



## 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)
- Guidance<sup>1)</sup> 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

<sup>1) &</sup>lt;a href="http://www.mrc.ac.uk/documents/pdf/guidance-for-applicants-and-award-holders/">http://www.mrc.ac.uk/documents/pdf/guidance-for-applicants-and-award-holders/</a>

## **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**

- Guidelines<sup>1)</sup> 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

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# 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.