

7.1. Where a project licence covers a broad category of substances (e.g. potential medicines or pesticides), but the specifics of the substance to be tested are not known (e.g. its disease indication or chemical series), consideration should be given to the development of a system which provides local oversight of the justification for the specific substances being tested, and which allows the opportunity for ASRU to review this.

We are in broad agreement with this expectation of applicants. It is also worth noting that there are already questions in the project application on local oversight for broad licences that provide a service. These questions are:

1. What is your process for accepting or rejecting work?
2. What specific criteria will you use to decide whether to accept or reject work?
3. Will others help you make decisions about accepting or rejecting work?

7.2. ASRU should develop a system for establishments to prospectively or retrospectively report the justification for each use of an animal test when non-animal methods are available.

PPLs must use a non-animal method if it is available, and they are able to achieve the scientific outcome using this method. If they are not able to use the non-animal method to achieve the scientific outcome, then ASRU's approach is:

1. For most new project applications or amendments, the applicant must provide scientific justification for using live animals and explain why the scientific outcome cannot be achieved by any non-animal methods which are available.
2. For projects that use animals for antibodies, the applicant must answer specific questions to further determine why the non-animal methods for generating antibodies are not suitable. If the licence is granted it will be under the condition that an annual report is carried out for AWERBs and inspectors to review during audits.
3. For regulatory licences, if a non-animal method is available but the applicant still wants to use animals then they need to complete a prospective authorisation form. Details of the test item should be provided in the form.

7.3. While acknowledging that ASRU is aware of these above difficulties, the ASC should review whether it is appropriate for generic service licences (including those for breeding and antibody production) to use the same harm-benefit framework as research licences, in cases where the eventual use of the substance is not considered.

This relates to point 7.1, as establishing mechanisms for the local oversight of the justification for specific substances would require a consideration of the harm-benefit framework to be used. In addition, Recommendation 6 of the report on Non-Human Primates Used in Service Licenses mentions that ASRU should consider how to encourage establishments through audits to empower AWERBs to assess ethical justification on a substance-by-substance basis, which includes consideration of the societal value and utility of each substance to be tested. ASRP will consider these points in order to address this recommendation.

8.1. Consideration of the 3Rs should be an active and ongoing process throughout the lifetime of the licence, considering best practices identified by the NC3Rs and other relevant bodies, and the relevant literature. In addition to reviewing project licences, the AWERB has a role in promoting the 3Rs and facilitating a broad uptake across the Establishment.

8.2. The AWERB should ensure that applicant has provided sufficient evidence of the consideration of potential replacements, including justification of why in vitro methods could not be used, and more indication of the applicant's plans to incorporate or investigate new methods.

8.3. More evidence is needed of the use of mechanisms to ensure that animal use and breeding is appropriately managed to reduce any potential for animals being bred for scientific purposes and not used.

As mentioned in 2.3, guidance has been published on the efficient breeding of GA animals. Section 4 of this document, on colony management, addresses how ASRU may approach ensuring that establishments are effectively matching the production of animals with demand. ASRU is undertaking a review of its current audit practices, with the intention of having a greater focus on assuring that AWERBs are fulfilling their full range of functions under ASPA. In addition, the ASC has been commissioned, by the Minister, for advice related to the effective functioning of AWERBs and Named Persons. As aforementioned, the NC3Rs and ASRU are conducting a review of ASRU's licence application form to ensure that robust information related to the 3Rs is elicited through a format which is clear and accessible.

9.1. Use of understandable language - establishments should be urged not to submit licence applications to ASRU until the AWERB lay member or another non-technical person has agreed that the NTS has adequately summarised the programme of work in non-technical language.

9.2. Aims and Objectives should provide a clear summary of work: the new e-licensing system should ask a question that will prompt the applicant to describe the proposed programme of animal experimentation.

9.3. It is important that the primary benefits presented are those expected of the programme of work within the licence itself, and that any potential wider benefits are described in realistic terms, rather than presented at too high a level - the benefits section of the NTS should focus on the benefits of the specific knowledge to be gained by the project and show restraint in presenting wider and future aspirations.

9.4. The NTS should include sufficient detail of expected harms, especially those involved in more severe or potentially controversial protocols - the new licence application system needs to state that all NTSs should clearly and accurately express whether the experimental protocols are mild, moderate or severe.

9.5. The 3Rs section of the NTS needs to explain the various steps taken to replace, refine and reduce in terms understandable by a lay audience.

9.6. Consideration might be given to sharing good examples of NTSs to provide help to applicants

Recommendations 9.1 - 9.6 are covered by review of the licence application journey being undertaken by NC3Rs and ASRU, and the commissions to the ASC regarding NTS. Additionally, examples of good responses in the various sections of the NTS are available in the PPL application guidance (page 5).

Thank you again for the valuable recommendations provided in the report. We will continue to engage with you on improvements within ASRU and look forward to continuing to work with you to deliver protections for animals used in scientific procedures.

Yours sincerely,

The Animals in Science Regulation Policy Unit