

LICENCE REFERRAL REVIEW

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1.0 Report of the Licence Referral Review Task and Finish Group

1.1 The Licence Referral Review subgroup (LRR) was established by the Animals in Science Committee (ASC) in July 2015 to review the process through which applications for project licences were selected by the Inspectorate for referral to the ASC Project Licence Application subgroup (PLA), so that they might advise the Secretary of State (SoS) on the granting of a licence.

2.0 Terms of reference

2.1 The LRR was tasked to produce recommendations which include, but are not limited to:

- Appropriateness or amendments required, to the current position.
- Identifying any drift in licencing recommendations, for instance around the length of time that animals might be allowed to be restrained in a primate chair, or the extent to fluid deprivation that was permissible to encourage training.
- Recommendations e.g. new threshold, modifications to the ASC licence application review process.
- The LRR identifies future work, including potentially other license types which might benefit from strategic review.
- Report and recommendations passed to ASC for discussion and ratification.

3.0 Membership

3.1 Members of the LRR are listed in Appendix 1.

4.0 Meetings

4.1 The LRR held teleconferences and face-to-face meetings on several occasions as listed in Appendix 2.

5.0 Background

5.1 The Guidance on the Operation of the Animals (Scientific Procedures) Act (ASPA)¹ provides that the SoS will seek specific or general advice, as appropriate, on applications involving:

- the use of wild-caught non-human primates;
- the use of cats, dogs, equidae or non-human primates in severe procedures;
- use of endangered species;
- projects with major animal welfare or ethical implications;
- projects involving the use of admixed embryos falling into category 3 of the AMS report on ACHM and category 2 where the predominance of an admixed embryo is unclear or uncertain (see Section 5.18.2);
- projects which may invoke any of the 'safeguard clauses' in the Directive with respect to the purpose of primate use, proposals for the use of a great ape, or proposals to cause long-lasting pain, suffering or distress that cannot be ameliorated
- projects of any kind raising novel or contentious issues, or giving rise to serious societal concerns.

5.2 At present this function is delegated by the ASC to the PLA, chaired by the Chair of the ASC (See Appendix 1), with the considerations of the subgroup being communicated to the full ASC at the next meeting. Since November 2015 all licence applications to be considered in this way have been circulated to the full ASC membership prior to the subcommittee meeting to allow any issues of concern to be raised, and issues raised in this way have also been notified to the applicants prior to their attendance at the ASC subcommittee meeting to allow them to prepare their response.

5.3 One purpose of the LRR was to establish whether, for some of the categories of applications referred to the ASC for specific advice, it might be possible for there to be in place some standing general advice that might be sufficient to obviate the need for detailed review of a specific licence. This would have potential benefits in the speed of licence approval, a reduction in the need for PLA meetings, thereby leading

¹ <https://www.gov.uk/government/publications/operation-of-aspa>

to a cost saving and/or freeing up time for the PLA to review licences not listed in 5.1 above or provide general advice to inspectors on certain types of licence.

- 5.4 The LRR took the opportunity in the context of their wider remit also to consider whether there were other issues relating to the work of the PLA where there were opportunities for improvement; and whether there were opportunities for the ASC to contribute to improvements in the process for licensing for applications not meeting the referral criteria in 5.1 above.

6.0 Information gathering

- 6.1 A review was undertaken of the characteristics of and outcome from the considerations given by the Animal Procedures Committee (APC), the predecessor of the ASC, and the PLA to the last 20 primate neuroscience applications which had been referred to it. Sixteen characteristics of interest were identified (listed in Appendix 3), including the recommendations of the APC and the PLA. The ASC secretariat then extracted those characteristics from each application, and LRR members reviewed these data and reached a judgement (individually) about (a) whether the recommendations of the APC and the PLA had identified major, moderate, minor or no issues of concern; and (b) whether these issues of concern might have been identified in advance given more detailed guidance to applicants and the inspectorate, obviating the need for a PLA meeting. To give summary estimates of the input judged to have been made by the APC and the PLA we took the median of the importance attributed to the issues raised.
- 6.2 A semi-structured telephone interview was conducted with nine members of the ASC to seek their views on the appropriateness of, and amendments required, to the current licence referral process, the PLA meetings and the follow up to the meetings.
- 6.3 Discussion with ASRU Inspectors both informally at an ASRU meeting held in September 2015 and formally through their attendance at a meeting of the LRR on 21 July 2016.

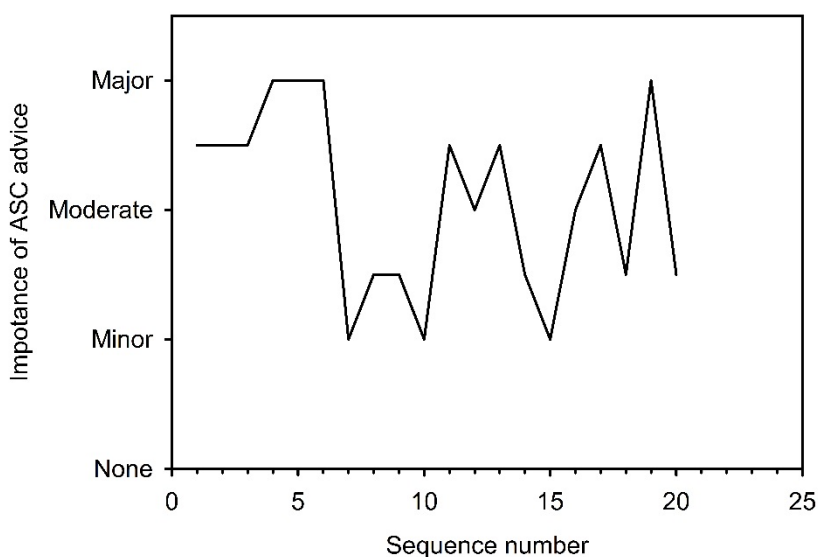
7.0 Findings

7.1 Of the 20 licences considered by the PLA the impact of their discussions was judged to range from minor to major (Table 1). The LRR noted that the PLA provides important advice and appears to provide good value.

Table 1

Impact	n (%)
Minor	3 (15%)
Minor to moderate	5 (25%)
Moderate	2 (10%)
Moderate to Major	6 (30%)
Major	4 (20%)

7.2 The LRR considered whether there was any change in this over time:



7.3 It appears that while there was some learning on the part of those advising on preparing licences for submission after the first five applications had been considered (manifest in fewer issues raised by the PLA), there were still applications being considered in the very recent past for which major issues were identified. Importantly, there was substantial heterogeneity in the issues raised by the PLA and the LRR did not consider that it would have been possible to create a scheme where these issues could have been identified in advance. LRR specifically reviewed each of the applications where the advice given was categorised as minor to determine whether the PLA made important recommendations, and came to the view that this was the

case. However, the LRR did agree that some of these issues might have been identified in a paper exercise, without the need for a face to face meeting.

7.4 Finally, LRR did not identify any trends in the severity of procedures in terms of for instance time spent in the primate chair or extent of fluid deprivation that might give cause for either concern or reassurance – within the limits of the information available the procedures applied for appeared to be constant over time.

Recommendation 1: That it is not possible to identify a subset of applications where general “standing” advice might obviate the need for Application subcommittee review.

Recommendation 2a: That ASC should explore the development of a secure online facility to allow ASC members to comment on applications prior to the PLA meeting. In this system, individuals should provide comments blinded to the comments of others, and nil returns – where the respondent has no comments – should be also be recorded. Subject to this facility being implemented, if no issues were raised during that period, an application might be recommended for approval without a face to face meeting of the PLA.

Recommendation 2b: That a decision to proceed without a face-to-face meeting could not be taken if any objection to this was raised by any member of the ASC. A face-to-face meeting would also take place at the request of the Chair, applicant or the Inspector assigned to the project licence application.

Recommendation 2c: That this procedure should occur alongside the current raising of issues for discussion in the PLA meeting.

7.5 We did not consider that introducing further iterations between the applicant and the ASC membership as part of this process would be possible given the time restrictions on the license approval process.

8.0 Results of the interviews with ASC members

8.1 Key issues raised by ASC members were discussed by the LRR during the meeting held of 21 July 2016. The LRR agreed that:

- all ASC members should continue to have sight of applications sent to it for review – not just the PLA
- in addition to forwarding questions related to the application, those members of the ASC who wish to attend an application meeting should be allowed to do so;
- the ASC Chair may wish specifically to invite a member of the ASC to the application meeting where they have expertise specific to a proposal being considered;
- membership of the PLA ought to be agreed by the wider ASC and reviewed in light of the current ASC recruitment round;
- the ASC Chair should remain the PLA Chair;
- inspectors should continue to observe the PLA meetings;
- terms of reference for the PLA should be developed (Appendix 4);
- quorum principles should be agreed.

8.2 These matters should be discussed at the next ASC meeting.

Recommendation 3a: ASC members wishing to attend PLA meetings should be allowed to do so.

Recommendation 3b: membership of the PLA should be reviewed and agreed by the wider ASC.

Recommendation 3c: Terms of reference and quorum principles should be developed

Recommendation 3d: The Chair of the PLA should ensure that relevant expertise is represented at sub-committee meetings.

Recommendation 3e: That in the event of the absence of a majority view concerning a project licence application, this would be indicated to the Minister in the letter containing the Committee's recommendations.

9.0 Other issues

9.1 Licences which are not referred to the PLA: the LRR considered whether the ASC might make a contribution to the consideration of other licences. In discussion with the Inspectorate it became clear that there were occasional situations where for instance the introduction of new research tools raised issues of a general rather than a specific nature, where the individual licence applications did not meet the threshold for referral under the terms of the Guidance to the Act outlined above. The LRR agreed that a process to allow this to occur might be helpful.

Recommendation 4a: That the Inspectorate should be invited to request advice (formal or informal) from the PLA in relation to general emerging issues in the licencing process

9.2 Further, the LRR was concerned that, because of the nature of the referral system, the applications which they saw were not at all typical; and that general (rather than specific) advice on applications not meeting the threshold for referral might be helpful as the Inspectorate sought to continue to function at the highest level. LRR agreed that this might be helpful, but were concerned to emphasise that this process was not intended to raise specific issues relating to specific licences which might call into question a licencing decision already made.

Recommendation 4b: That the PLA should from time to time review a selection of licences awarded in a given area, and make any general observations which they consider appropriate.

Appendix 1: Membership

Licence Referral Review subgroup

Professor Malcolm Macleod – Chair

Dr Gilly Stoddart – Deputy Chair

Dr Sophie Dix

Dr Huw Golledge – Full Member from commencement. Co-opted as of May 2016

Professor Sarah Wolfensohn

Professor Gavin Woodhall – Full Member from commencement. Co-opted as of May 2016

Appendix 2: Meetings

2015

26 October - ASC Main Meeting

31 November – License Referral Review Teleconference

01 December – ASC Subgroup Chair's Teleconference

2016

25 January – ASC Main Meeting

22 February – ASC Agenda Setting Meeting

05 May – ASC Main Meeting

15 June – License Referral Review Teleconference

21 July – License Referral Review Meeting

Appendix 3: Project licence characteristics considered during the review

1) Title
Disease Model/Biological Process being studied
2) HBA
HBA Assessment by ASRU
List of harms stated by Applicant
3) Procedures for each protocol
Duration of Experiment
Days of Experiment (per week)
Total duration of experiment
Fluid restriction
Food restriction
Head post fixation used?
Head post fixation duration
Is a Primate chair used
Training method for habituating the animal to primate chair
Details of humane endpoints
Screening for suitability for use in awake-behaving experiments
Is there provision for re-use
Stated maximum number of operations on animals
4) Statistics
What information has been included on statistics
5) 3R's
Improvements in 3R's compared with previous licensed work
Is there consideration of <i>in vitro</i> and <i>in silico</i> methods
<i>Evidence of continuing programme of refinement</i>
6) Species Choice
Justification of species selection
Does the licence involve analogous severe procedures on another species (non primate)
7) Severity
Has the band been changed following discussion with Inspectorate
8) Retrospective Review
Details of retrospective severity assessment requirements on the licence
Attempts to assess lifetime experience
Attempts to assess cumulative severity
Proposal to collect potential welfare-related metrics

<u>9) Applicants Track Record</u>
How much published work?
<u>10) Multiple Licences/Evolution of Licences</u>
Refinements/Replacements from previous licence
experimental methodology progression
Is the harm per animal decreasing
<u>11) Translational Benefit</u>
What were the stated purposes of the work
<u>12) Funding & Peer Review</u>
Does the application reference funding as a justification for approval
Does the application reference peer review as a justification for approval
Does the application reference review by NC3R's (or equivalent) as a justification for approval
<u>13) Administrative Issues</u>
Date of first contact
Date of receipt of complete application
Date of ASC referral
Date of decision notification
Key issues raised by Inspectorate prior to submission of completed application
<u>14) Other Salient Issues</u>
Summary
<u>15) Issues Beyond Specific Licence Being Reviewed</u>
Request retrospective assessment of actual severity on the licence that is being replaced
Request evidence behind the above assessment
Were there any infringements/potential infringements on licence post approval
<u>16) ASC/APC Advice</u>
Details on Recommendation Letter sent to ASRU e.g.:

Appendix 4: Developed Terms of Reference for the PLA in response to this review

Home Office Animals in Science Committee (ASC)

Project Licence Application (PLA) Subgroup

Terms of Reference

1.0 Purpose

- 1.1 To provide timely and independent scientific scrutiny of project license applications referred to it by the Home Office's Animals in Science Regulation Unit (ASRU).

2.0 Governance

- 2.1 The PLA subgroup is a standing subgroup of the ASC and is chaired by the ASC Chair, or their nominated deputy. All members of the ASC are privy to the applications under review and are able to set questions to seek clarification from the applicant around technical or ethical issues. Technical issues might include further details of the procedures proposed, and ethical issues might include further discussion of ethical arguments made. The PLA subgroup acts under delegated authority on behalf of the ASC in the decision-making process. The outcomes of reviews and any recommendations made are reported to the ASC at its quarterly meetings.

3.0 Licences Referred for Review

- 3.1 Under the Animals (Scientific Procedures) Act 1986 [A(SP)A] (section 9(1)), the Secretary of State will refer certain project licence applications to the ASC for advice, as appropriate, on applications involving:
 - the use of wild-caught non-human primates;
 - the use of cats, dogs, equidae or non-human primates in severe procedures;
 - use of endangered species;
 - projects with major animal welfare or ethical implications;
 - projects involving the use of admixed embryos as advised in the 'Guidance on the use of Human Material in Animals'²;
 - projects which may invoke any of the 'safeguard clauses' in the Directive 2010/63 with respect to the purpose of primate use, proposals for the use of a great ape, or proposals to cause long-lasting pain, suffering or distress that cannot be ameliorated;
 - projects of any kind raising novel or contentious issues, or giving rise to serious societal concerns.
- 3.2 In addition the Inspectorate can request advice (formal or informal) from the PLA subgroup in relation to general emerging issues in the licensing process. Emerging issues will also be discussed with the whole ASC as necessary.

² <https://www.gov.uk/government/publications/guidance-on-the-use-of-human-material-in-animals>

3.3 The PLA subgroup can also review a selection of licences already awarded in a specific research area and/or a random selection of licences awarded within a certain timeframe, to provide context for their considerations of licences under 3.1 or to make any general observations which they consider appropriate. These activities may be delegated to the Licence Analysis (LA) Task and Finish group by agreement between the Chair of the PLA subgroup and the Chair of the LA Task and Finish group.

4.0 Membership

4.1 The PLA subgroup is chaired by the Chair of the ASC with membership (specialist and lay) drawn from the ASC.

4.2 Usually, the standing membership of the PLA subgroup will be at least 5 members of the ASC of which at least two shall be lay members.

4.3 The membership of the subgroup will be reviewed by the Chair and secretariat and supplemented if necessary depending on the availability of the members, additional expertise required, and where conflicts of interest prevent participation of a standing member.

4.4 Members of the ASC, that are not standing members of the PLA subgroup, shall attend PLA subgroup panels if they wish to do so.

5.0 Duration

5.1 The PLA subgroup is an ASC standing group. Meetings are convened as appropriate to ensure the expeditious review of applications within the legal timeframe of 55 days following the submission to ASRU of a 'correct and complete' application.

6.0 Meetings and working methods

6.1 All licence applications to be considered by the subgroup will be circulated to the full ASC membership prior to the subgroup meeting to allow for any issues of concern to be raised.

6.2 Concerns raised by ASC members will be compiled by the secretariat and sent to the applicant to enable them to prepare responses prior to attending the PLA subgroup meeting. Where a large number of concerns have been raised it is the responsibility of the subgroup Chair to prioritise these.

6.3 The quorum for meetings of the PLA subgroup shall be four persons, with at least two lay members and two non-lay members, including the Chair. In this context, the term 'lay' is defined as members of the Committee who are not directly involved in research using animals.

6.4 In addition to PLA subgroup members, the assigned Inspector from ASRU, and other ASRU representatives as necessary, may attend the projects licence application panel meeting to provide relevant information as requested by the Chair of the PLA subgroup.

- 6.5 The Project Licence Applicant will be provided with the opportunity to present to the PLA subgroup prior to discussion of the concerns raised. Following the discussion the PLA subgroup will reach an agreement as to whether they will recommend that the project licence should be granted, granted subject to amendments or rejected. In licences considered under 3.2 and 3.3 above, attendance of the Project Licence Applicant will not be required unless specifically invited.
- 6.6 Decisions on licence applications will be considered and recommended by the panel attendees and the Secretary of State will be informed of the range of views provided. Any abstentions from the agreement of the subgroup will also be indicated to the Minister in the letter containing the PLA subgroup's recommendations.

7.0 Confidentiality

- 7.1. PLA subgroup members will not misuse information gained in the course of their public service for personal gain or for political purpose, nor must they disclose any information which is confidential in nature or which is provided in confidence without authority. This duty continues to apply after any member has left the Committee.
- 7.2. Protecting health and safety is a particular concern for people and establishments involved in animal research and confidentiality remains obligatory for people or place names. The Government also reaffirms its legal responsibility towards safeguarding confidentiality of information that constitutes intellectual property, whilst supporting a more open and transparent environment surrounding the use of animals in scientific research and increasing public understanding of the use of animals where no alternative exists. A(SP)A clause (section 24) imposes a very broad duty of confidentiality on everyone working under the Act. Section 24 denotes that the Home Office cannot release any information received in confidence under ASPA, even when the provider has no objection to its disclosure. This also applies to ASC members and particularly in respect of matters relating to licences and applications for licences.

8.0 Secretariat

- 8.1 The Secretariat will coordinate availability, forward licence applications, arrange meetings as required and collate comments/ issues.
- 8.2 Recommendations made by the subgroup will be drafted by the Secretariat, reviewed by the subgroup and ratified by the Chair before being forwarded to ASRU's Head of Compliance. It is the responsibility of the Head of Compliance to seek agreement from the Secretary of State and to ensure that a process is implemented to ensure appropriate and timely feedback to the ASC. It would be unusual for this feedback to be delayed beyond the time the Project Licence Applicant received a final decision on their application.

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Date of ASC sign-off [insert date of ASC sign-off in the format day/month/year]

Document control				
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1.0	Draft prepared by PLA subgroup	PLA subgroup	M Macleod	26/07/17
2.0	Revised draft prepared by secretariat for ratification by PLA subgroup Chair and Deputy Chair	B Mavromatis and K Homer	J Wallace	08/09/17