### The ARRIVE Guidelines Checklist

| Item No | Item  | RECOMMENDATION | Reported on Page Number/Line Number | Reported on Section/Paragraph |
|---------|-------|----------------|------------------------------------|-----------------------------|
| 1       | Title | Provide as accurate and concise a description of the content of the article as possible. | Page 1 line 1–3 | Title |
| 2       | Abstract | Provide an accurate summary of the background, research objectives, including details of the species or strain of animal used, key methods, principal findings and conclusions of the study. | Page 2 line 32–55 | Abstract |
| 3       | Background | a. Include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale.  
       |       | b. Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study’s relevance to human biology. | Page 2 line 63–66  
Page 3 line 67–99  
Page 4 line 100–110 | Introduction Paragraph 1–2 |
| 4       | Objectives | Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested. | Page 4 line 111–119 | Paragraph 2 |
| 5       | Ethical statement | Indicate the nature of the ethical review permissions, relevant licences (e.g. Animal [Scientific Procedures] Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research. | Page 4 line 130–132 | Method paragraph 4 |
| 6       | Study design | For each experiment, give brief details of the study design including:  
a. The number of experimental and control groups.  
b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when).  
c. The experimental unit (e.g. a single animal, group or cage of animals). A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out. | Page 5 line 139–143  
Page 5 line 155–165 | Method Paragraph 5  
Paragraph 7 |
| 7       | Experimental procedures | For each experiment and each experimental group, including controls, provide precise details of all procedures carried out. For example:  
a. How (e.g. drug formulation and dose, site and route of administration, anaesthesia and analgesia used [including monitoring], surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including supplier(s).  
b. When (e.g. time of day).  
c. Where (e.g. home cage, laboratory, water maze).  
d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used). | Page 5 line 139–165 | Method Paragraph 5–7 |
| Section | Page | Method | Paragraph |
|---------|------|--------|-----------|
| Experimental animals | Page 4 line 112-117 | Method Paragraph 4 |
| Housing and husbandry | Page 5 line 133-137 | Method Paragraph 4 |
| Sample size | Page 5 line 155-165 | Method Paragraph 7 |
| Allocating animals to experimental groups | NA | NA |
| Experimental outcomes | NA | NA |
| Statistical methods | Page 5 line 167-180 | Method Paragraph 8-9 |
| RESULTS | | | |
| Baseline data | NA | NA |
| Numbers analysed | Page 6 line 182-198 Page 7 line 199-220 | Result Paragraph 10-11 |
| Outcomes and estimation | Page 7 line 222-231 Page 8 line 232-245 | Result Paragraph 12-13 |
| Adverse events | NA | NA |
DISCUSSION

Interpretation/scientific implications

| Page | Paragraph |
|------|-----------|
| page 8 247-264 | Discussion 14-18 |
| Page 9 265-297 |  |
| Page 10 298-329 |  |
| Page 11 331-335 |  |

- Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature.
- Comment on the study limitations including any potential sources of bias, any limitations of the animal model, and the imprecision associated with the results. 
- Describe any implications of your experimental methods or findings for the replacement, refinement or reduction (the 3Rs) of the use of animals in research.

Generalisability/translation

| Page | Paragraph |
|------|-----------|
| Page 10 338-347 | 19 |

Comment on whether, and how, the findings of this study are likely to translate to other species or systems, including any relevance to human biology.

Funding

| Page | Acknowledgements |
|------|------------------|
| Page 10 351-356 |  |

List all funding sources (including grant number) and the role of the funder(s) in the study.

References:

1. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. PLoS Biol 8(6): e1000412. doi:10.1371/journal.pbio.1000412

2. Schulz KF, Altman DG, Moher D, the CONSORT Group (2010) CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ 340:c332.

From:
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References:

1. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. PLoS Biol 8(6): e1000412. doi:10.1371/journal.pbio.1000412

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*As the checklist was provided upon initial submission, the page number/line number reported may be changed due to copyediting and may not be referable in the published version. In this case, the section/paragraph may be used as an alternative reference.