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

Rethinking the project licence application and assessment process to maximise 3Rs impacts

Recommendations from the NC3Rs

Pioneering Better Science

Contents

Executive summary

The NC3Rs was commissioned by the Home Office's Animals in Science Regulation Policy Unit (ASRP) to review how the principles of the 3Rs – replacement, reduction and refinement – are incorporated into the project licence (PPL) application and assessment process. Our review examined the structure, content and function of the current PPL form, how it is used by applicants, Animal Welfare and Ethical Review Bodies (AWERBs) and the Animals in Science Regulation Unit (ASRU), and how effectively it supports the harm-benefit analysis that sits at the heart of the Animals (Scientific Procedures) Act 1986 (ASPA) and the practical implementation of the 3Rs.

Under the ASPA, the PPL authorises regulated procedures on protected animals for a specified programme of work. It forms a central part of the UK legislation and a key framework for ensuring animals are protected by the full implementation of the 3Rs. Over recent years, various reports (e.g. the Rawle report[1]) have highlighted opportunities to improve application of the 3Rs in the licensing process. Using these as a foundation, we conducted a detailed analysis of the PPL form, supported by extensive consultation with stakeholders from the regulated community. Our findings reinforce opinions expressed by many stakeholders that the PPL form could be significantly improved to better support the effective presentation, assessment and implementation of the 3Rs. The PPL form is lengthy, with information relevant to the 3Rs often fragmented or duplicated across multiple sections. This can make it challenging for applicants to present information coherently, and for AWERBs, ASRU and establishments to identify and assess the information most relevant to the scientific justification of animal use, animal welfare and regulatory oversight.

We set out recommendations for significant changes to the PPL form that represent one of the most substantial evolutions of the licensing process in the last decade. The 12 recommendations – summarised in Table 1 – strengthen the protection of animals and the application of the 3Rs, improve the clarity and efficiency of the licence assessment process, and

[1] 'The role of review and regulatory approvals processes for animal research in supporting implementation of the 3Rs' was commissioned by the NC3Rs and published in 2023.

support researchers, AWERBs and ASRU with their responsibilities. Our recommendations enable greater flexibility to implement refinements, encourage the use of more relevant indicators of animal suffering, and promote the harmonisation of severity limits and humane endpoints. Alongside these benefits, the recommendations offer operational gains by reducing the length of a typical PPL application by around a quarter, streamlining the review process for AWERBs and ASRU and facilitating compliance monitoring, while freeing-up capacity to focus on other responsibilities, including the implementation of the 3Rs in practice.

In this report we describe our objectives and methodology, the current format of the PPL application form and assessment process for background and context, and the rationale for our recommendations including ensuring legal compliance, operational feasibility and continued public confidence in the regulation of animal research. Should the recommendations be taken forward by the Home Office, their implementation will require close working with the regulated community. This will help ensure that the changes are understood and can be actioned effectively to enable a smooth transition for applicants, AWERBs and the regulator, in order to deliver the intended benefits of our recommendations to the licensing system and how the 3Rs are embedded within it.

Table 1: Recommendations for improving the licence application and assessment processes

Theme	Recommendation
Theme 1 Strengthening the scientific rationale for animal use	1. Information on the choice of model and scientific background should be consolidated into a new ***Project overview*** section.
	2. New questions and guidance on the justification for animal use and the evaluation of replacement strategies should be adopted.
	3. Updated questions and guidance on the benefits of the research should be implemented.
Theme 2 Improving the description of harms and refinement controls	4. Information on harms to animals should be consolidated into the ***Project overview*** section.
	5. New questions and guidance on harms to animals and refinement controls should be adopted.
	6. Further work on defining severity and cumulative suffering should be commissioned.
	7. The ***Protocols*** section should be streamlined to improve the assessment of the PPL.
	8. The description of ***Licence steps*** should focus on the impacts on animal welfare rather than technical detail.
	9. A library of standard ***Licence steps*** should be generated.
Theme 3 Promoting and facilitating application of the 3Rs on the ground	10. The ***Project overview*** section should be published.
	11. The Home Office should promote the use of study plans and set their minimum information requirements.
	12. Establishments should have processes in place to support the use of study plans.

Objectives and methodology

Following discussion with ASRP over the summer of 2024, the NC3Rs was subsequently invited to review how the principles of the 3Rs are applied within the PPL application process. Our review focused on improving the quality of 3Rs information within PPLs and facilitating the assessment of it by AWERBs and ASRU. The initial scope of the review was limited to the 3Rs-relevant questions within the PPL application form. However, because these questions are distributed throughout the form, with a high degree of repetition, and do not capture opportunities to apply the 3Rs after licence approval, the scope was subsequently broadened to consider the entire licensing process. This wider perspective enabled the development of recommendations that strengthen the application of the 3Rs, improve the clarity and efficiency of the licencing process, and support applicants, establishments and ASRU in meeting their responsibilities at a time of considerable public and parliamentary scrutiny of the use of animals in science and its regulation.

We carried out an in-depth analysis of the current PPL application form and review process for a standard research PPL (excluding higher education licences). This included reviewing the questions in the PPL application form and associated guidance within ASPeL (ASRU's digital platform for managing licences), as well as the Guidance **Notes for Project Licence Applications** which was published in February 2024. We focused on identifying the minimum information required in the PPL to enable effective implementation of the 3Rs and meet the legal obligations of the ASPA.

To evaluate both the limitations of the current PPL form and the implications of the recommendations we were considering, we conducted a SWOT analysis examining the strengths, weaknesses, opportunities and threats related to both. We then consulted with 25 stakeholders from across the sector, including senior individuals working under the ASPA in a range of capacities such as researchers, AWERB members and named persons in different settings (academia, industry and contract research organisations), as well as representatives from the RSPCA, the Animals in Science Committee, ASRU,

ASRP and various membership organisations. Semi-structured interviews explored:

- Stakeholders' experience of the PPL application and review processes.
- Which parts of the application best support assessment of the 3Rs.
- The impact of streamlining and consolidating related questions in the PPL application form.
- Opportunities to enhance 3Rs implementation through the use of supporting documents such as standard operating procedures and study plans.
- Areas where the current PPL application form creates inefficiencies, confusion or unnecessary administrative burden.

Based on the evidence gathered, we developed a set of draft recommendations which were subsequently road-tested with key organisations to assess how they would support the work of AWERBs, provide an efficient process for applicants, enable effective regulatory assessment and influence public confidence in the appropriate oversight of animal research.

Context for the NC3Rs review

Under the ASPA, all work involving regulated procedures on animals must be authorised through a PPL approved by the Secretary of State via ASRU. PPL applications are submitted through ASPeL. Each application contains detailed scientific justification, protocols, severity limits and refinement measures set out in various sections and sub-sections (see Table 2), plus a separate non-technical summary (***NTS***) section, which outlines at a high-level the proposed programme of work. Prior to submission, PPL applications (including the ***NTS*** section) are reviewed by the establishment's AWERB, with input from named persons (the named veterinary surgeon, and named animal care and welfare, named training and competency and named information officers) and others who provide species-specific, technical and welfare expertise to support the identification and implementation of appropriate 3Rs measures. The application is subsequently submitted to ASRU to undertake the formal evaluation, which includes a harm-benefit analysis. Following approval, the

NTS section is separated from the licence and used by ASRU to produce a non-technical summary that is published on the Home Office website in order to provide information for the public on the use of animals under the ASPA. The PPL itself remains confidential and serves as a key regulatory document that can be used for assuring compliance. PPL holders have an ongoing legal responsibility to apply the 3Rs throughout the lifetime of the project. Meeting these responsibilities requires PPL holders to keep their experimental plans under active review and to adopt new 3Rs approaches where appropriate.

Table 2: Sections and sub-sections of the current PPL application form

Sections	Sub-sections
Introductory details	-
NTS	Aims; Benefits; Project harms; Fate of animals; Replacement; Reduction; Refinement
Applicant information	Experience; Funding; Training
Project location	Establishments; Transfer and movement of animals; Places other than licensed establishments
Project plan	Scientific background; Action plan; General principles
Protocols	Protocol details; Animals used in this protocol; Genetically altered animals; Steps; Fate of animals; Animal experience; Experimental design; Protocol justification
Use of animals	Cats, dogs and equidae; Non-human primates; Purpose bred animals; Endangered animals; Animals taken from the wild; Feral animals
Other considerations	Neuromuscular blocking agents; Re-using animals; Commercial slaughter; Animals containing human material; Keeping animals alive; Setting animals free; Rehoming animals

Overview of the NC3Rs recommendations

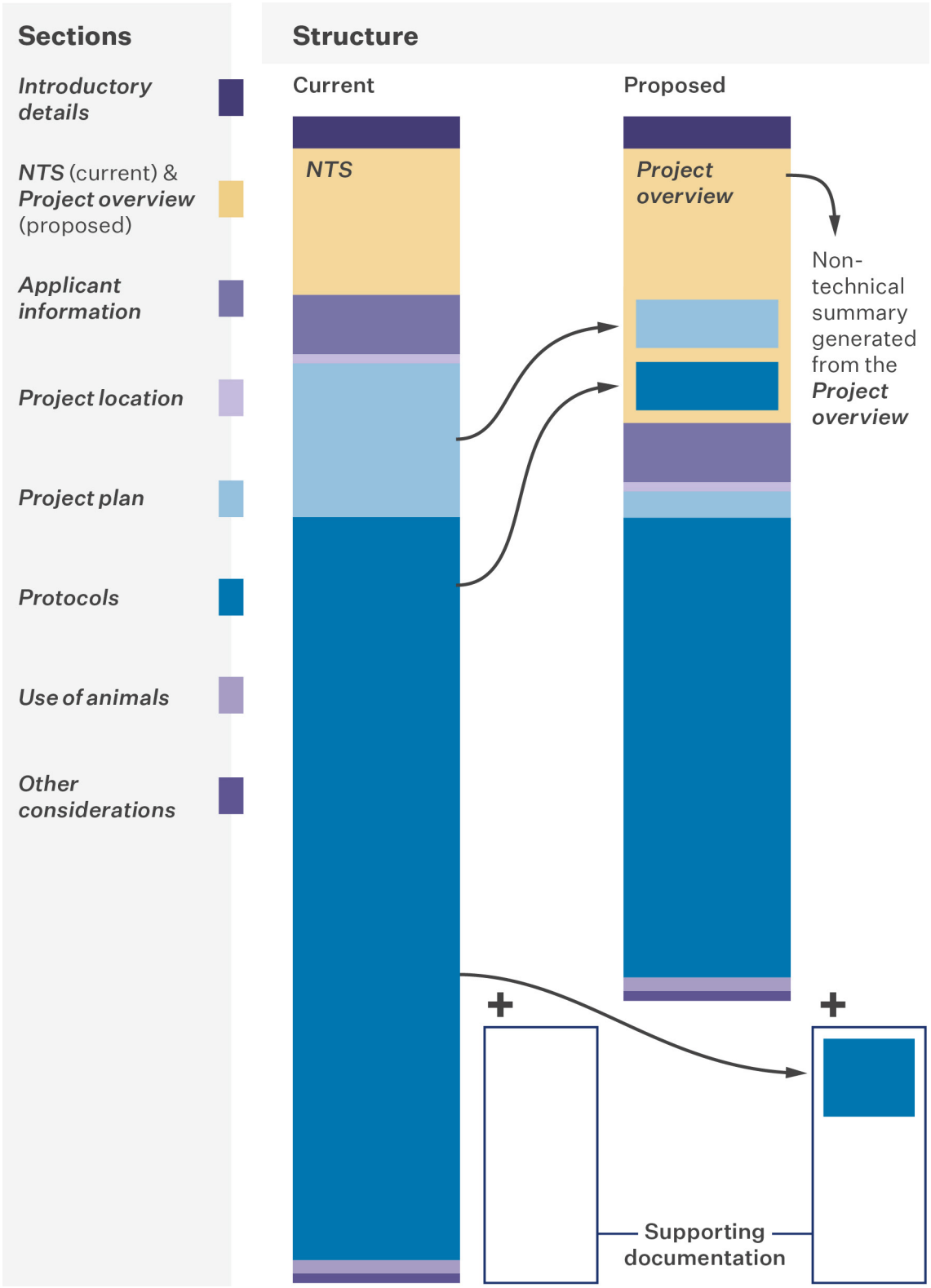
Our analysis highlighted a series of structural limitations in the current PPL application form and related assessment workflow. The format of the form does not always enable applicants to set out a clear and coherent explanation of how the 3Rs have been applied, and its structure can make it difficult to present and locate information that is required for considering the justification for animal use and the conduct of the harm-benefit analysis. The form is overly complex, with some licences extending to several hundred pages as a result. Key information relevant to the 3Rs is spread across multiple sections in the application form and is frequently duplicated – this is particularly the case with the ***NTS section***, which despite having a different purpose, has the same information requirements as other sections in the PPL form. Completion of the application can be burdensome for applicants, and concomitantly the licence structure makes it difficult for named persons, AWERBs and ASRU to efficiently identify and assess the information most relevant to protecting animals and implementing the 3Rs. Inconsistencies in guidance (between ASPeL and the **Notes for Project Licence Applications**) further undermine clarity and can have unintentional consequences, which do not always result in best practice being implemented.

PPL applicants are required to provide detail on their plans that is either too generic to be meaningful or too specific to remain accurate as studies progress. Important practical information for day-to-day oversight is often captured outside the PPL in supporting documents such as study plans that are used by some institutions to manage individual experiments and assure compliance with the licence conditions. PPL applications do not always include information required by AWERBs which leads to additional requests for further context to assess the project, with locally developed question sets sometimes used to during reviews, for example, to assess whether opportunities to replace animal use have been thoroughly investigated. At the same time, the licensing process provides limited opportunities to share good practice between institutions and research groups due to confidentiality

constraints, contributing to inconsistent standards and reduced visibility of 3Rs approaches. Given the time and resources required to prepare and review a PPL, not sharing 3Rs advances is a missed opportunity.

To tackle the various limitations with the current PPL application and assessment processes, we have developed 12 recommendations for the Home Office to consider that are designed to strengthen the scientific rationale for animal use, improve the description of harms and refinement controls and facilitate the application of the 3Rs in practice. Addressing the structure of the PPL form is essential to achieving these aims. Central to our recommendations is the introduction of a new ***Project overview*** section, which consolidates key information that is currently spread across the ***NTS***, ***Project Plan*** and ***Protocols*** sections in the PPL application form. This change enables clear articulation of the knowledge gap, scientific objectives, model choice, expected harms to the animals and refinement strategies, while reducing duplication elsewhere in the form. In parallel our recommendations also streamline the ***Protocols*** section by introducing ***Licence steps*** and ***Protocol steps***, reducing repetition and focusing procedural descriptions on the harms to the animals rather than technical detail in order to strengthen the protection of animal welfare and the assessment of cumulative suffering. With the changes we are proposing we estimate that the overall length of the PPL application could be reduced by around a quarter. In Figure 1 and Annex 1, we provide a comparison of the current PPL structure and the revised format to illustrate how the information requirements have been streamlined. These efficiencies are further supported by our recommendation to make greater use of existing documentation, such as study plans, as a practical mechanism to strengthen the application of the principles of reduction and refinement at the level of individual studies.

Figure 1: Schematic of proposed changes to streamline the PPL application form



*This figure is based on an example PPL of 60 pages in length. By consolidating information into the **Project overview** section and removing duplication in the **Protocols** section, the PPL's length could be reduced by 15 pages, an estimated 25% reduction. Supporting documentation refers to standard operating procedures and study plans.*

Rationale for the NC3Rs recommendations

In this section we describe the detailed rationale for the recommendations which we have grouped into three thematic areas. In some cases, the underlying reasoning for individual recommendations is closely linked and where this is the case we have combined the explanations for clarity and completeness.

Theme 1: Strengthening the scientific rationale for animal use

Theme 1 focuses on strengthening the scientific rationale for animal use, including better articulation of the benefits of the research and improving consideration of strategies to replace the use of animals. The recommendations in Theme 1 support a streamlined PPL application form with the introduction of a new ***Project overview*** section that enables the knowledge gaps, objectives and anticipated outputs of the work to be clearly described, which in turn facilitates the assessment of the overall benefits of the proposed research.

Recommendation 1:	Information on the choice of model and scientific background should be consolidated into a new ***Project overview*** section.
Recommendation 2:	New questions and guidance on the justification for animal use and the evaluation of replacement strategies should be adopted.
Recommendation 3:	Updated questions and guidance on the benefits of the research should be implemented.

In the current PPL application form, information on the scientific background of the work, rationale for animal use and choice of model is distributed between the ***NTS*** and ***Project plan*** sections, with applicants often providing extensive and generic details on the rationale and benefits of the work without articulating the specific knowledge gap they intend to address. Recommendation 1 addresses this by creating a new section – the ***Project overview***. This replaces the current ***NTS*** section which is not currently retained as part of the licence once approved. The ***Project overview*** section would form an integral part of the PPL and consolidate information essential to the harm-benefit analysis in one place rather than summarising it, thus avoiding the repetition of information currently occurring in the ***NTS*** section.

The ***Project overview*** includes six sub-sections, as shown in Table 3, which both combines new questions and consolidates questions that are currently distributed across various sections in the PPL form. The question set for the ***Project overview*** section can be found in Annex 2. This new organisation of information will enable researchers to better describe how the animal studies sit within their wider programme of work, including the rationale for the choice of species, strain, sex and specific models/procedures. Implementation of recommendation 2 also encourages the demonstration of how findings from previous work have been applied and how non-animal methods are being integrated – including approaches for identifying and keeping up to date with emerging replacement opportunities.

The consolidation of information into the ***Project overview*** section and the implementation of recommendation 3 on new guidance for describing the benefits of the research will provide AWERBs and ASRU with a comprehensive picture to assess the impacts of the work, including how likely they are to be realised. In turn this supports a more robust evaluation of the need to use animals, helping to address issues identified in the **Rawle Report** and by the **Animals in Science Committee** and the **RSPCA**.

Table 3: Content of the current NTS section compared with the new *Project overview* section

Current PPL structure	Recommended PPL structure
NTS ▪ Aims ▪ Benefits ▪ Project harms ▪ Fate of animals ▪ Replacement ▪ Reduction ▪ Refinement	***Project overview*** ▪ Aims ▪ Benefits and outputs ▪ Choice of model and replacement ▪ Project harms and refinements ▪ Reduction ▪ Fate of animals

The question set for the ***Project overview*** is longer than the current ***NTS*** section, with 33 questions (compared to 25 currently). It captures information at a more granular level and by combining questions into one section, it enables the shortening of other sections of the PPL form where questions are currently duplicated (see Figure 1). It will be essential for ASRU to provide comprehensive examples of ***Project overviews*** for different disciplines or licence types to illustrate the appropriate level of detail required. Training for applicants and AWERBs will also be important to ensure the successful deployment of the new ***Project overview*** question set.

The ***Project overview*** section is designed to be used for all licence types (excluding higher education licences). For standard research PPLs, this enables the removal of most of the current ***Project plan*** section, with only a question on animal transfer from previous licences and three filter questions to identify other licence types (e.g. service, vaccine manufacture or regulatory work) retained. These licence types currently trigger a subsequent series of questions that have not been included in our review. In considering the implementation of the recommendations in Theme 1, ASRU should undertake an assessment of the minimum information required, in addition to the

Project overview, for an appropriate harm-benefit analysis to be conducted for licences involving service, vaccine manufacture or regulatory work. This would also address recommendations made in the Animals in Science Committee's **report on the use of non-human primates in service licences** and its 2020 **licence analysis review**.

Theme 2: Improving the description of harms and refinement controls

In Theme 2, we set out six recommendations to create a clearer and more coherent framework for describing harms to the animals used and the measures in place to minimise these. By consolidating information that is currently spread across the licence, strengthening how severity and cumulative suffering are assessed, and streamlining protocols and step descriptions, the recommendations reduce the duplication of information and make animal welfare considerations easier to evaluate and address.

Recommendation 4:	Information on harms to animals should be consolidated into the ***Project overview*** section.
Recommendation 5:	New questions and guidance on harms to animals and refinement controls should be adopted.

Harms to animals are currently described within both the ***NTS*** and the ***Protocols*** sections of the PPL application form. This often results in inconsistencies in the information provided, making it difficult to assess the overall experience of the animals and the level of harm caused. In recommendation 4 we propose consolidating this information into a new ***Project harms and refinements*** sub-section within the ***Project overview*** (see Annex 2). This streamlined structure will provide a more accurate account

of the expected harms to the animals and the measures in place to minimise these. As part of this we have re-worked and re-organised questions from the current PPL form – the use of these questions as in recommendation 5 will enable applicants to consistently describe how new opportunities to improve animal welfare are identified and the mechanisms in place for incorporating these into the work. These changes will enable named persons, AWERBs and ASRU to fully assess progress in implementing refinements and where opportunities to improve animal welfare are not routinely being adopted. Auditing this information will also enable ASRU to identify and promote examples of best practice, supporting the principles of the recent **Animals in Science Committee's recommendations** on strengthening leading practice.

Recommendation 6:	Further work on defining severity and cumulative suffering should be commissioned.

The questions in the ***Project harms and refinements*** sub-section will require applicants to describe the impact of procedures, handling, housing and husbandry on the animals under both typical and worst-case scenarios, including where animals are used across multiple protocols. This will provide a clearer account of the expected level of suffering and enable AWERBs and ASRU to more effectively evaluate the overall impact on the animals. However, it is important to note that assessment of severity and cumulative suffering remains challenging and this was an area highlighted by many of the stakeholders we consulted. Severity classifications – sub-threshold, mild, moderate, severe and non-recovery – are used to define the expected levels of pain, suffering, distress and lasting harm. There is considerable scope to improve consistency in how severity classifications are understood and applied by the regulated community, not least because this would support a more accurate assessment of cumulative suffering. Various organisations, including the **Animals in Science Committee**, have highlighted the importance of clarity in assessing severity and cumulative suffering, however there remains a critical need for further work in this area to address key knowledge gaps. We propose in recommendation 6 the commissioning of

further work to improve the definition and categorisation of severity and the assessment of cumulative suffering, in order to support much-needed guidance for applicants, AWERBs and ASRU on how to apply these effectively to protect animals.

Recommendation 7:	The ***Protocols*** section should be streamlined to improve the assessment of the PPL.

The ***Protocols*** section currently accounts for the majority of the PPL form. It often includes multiple protocols, depending on the nature of the work. Each protocol includes a series of steps, describing in detail the procedures to be carried out on the animals. In many cases, information is repeated either to comply with the basic information requirements of each protocol or because a step is used in several protocols. There is an opportunity to streamline the information required by dividing it into two new sub-sections – ***Licence steps*** and ***Protocol steps*** – and reducing the level of information required in the ***Protocols*** section through the introduction of the ***Project overview*** (as described in recommendation 4). We estimate that the implementation of recommendations 4 and 7 will reduce the overall length of the ***Protocols*** section by almost 40%[2].

The ***Licence steps*** compiles all of the steps used within the PPL so that they are only described once, rather than being repeated across multiple protocols as is the current case. This change shortens the length of each protocol, removes unnecessary duplication and reduces the burden on AWERBs and ASRU who otherwise need to examine identical information several times.

The ***Protocol steps*** sub-section then summarises the sequence of steps that will be used by cross-referencing to the ***Licence steps*** sub-section. Information is provided in a table format that describes both the typical and the worst-case scenario for each protocol, for example the typical scenario may be a surgery followed by a single behavioural test, while the

[2] This figure is based on an example PPL with a ***Protocols*** section of 40 pages that includes three protocols with five steps each. If the total length of the ***Protocols*** section is 40 pages, and of the 15 steps described, five are duplicated across protocols, removing duplicated steps and consolidating the ***Fate of animals***, ***Animal experience***, ***Experimental design*** and ***Protocol justification*** sub-sections into the ***Project Overview***, reduces the ***Protocols*** section by 15 pages, equating to a 38% reduction.

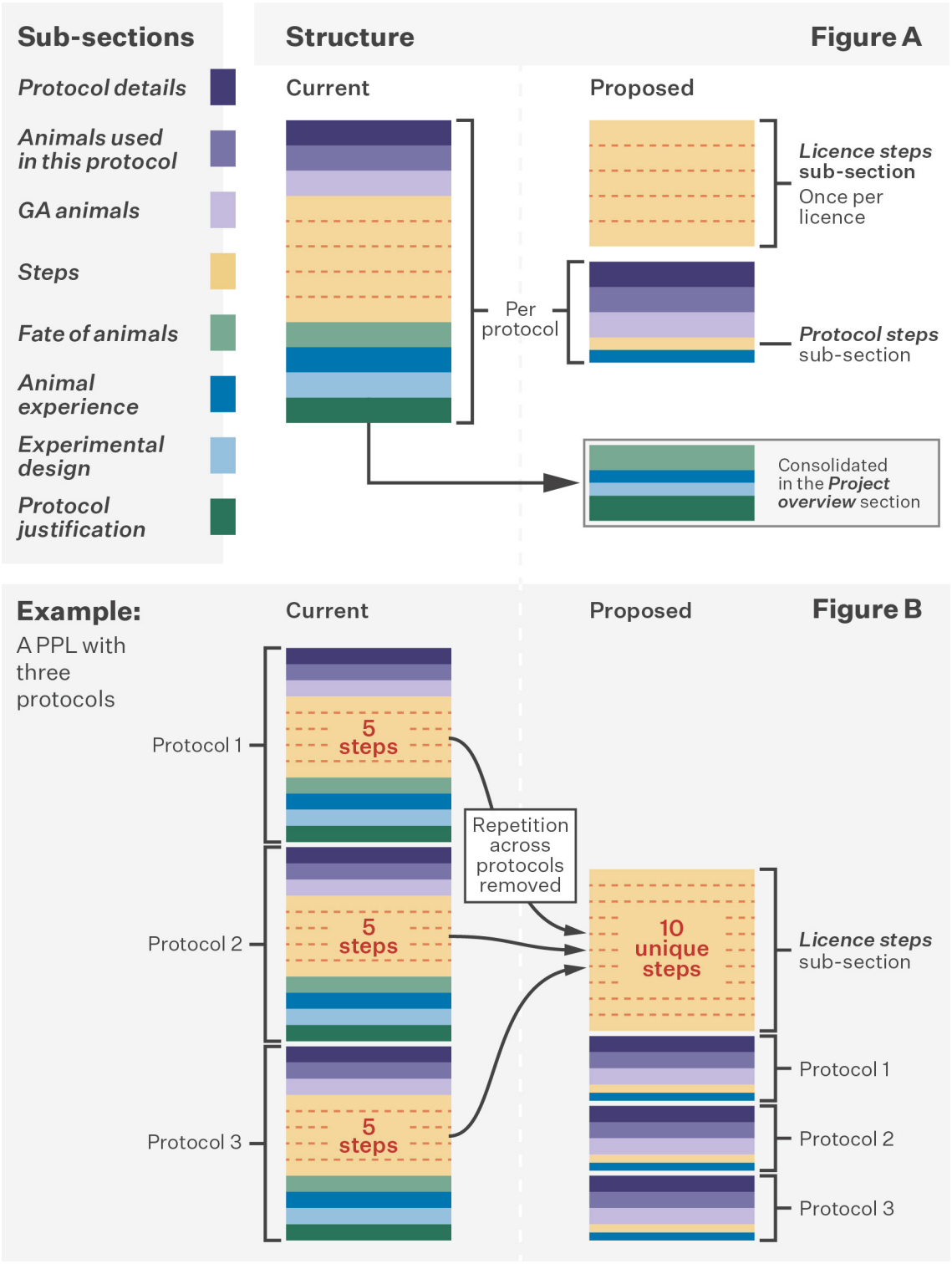
worst-case scenario may include an additional surgical intervention and multiple behavioural tests. This approach provides a clearer account of how steps are combined within a protocol and addresses limitations in the current PPL where steps are labelled mandatory or optional but AWERBs and ASRU have no indication of which optional steps will be used together in the same experiment, making it difficult to assess the harms to the animals and their overall experience. Table 4 and Figure 2 highlight the impact of recommendation 7 on the structure of each protocol.

Table 4: Recommended changes to streamline the Protocols section

Sub-section	Recommended changes
Licence steps	New sub-section to compile descriptions of steps. There is no duplication, each step is only described once per PPL.
Each protocol	
Sub-section	**Recommended changes**
Protocol detail	Unchanged.
Animals used in this protocol	Unchanged.
GA animals	Unchanged.
Protocol steps	Table listing steps for typical and worst-case scenario.
Animal experience	Reduced to a single question on general humane endpoints. Information on the typical and worst-case experiences for animals in each protocol is no longer needed as it is consolidated into the ***Project overview*** section.

*In the recommended structure of the **Protocols** section, the sub-sections **Fate of animals**, **Experimental design** and **Protocol justification** are removed because the information they contain is consolidated into the **Project overview** section.*

Figure 2. Recommended *Protocols* section compared with the current structure



*A. Schematic of proposed changes to the **Protocols** section to remove duplication of information.*

*B. Examples of the changes in practice for a PPL with three protocols that include five steps each – of these 15 steps, five steps are duplicated across the protocols. The introduction of the **Licence steps** sub-section removes this duplication, reducing the total number to ten distinct steps.*

The revisions to the ***Protocols*** section that we are recommending, further allow the length of each protocol to be reduced by deleting the sub-sections ***Fate of animals*** and ***Protocol justification***, and instead consolidating this information into the new ***Project overview*** (Annex 2) rather than having it duplicated in each protocol and in the ***NTS*** section as is currently the case. We are also proposing that the current ***Animal experience*** sub-section can be reduced, as information on the typical and worst-case experiences for animals in each protocol will be captured within the ***Project overview*** with no need to duplicate it.

Currently, information on humane endpoints is required in several places in the ***Protocols*** section. Humane endpoints are required for each step within a protocol and in the ***Animal experience*** sub-section, where there is a requirement for information on 'general' humane endpoints to be used for each protocol. This creates inconsistencies in the type of information applicants provide and confusion on how the humane endpoints will be used in practice once the PPL is approved. Some PPL applicants use the ***Animal experience*** sub-section to describe humane endpoints associated with adverse effects arising from a combination of steps while others provide a compilation of all humane endpoints which have already been described for every step in the protocol. The latter is problematic because there is a risk that PPL holders use the general humane endpoints in all experiments, rather than humane endpoints tailored to each experiment, which in most cases would not involve every optional step listed in the protocol. At the study level, this makes it difficult to demonstrate how animal suffering is being minimised. It is essential that ASRU provides clear guidance on what should be included in the general humane endpoints and how this information should be used in practice. Alongside this, we set out in recommendation 11 the use of study plans to tailor humane endpoints for specific experiments that are permitted within a protocol.

In the streamlining of the ***Protocols*** section, we are also recommending that the experimental design requirements are no longer included within each protocol and instead relevant information should be captured only in the ***Project overview*** section. This would encompass details on how the number

of animals used will be kept to the minimum necessary, the overarching principles that the PPL applicants/holders will follow to ensure that the findings are reliable, and information on the statistical expertise in place to support the work. Since the detailed experimental design information currently required for each protocol is unlikely to reflect all studies to be conducted over the five-year duration of a PPL, the use of study plans provide a more effective mechanism for describing and reviewing the design of individual experiments and we are recommending that their use becomes standard practice. This would enable relevant information on the reliability and reproducibility of experiments to be reviewed locally and verified through audits by ASRU – this is expanded on in recommendation 11.

Recommendation 8: The description of ***Licence steps*** should focus on the impacts on animal welfare rather than technical detail.

In the current PPL form, the steps in the protocols are primarily assessed based on a narrative description of the techniques, adverse effects and humane endpoints. Existing guidance in ASPeL encourages these descriptions to be sufficiently broad to allow flexibility but in practice they are often lengthy and can include technical information that has no bearing on the protection of animal welfare. As a result, even minor methodological variations may require licence amendments despite having no impact on the level of animal suffering, and AWERBs and ASRU are required to assimilate detailed procedural descriptions that add little value to the harm-benefit analysis.

The introduction of the new ***Licence steps*** as set out in recommendation 7 provides an opportunity to evolve how the impact of the regulated procedures on animal welfare is described. Recommendation 8 proposes that ***Licence steps*** capture only the information necessary for assessing the harms to the animals involved, rather than the precise procedural method to be used. This avoids unnecessary technical detail and, by highlighting the information

specifically relevant to animal welfare, it promotes a more considered evaluation of the harms to animals. Importantly this recommendation provides PPL holders with the flexibility to use the most appropriate or most refined method without requiring amendments (provided they remain within the authorised limits of suffering specified in the step). This aligns with recent **recommendations** from the Animals in Science Committee on strengthening leading practice and facilitating the implementation of refinements.

We propose that the narrative detail in the ***Licence steps*** focuses on a short summary of the procedures, with the harms to the animals structured around four core elements that highlight the aspects of each step most relevant to animal welfare: the procedural limits, likely adverse effects, refinement controls and monitoring, and humane endpoints. These are described in Table 5.

Table 5. Recommended changes for *Licence steps*

Information required	Rationale
Step name and number	This enables rapid identification of each unique step to list the steps used in each protocol (in the ***Protocol steps*** sub-section – see recommendation 7)
Step description	Short summary of the procedures in a few sentences. This includes key information such as the route for dosing and sampling procedures.
Species and relevant animal characteristics	Restricting a step to animals with shared welfare considerations enables streamlining of individual steps, it promotes the use of relevant indicators of suffering and limits tailored to the animals under study.
Procedural limits	For example, frequency of dosing, duration of procedures, maximum number of procedures, and minimum interval between procedures. Currently this information can be included as part of the narrative step description but the requirement to specifically and consistently provide it is new.
Likely adverse effects	An outline of the adverse effects for steps likely to result in more than transient discomfort. This requirement is included in the current PPL form.
Refinement controls and monitoring	This includes three different elements that require the provision of more detailed information than is the case in the current PPL form: i. The methods that will be used to reduce the occurrence or severity of adverse effects (e.g. using ultrasound guidance to avoid invasive surgery, or administration of tamoxifen in the diet instead of by oral gavage). ii. How and at what frequency animals will be monitored. iii. The measures that will be taken to ameliorate any adverse effects observed.
Humane endpoints	An outline of the humane endpoints in place for each step. This requirement is included in the current PPL form.

Differences in animal characteristics such as species, sex or age can influence procedural limits, expected adverse effects, appropriate refinements and relevant humane endpoints. Separate ***Licence steps*** would be required in these instances to ensure that animals are assessed and protected accordingly, and that the limits authorised in the licence accurately reflect the welfare implications. While this approach may increase the number of steps within a licence, the individual steps themselves become more streamlined, as they focus on a single species or animals with shared welfare considerations. This also aligns with current ASRU practice, where inspectors are increasingly requesting that species are separated into distinct steps.

Some stakeholders consulted raised concerns that the ***Licence steps*** descriptions that we are recommending could make it more difficult for named persons, AWERBs and ASRU to scrutinise the procedures effectively. However, our recommendation mitigates this risk by introducing dedicated information requirements that clearly define the limits applicable to each step and set out the refinements that will be implemented. When considered alongside the expected adverse effects and the humane endpoints tailored to the animals under study, this provides a more targeted and comprehensive consideration of the harms to the animals than is possible with the current licence structure. Our recommendation will enable AWERBs and ASRU to identify opportunities for further refinement more easily and to challenge applications where appropriate measures are not in place to protect animals. It is however important to note that in implementing this recommendation ASRU will need to ensure that the PPL application retains the minimum level of procedural detail necessary for essential legal checks and maintaining effective regulatory oversight.

Recommendation 9:	A library of standard ***Licence steps*** should be generated.

We are recommending that a practical mechanism to promote the adoption and dissemination of best practice is to establish a library of standard steps,

pre-approved by ASRU, that applicants can select for inclusion in their PPLs[3]. The library would enable a harmonised approach to setting severity limits and humane endpoints for similar procedures, both within individual establishments and across the UK.

Consultations with stakeholders indicated that a high proportion of procedural steps – up to 80% – are for common procedures that could be standardised, offering substantial efficiency gains. In the current PPL process, some institutions already use standardised wording for common procedures. A library of pre-approved ***Licence steps*** on a national scale would deliver substantial benefits, including greater consistency across PPLs and simpler compliance monitoring for establishments by removing discrepancies introduced when similar steps are reviewed by different AWERBs and inspectors. It would also significantly reduce the time required to draft, review and oversee PPLs, freeing-up resources for applicants, named persons and AWERBs to focus more effectively on implementing the 3Rs in practice. Importantly, this recommendation operationalises the Animals in Science Committee's **proposed framework** for embedding expected standards across the sector as well as recommendations in the **Rawle report** on facilitating the sharing of 3Rs advances.

We envisage two mechanisms for implementing recommendation 9, with ASRU playing a key role in both. A bottom-up approach in which establishments can flag to ASRU the ***Licence steps*** that are commonly used within their facilities. This would allow for frequently used procedures to be identified across the sector and prioritised, for example the most commonly used dosing and sampling procedures. A complementary top-down approach could also be implemented, in which various organisations such as the IAT, LASA, LAVA, NC3Rs and RSPCA would work with ASRU to identify areas for the development of standard ***Licence steps***, for example based on those that involve severe suffering with significant opportunities for refinement. In either case it would be essential to ensure wide input from a range of experts and organisations, including named persons and learned societies, with a working group format the most appropriate mechanism for developing consensus and periodic review to ensure that standard steps remain up to date. Some

[3] Note that the recommendation is different from the approach that ASRU has taken by publishing standard protocols for breeding genetically altered animals, which provide standard wording that applicants can edit and therefore still require detailed review by AWERB and ASRU.

stakeholders expressed concerns about the challenge of harmonisation, however the focus on ***Licence steps*** rather than entire protocols provides a modular system that offers a flexible and practical solution, reducing administrative burden while maintaining appropriate oversight to protect animals.

The library of standard ***Licence steps*** could be developed over time, with PPLs including a mixture of pre-approved standard steps and steps drafted by applicants. To realise the efficiency gains of such a library, standards steps would need to be un-editable, clearly labelled as pre-approved and easily distinguishable from applicant-drafted ***Licence steps***. This would enable AWERBs and ASRU to focus on assessing the impact on animals of the combination of steps, rather than re-evaluating the content of standard steps. Applicants would retain the flexibility to draft their own steps when the procedures they need are not included in the library, or when there is scientific justification for using different severity limits than those described in the standard ***Licence steps***. However, choosing a manual step for a procedure already included in the library would trigger scrutiny to ensure that any divergence in the proposed severity limits is fully justified.

Despite the requirements of **Standard condition 4 for personal licence holders** to ensure that pain, suffering, distress and discomfort are reduced to the absolute minimum necessary, a potential risk identified by stakeholders with recommendation 9 is that applicants might select standard ***Licence steps*** with higher severity limits than needed. This risk already exists under the current licensing system, where applicants will sometimes try to cover all possible eventualities (including unlikely adverse effects) to avoid compliance breaches or the need for licence amendments. The use of standard ***Licence steps*** does not increase this risk but in any case, in considering implementation of recommendation 9, ASRU should take the opportunity to work with the sector to identify remedial measures to avoid this practice.

Theme 3:
Promoting and facilitating application of the 3Rs on the ground

In Theme 3, we set out three recommendations designed to strengthen the mechanisms that promote and support the application of the 3Rs in practice. By improving the accessibility and use of information in the PPL, embedding study plans within the licensing framework, and clarifying oversight and accountability, these recommendations aim to drive more transparent and effective implementation of the 3Rs.

Recommendation 10: The ***Project overview*** section should be published.

In line with legal requirements, ASRU publishes non-technical summaries of approved PPLs on the **Home Office's website** each quarter. These summaries are currently generated from the ***NTS*** section of the PPL application form and are intended to inform the public about the use of animals in scientific procedures under the ASPA. Despite the length of many non-technical summaries (which can range from 4 to 23 pages[4]) the **Animals in Science Committee** and others have highlighted that it is commonplace for these not to provide sufficient or useful information and in many cases the use of specialist and technical language limits accessibility for public audiences.

In recommendation 10, we propose that the new ***Project overview*** section described in Themes 1 and 2 is made publicly available to meet the legal requirements of the ASPA[5]. The use of the ***Project overview*** for this function rather than a separate ***NTS*** section as is the current case will benefit applicants by avoiding the need to provide similar information in multiple places in the PPL. In order to maintain public accountability and trust, we recommend publishing a complementary short and genuinely lay summary to accompany the ***Project overview***. Allowing applicants to use generative

[4] This analysis is based on 446 non-technical summaries published on the Home Office website for PPLs approved in 2025. The average length was nine pages.

[5] Section 5A of the Animals (Scientific Procedures) Act 1986 details the information requirements of the non-technical summary.

AI[6] to draft this summary could help ensure that the language is clear and accessible, while applicants would remain responsible for ensuring that the final version accurately reflects the PPL.

In developing recommendation 10 we have considered how transparency can be strengthened while continuing to protect PPL holders and their establishments, and safeguard confidential or commercially sensitive information. The new ***Project overview*** section does not include any personal details about the PPL holder and their establishment. We are also proposing that publication of the ***Project overview*** section omits responses to the three questions relating to the scientific background and outputs of the work, which frequently reference previous studies or proprietary information (questions 4, 5 and 6 in Annex 2). Although the detailed responses to these questions are essential for AWERBs and ASRU to assess the PPL application and conduct a harm-benefit analysis, a high-level description of this information in the short lay summary should be sufficient to meet the legal requirements of the ASPA.

There are also additional advantages of publishing the ***Project overview*** in terms of providing a mechanism for sharing 3Rs innovations across the sector. Information on refinements and the non-animal models that are used alongside *in vivo* work could provide general pointers for other researchers to identify approaches that are relevant to their own studies. The current publication format with non-technical summaries compiled in a series of long PDF documents (typically 1,000 pages long), does not support this type of use. Valuable information that could be used by others without revealing intellectual property is not being shared. This could be addressed by publishing ***Project overviews*** in a searchable database, which would enable PPL applicants and named information officers to identify 3Rs approaches relevant to particular research areas. While ***Project overviews*** will not identify the applicants or include detailed methodological descriptions, the database would help raise awareness of the techniques mentioned (which may be published for other applications) and prompt further investigation into opportunities to apply the 3Rs several years before the research described in the PPL is published in the scientific literature.

[6] The Animals in Science Committee recently published a letter to the Home Office minister recommending investigating the use of generative AI in licensing **www.gov.uk/government/publications/generative-ai-in-animals-in-science-letter-to-lord-hanson/generative-ai-in-animals-in-science-letter-to-lord-hanson-accessible**

Recommendation 11:	The Home Office should promote the use of study plans and set their minimum information requirements.

We recommend that the Home Office promotes the use of study plans to help researchers and named persons translate information set out in the PPL into individual experiments that are permitted under the licence authorisation. The ultimate goal of recommendation 11 is for study plans to become the expected standard, with institutional oversight for their use embedded within the ASRU audit process.

Recommendation 11 is not intended to dilute the information required in the PPL, rather study plans provide a structured framework for detailing the specifics of an individual experiment, capturing information that cannot be defined at the PPL level, given that it focuses on a multi-year programme of work. They typically include the animals to be used, the monitoring regime and humane endpoints, and, in some cases, the experimental design. By complementing standard operating procedures, study plans form part of the complete documentation for an experiment, ensuring that day-to-day implementation aligns with the legal limits set out in the PPL. Many animal facilities are already using study plans for record-keeping, compliance monitoring and as evidence during ASRU audits. Their routine use supports clear communication, strengthens collaboration between researchers, named persons, research support staff and statisticians and bolsters institutional mechanisms for ensuring that work is conducted in line with regulatory requirements and best practice.

Within the legal framework of a PPL, study plans provide an important mechanism for achieving reduction and refinement. They ensure that the design, methodology and animal care arrangements are tailored to the specific scientific aims of each study, which is more effective than relying on the high-level information required for a five-year programme of work that a PPL encompasses. Study plans prompt researchers to consider clinical

signs, humane endpoints, monitoring regimes and refinements at the level of the individual experiment, thus helping to reduce the risk of applying generic, protocol-level humane endpoints that are not tailored to the specific steps involved. Within the upper limits authorised in the licence, they can be used to identify opportunities for further refinements – such as reducing injection volumes or shortening the duration of procedures – that can be appropriately implemented for a given study. In practice, this means the list of adverse effects set out in the PPL can be narrowed within the study plan, providing additional opportunity to refine corresponding humane endpoints and reduce suffering below the maximum level permitted.

Study plans provide a mechanism to optimise the experimental design at the level of each study, something that cannot be described effectively at the PPL level. This places greater emphasis on the specific measures in place to minimise subjective bias and enhance reliability; it also provides an opportunity to verify that the number of animals proposed is genuinely the minimum required to meet the study's objectives. The increased granularity enables establishments to support applicants in the use of appropriate experimental design and robust methodology that yield reliable and reproducible findings.

The promotion of study plans by the Home Office would signal their importance to PPL holders and empower establishments to deploy them consistently. At present, the use of study plans varies between establishments, from adopting study plans for all *in vivo* work to not using them at all. Study plans serve different functions depending on the facility – including compliance with Good Laboratory Practice standards or the PPL – meaning that their structure and level of detail can differ substantially. Given this variability, we recommend that, in consultation with the regulated community, ASRU defines the minimum information that any study plan should include to provide a meaningful description of study-specific harms, refinements and experimental design. The **ARRIVE study plan**[7] that was published in 2024 provides a sensible starting place for these discussions. Importantly, provided that study plans meet the minimum information

[7] The ARRIVE study plan operationalises all of the information required to comply with the international standard set by the **ARRIVE reporting guidelines**.

requirements set by ASRU, establishments should have the flexibility to determine the most appropriate format to fit their internal processes, avoiding unnecessary administrative burden and duplication of effort.

Recommendation 12:	Establishments should have processes in place to support the use of study plans.

For recommendation 11 to be effective, establishments will need to have appropriate processes in place to enable researchers to use study plans effectively. This should include assistance for drafting study plans and mechanisms for input from key individuals such as named persons. The range of knowledge required to support the use of study plans is broad, and some of the stakeholders we consulted expressed concerns that not all establishments will have the capacity to cover all relevant domains, for example access to statistical expertise for animal studies varies across the sector. The **ARRIVE study plan** is useful in this case as it includes guidance that helps researchers independently design reliable experiments, identify the measures they will use to ensure results are robust and determine the minimum number of animals required.

An important consideration in implementing recommendation 12 is whether institutions should have a formal approval process for study plans. Some stakeholders raised concerns about the resources needed to provide input and review them. The changes that we are recommending for the PPL form will free-up time for named persons and others that can be redirected to supporting the use of study plans. Flexibility to develop oversight mechanisms suited to local circumstances and working practices is however essential and should be taken into account when considering recommendation 12. Some organisations will have the capacity and existing processes for AWERBs or animal facilities to review and approve study plans for all animal studies, while others may opt to limit checks to confirming that a complete study plan is in place rather than requiring formal approval of its content, or to only review those involving severe suffering or novel procedures.

Careful onward discussion between the Home Office and the regulated community will help ensure that study plans are integrated proportionately into local governance processes.

Acknowledgements

The NC3Rs expresses its sincere gratitude to the individuals and organisations across the sector who contributed to this review, either as part of the consultation or by providing feedback on the draft recommendations.

Annex 1: Summary of the impact of the NC3Rs recommendations on the sections of the current PPL form

Sections	Sub-sections
Introductory details	Unchanged.
NTS	All questions consolidated into the new ***Project overview*** section.
Applicant information	Unchanged.
Project location	Unchanged.
Project plan	***Scientific background*** and ***Action plan*** sub-sections removed – all questions related to standard research licences consolidated into the new ***Project overview*** section, ASRU to assess whether additional information is required for licences that include services, vaccine manufacture or regulatory work. ***General principles*** sub-section removed – all questions consolidated into the new ***Project overview*** section.
Protocols	***Fate of animals*** and ***Protocol justification*** sub-sections removed – all questions consolidated into the new ***Project overview*** section. ***Animal experience*** sub-section reduced – most questions consolidated into the new ***Project overview*** section, ASRU to clarify requirements on general humane endpoints. ***Experimental design*** sub-section removed – questions related to overarching principles consolidated into the new ***Project overview*** section, remaining questions covered in study plans instead. ***Steps*** sub-section replaced by a new ***Licence steps*** sub-section to compile distinct step descriptions across all protocols and new ***Protocol step*** sub-section to list sequences of steps to be used.
Use of animals	Unchanged.
Other considerations	Unchanged.

Annex 2:
Question set for the new *Project overview* section

Sub-Sections	Question and guidance
Aims	**1. What is the aim of this project?** Keep this to a short one or two sentence summary using non-technical language.
Aims	**2. Key words that describe this project.** Choose up to 10. Try to capture the academic field and the context of the work, for example: cancer, stem cells, therapy. If development of a 3Rs approach is a key focus of the work, keywords such as replacement, reduction and refinement can also be used.
Aims	**3. Objective title (add as required).** Describe clear and realistic objectives that support your overall project aim. Avoid broad terms like "cancer" or "nervous system" without explaining exactly what you are studying. Objectives may be framed as questions where this aids clarity. It should be possible to determine in five years' time whether or not your objectives were met, assuming all lines of enquiry are pursued. You may not be able to identify all objectives at the time of application. Additional objectives can be added as amendments if they fit within the overall aim. Objectives should reflect the intended outcomes, rather than the methods used to achieve them.
Aims	**4. Describe how each of these objectives relate to each other and help you to achieve the aim of this project.** Describe how different objectives within your project depend on each other, including any decision points where progress may be paused or redirected (e.g. go/no-go criteria). This section should link objectives to protocols, explaining how objectives will be addressed. Provide an outline of the stages of the programme of work and indicate – using protocol numbers – how each protocol contributes to each objective. Where helpful, include annotated flow charts and decision trees (.jpg and .png files) to illustrate how objectives relate to each other.
Benefits and outputs	**5. Briefly summarise the state of scientific knowledge and the knowledge gap to show how you arrived at the starting point of this project.** Be specific and relevant to your project aim. There is no need for a detailed overview of the entire field but provide insight to how you came to the start of this current project licence. If the work involves translational, veterinary or clinical applications, explain the prevalence and severity of the condition, availability of current treatments and why a different therapeutic approach is necessary.

Sub-Sections	Question and guidance
Benefits and outputs	**6. Describe the impact of this project, what new knowledge and outputs are you likely to generate?** Why is it important to undertake this work and what part of the knowledge gap will it address? Expand on your aim and objectives and include what you hope to learn or discover by doing this project. Include details of the outputs likely to be produced by the end of this Project Licence such as data, methods, medicines, vaccines or new models that others might benefit from in future research.
Benefits and outputs	**7. Who or what will benefit from the project outputs and how?** Consider short (<1 year), medium (1-5 years) and long-term (>5 years) beneficiaries of the research and provide both a local and broader context to the benefits. Explain how each type of beneficiary is expected to benefit and if applicable, the added value of offering this work as a service to others.
Benefits and outputs	**8. How will these benefits be shared and disseminated?** Describe how you will disseminate new knowledge – this includes research methods and protocols, as well as findings from approaches that were not successful. Outline your strategy for open and reproducible research and making resources (e.g. methods, protocols, data, animals, tissues) available and useful to other researchers. You should refer to tools or resources you use to support maximum impact of data/knowledge sharing such as the ARRIVE guidelines (https://arriveguidelines.org) or the FAIR Data Principles (https://doi.org/10.1038/sdata.2016.18).
Benefits and outputs	**9. Will your project result in the development or validation of novel approaches that would replace, reduce or refine the use of animals in research and/or testing?** Provide details of any models, tools or resources you will develop to replace or reduce animal use or support better animal welfare.
Benefits and outputs	**10. How will you ensure that any findings obtained are reliable, valid and accurate?** Your response should address the strategies, tools and resources you will use to minimise the risk of bias in your experiments, such as the use of randomisation, masking/blinding and *a priori* inclusion/exclusion criteria to minimise potential confounders. Further information on rigorous study design can be found on the NC3Rs' Experimental Design Assistant website: https://eda.nc3rs.org.uk.

Sub-Sections	Question and guidance
Choice of model and replacement	**11. Describe the animal models you will use in each protocol of this licence.** Models may include wild-type or genetically altered animal strains, surgically or chemically induced models of disease or models of biological or behavioural processes. For each model include the species and relevant animal characteristics. Where multiple models are used in the licence, provide a clear breakdown of the known phenotypes (spontaneous or induced) or features of the model. You may wish to use a table. If producing data for regulatory authorities, what tests will be performed?
Choice of model and replacement	**12. Why do you need to use animals to achieve the aim and objectives of your project?** For each animal model provide insight into why animals are necessary to achieve your scientific objectives and, where relevant, why they are representative of the diseases/conditions being studied, including reference to the specific aspects of physiological processes/anatomical structures/ cognitive functions that are of scientific interest. For each model include a justification for the species, strain and life stages you are using. For human-focused research, ensure that you describe the relevant similarities between the animal model and the human. Evidence that progression into live animals is a logical and necessary next step. If producing data for regulatory authorities, how have you determined that an *in vivo* test is required?
Choice of model and replacement	**13. What makes the selected animal models the most appropriate for achieving the aim and objectives of your project and how have you selected these to ensure the lowest harms to the animals involved?** Where there are multiple options to induce a condition or disease, explain why the animal models you have chosen are the most suitable and least harmful for addressing your project goals. Where you are using protocols with severe suffering ensure that a clear justification is provided for why the animals need to experience the highest severity level. You should consult and refer to any published guidelines to demonstrate evidence-based choices of models to ensure your scientific objectives are achieved with the minimal amount of animal suffering.
Choice of model and replacement	**14. How are you integrating other approaches (e.g. *in vitro* or *in silico* models, clinical work and the use of non-protected animals) into your research to complement the *in vivo* work described in this licence?** Describe any key *in vitro*, *ex vivo*, *in silico*, non-regulated animal work or clinical work that will precede, or be run alongside your *in vivo* work. Explain how these will inform and optimise the animal studies included in this licence (e.g. indicate where go/no-go criteria will be applied).

Sub-Sections	Question and guidance
Choice of model and replacement	**15. How do you identify potential alternatives to using protected animals in your research? What steps will you take to stay informed about emerging replacement approaches that could reduce or eliminate the need for animals in your work?** Describe the steps that you have taken to ensure that there are no alternatives to the use of protected animals for the objectives of your project. You should specifically describe the literature and databases that you have utilised and the search methods and terminology that you have employed. You may find it helpful to consult Replacing Animal Research's Replacement Checklist (https://replacinganimalresearch.org.uk/resources/replacement-checklist/). Describe how you will keep abreast of new opportunities that would enable the use of animals in this project to be replaced. For example, include the networks that you participate in and other relevant sources of information.
Choice of model and replacement	**16. Which approaches that could be used to replace the use of live animals (e.g. *in vitro* or *in silico* studies) did you consider for achieving the aim and objectives of this project? Explain why they were not suitable.** Explain the specific aspects related to the processes/functions/anatomy of interest that can be replicated outside of a living organism (e.g. through the use of *in vitro* or *in silico* approaches). Provide examples of the models available and why these approaches are not sufficient to address the objectives of this project. Have you tried addressing any of the objectives of this licence without using live animals? If so, what did you try and why was it not feasible?
Choice of model and replacement	**17. Which non-protected species or life stages did you consider to replace all or part of the use of protected animals in this licence? Explain why they were not suitable.** Explain what species not protected under ASPA (e.g. many invertebrate species) or immature non-protected life stages were considered and why they are not sufficient to address the objectives of this project.
Choice of model and replacement	**18. Will all your experiments use male and female animals to maximise the generalisability of the findings? If not, specify which experiments will use animals of a single sex and provide a justification for this choice.** Further advice on incorporating animals of different sexes into the study design and analysis is available, for example as part of the Sex Inclusive Research Framework (https://doi.org/10.1038/s41467-025-58560-5).
Project harms and refinements	**19. Enter the estimated number of animals of each type used in this project.** Animal type refers to species and can be selected from a drop-down menu.

Sub-Sections	Question and guidance
Project harms and refinements	**20. What are the expected severities and the proportion of animals in each category (per animal type)?** The expected severities may include non-recovery, sub-threshold, mild, moderate, and severe. Further information regarding the severity classification of procedures can be found in Appendix G of the Guidance on the Operation of the Animals (Scientific Procedures) Act 1986 (**https://assets.publishing.service.gov.uk/media/66e0233ab1a8879e443282a0/Guidance_on_the_operation_of_ASPA_-_December_2023.pdf**).
Project harms and refinements	**21. For each protocol describe what will be done to the animals, the expected level of impact these procedures would typically have and the worst-case scenario that any animal could experience.** Outline what will be done to the animals and the expected impact and potential adverse effects of these procedures. Provide details of the typical and worst-case levels of pain, suffering and distress that an animal may experience under each protocol. Your response should justify the chosen severity classification of each protocol and consider the cumulative effect of combined procedures, the amount of time an animal will remain on the protocol and any impact arising from housing, handling and husbandry conditions (e.g. single housing, methods of restraint etc.). Diagrams can be used to improve clarity.
Project harms and refinements	**22. Explain whether animals will be used in multiple protocols and describe how this may impact on the overall experience of those animals.** Describe the cumulative effect of any combination of procedures the animals will undergo across multiple protocols and how this will impact on the overall experience of these animals. Consider the amount of time an animal will remain under study and whether there is re-use or continued use of animals between protocols.
Project harms and refinements	**23. How will you minimise harms and improve animal welfare across all aspects of your protocols?** Describe the techniques, procedures and approaches you will use to reduce pain, suffering or distress for animals across all your studies. This should include refinements to housing, handling and husbandry practices that help improve welfare. Also, if relevant, explain why your scientific objectives cannot be met with earlier humane endpoints or without animals showing clinical signs.
Project harms and refinements	**24. Describe any refinements that have emerged over the last five years that you have been able to incorporate into your plans to minimise harms and improve animal welfare.** This can include refinements you have developed in your lab, identified through collaborators or through the scientific literature.

Sub-Sections	Question and guidance
Project harms and refinements	**25. How do you stay up to date with refinements that minimise harms and improve animal welfare within your field and what mechanisms are in place to ensure you are able to implement these during the project?** Describe how you keep informed about new refinement opportunities, including professional networks, meetings and conferences you engage with. Describe how you assess, adopt and embed relevant refinements into your studies to ensure that they are effectively implemented throughout the project to minimise harms and improve animal welfare.
Project harms and refinements	**26. What published best practice guidance and resources will you use to improve the welfare of the animals used in your protocols?** Provide model-specific examples from the literature of refined procedural or husbandry methods that you will use to inform your study plans (e.g. IMPROVE guidelines for ischaemic stroke models, RSPCA guidance on avoiding and reducing severe suffering, etc.). Where applicable, explain how adherence to these standards will help reduce pain, suffering, or distress in the animals.
Reduction	**27. How have you estimated the numbers of animals required for this project, and why is this number appropriate to achieve your scientific objectives?** Where appropriate, outline the principles of experimental design you will apply at each stage of the work, indicating how you will select the number of experimental groups and group sizes. Where applicable, include a sample size calculation to demonstrate your approach at the experimental level, and indicate how this scales to the overall numbers requested for the Project Licence. The justification should be robust and demonstrate that the planned numbers are sufficient to generate reliable, decision-informing results without the need to repeat experiments unnecessarily. The overall number of animals requested and the justification should also take into account the numbers of animals expected to be excluded from studies. Note that reducing animal use is not simply about using fewer animals – experiments with group sizes that are too small can lead to inconclusive or unreliable results and ultimately waste animals.
Reduction	**28. What statistical support is available to advise on study design and ensure that animal numbers are appropriate and kept to the minimum necessary to meet your scientific objectives?** Describe the sources of statistical support you will draw on when planning your studies. This may include institutional biostatisticians, expertise within your research group or external consultants.

Sub-Sections	Question and guidance
Reduction	**29. What measures will you implement to reduce the number of animals used in your project?** Describe strategies that you will use to minimise the number of animals used. This may include optimising breeding strategies, conducting feasibility or pilot studies to avoid unnecessary full-scale experiments, or streamlining experimental design to limit surplus groups (e.g. unnecessary satellite groups).
Reduction	**30. What measures will you take to maximise the amount of knowledge gained from each animal?** Describe the strategies you will apply to maximise the amount of useful data obtained for each animal. In your response, consider whether any additional harms might result from collecting more data per animal and how you will ensure that any such burden remains justified and within acceptable limits.
Fate of animals	**31. What will happen to animals used in this project at the end of each protocol?** Describe the intended fate of animals at the end of each protocol (e.g. euthanasia, re-use, re-homing or setting free). Animals may only be kept alive if a veterinary surgeon or other competent person confirms this is appropriate. Any plan to re-use, re-home or set free animals must be specifically justified. Refer to the Advice Note on re-homing and setting free of animals (**https://assets.publishing.service.gov.uk/media/5a82e2ab40f0b6230269d373/Advice_Note_Rehoming_setting_free.pdf**) for further guidance.
Fate of animals	**32. Will you be using non-schedule 1 killing methods on a conscious animal?** Answer "Yes" only where animals will be killed while conscious using a method not listed in Schedule 1 (e.g. decapitation of conscious neonates).
Fate of animals	**33. (If yes to 32) For each non-schedule 1 method, explain why this is necessary.** N/A

The Project overview section will be publicly available. However, the responses to questions shaded in grey (questions 4, 5 and 6) will be removed to avoid the risk of sharing proprietary or identifiable information. Although the detailed responses to these questions are essential for AWERBs and ASRU to assess the PPL application and conduct a harm-benefit analysis, a high-level description of this information in the short lay summary should be sufficient to meet the legal requirements of the ASPA.

Annex 3:
List of abbreviations and acronyms

Abbreviation	Definition
ASPA	Animals (Scientific Procedures) Act 1986
ASPeL	Animals in Scientific Procedures e-Licensing
ASRP	Animals in Science Regulation Policy Unit
ASRU	Animals in Science Regulation Unit
AWERB	Animal Welfare and Ethical Review Body
IAT	Institute of Animal Technology
LASA	Laboratory Animal Science Association
LAVA	Laboratory Animal Veterinary Association
NTS	Non-Technical Summary
PPL	Project Licence
RSPCA	Royal Society for the Prevention of Cruelty to Animals

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