



Strengthening the peer review of in vivo research proposals

Supporting the 3Rs and better reproducibility

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- MRC is a major UK funder of animal research (around 1/3 of all MRC funded projects involve animal use)
- Guidance¹⁾ has existed for some time about information applicants needed to provide to justify animal use – but is often ignored!
- Increasing awareness of the challenge of reproducibility of research findings, especially in animal research

¹⁾ <http://www.mrc.ac.uk/documents/pdf/guidance-for-applicants-and-award-holders/>

MRC experience

- Issues about inadequate information in in-vivo proposals previously identified – especially experimental design and justification of numbers
- Addressed on a piece meal basis by Boards e.g. Conditional awards & general feedback
- MRC funding *may* influence AWERB and Home Office reviews of licence applications – so our assessment must be robust
- Working group to look at adequacy of applications and MRC guidance formed in July 2012

Cross-Board Appraisal Exercise

- Rapid, simple appraisal of all (post-triage) applications to all 4 Boards in autumn 2012
- Checklist for each application involving animals on:
 - Is the need to use animals justified?
 - Is the choice of species/model justified?
 - Is the experimental approach and rationale clear?
 - Is the choice of sample size justified?
 - Are the planned statistical analyses clear?
 - Are there any plans to reduce experimental bias?
 - Is this an example of a particularly strong/poor justification?

Appraisal results

(68 applications with completed pro formas)

Generally well justified:

- Need to use animals
- Model chosen
- Experimental rationale and planned design

Generally poorly described/justified:

- Choice of sample size (clear in just over 50% [64% awarded])
- Proposed statistical analyses (clear in 36%)
- Plans to minimise experimental bias (clear in only 11%)

Updated Guidance

- Guidelines¹⁾ updated in light of findings, to clearly define expectations of the type and level of information proposals should include
- New section on 'Statistical Considerations'
- Guidance on where information should be provided within a proposal
- Proposal form questions updated
- Non-prescriptive, covers range of experimental types

1) <http://www.mrc.ac.uk/documents/pdf/guidance-for-applicants-and-award-holders/>

Examples of issues to be addressed regarding experimental design

- the **avoidance of bias** (for example blinding of observers);
- how **randomisation** will be carried out (if used) or why it is not appropriate if it will not be used;
- a clear **definition of the experimental unit** in the analysis and the implications thereof;
- a principled justification of the **adequacy of the numbers of animals** to be included so as to be able to minimise the likelihood of spurious results due to the play of chance alone;
- the **number of different time points** at which measurements will be made on each animal;
- a description of the **statistical analysis methods** that will be used, explaining how they relate to the experimental design
- an indication of the number of **independent replications** of each experiment to be performed with the objective of minimising the likelihood of spurious nonreplicable results.

Key points

- New guidance explicitly covers avoidance of bias – not just adequacy of sample size
- New guidance may lead to more expensive applications and sometimes bigger numbers per experiment – this is understood by funders
- Researchers should design studies that maximise chance of a reproducible and valid result
- New guidance is aimed at increasing validity and reproducibility of what is funded
- **Our policy is not all about reducing numbers *per se*.** Poorly designed or inadequately powered studies are unethical.