Not All Mice Are the Same: Standardization of Animal Research Data Presentation

As the editors of several journals, we have joined forces to highlight the importance of providing essential details related to animal experiments, particularly for studies that include mouse work. This is a critical issue that partially underlies the problem of irreproducible results that is attracting international attention[1] as well as the attention of funding agencies such as the National Institutes of Health.[2] For mouse studies, this can be a daunting problem given that many manuscripts do not provide sufficient details regarding the number of animals used for a given experiment, the sex of the animals, their age, and in some cases identification of the background genetic strains. Other variables that can also play an important role in shaping experimental findings and conclusions are the microbiome,[3] making co-housing of control and genetically altered animals essential, diet, and even the composition of animal bedding.[4]

Several journals have supported the ARRIVE (Animal Research: Reporting of In Vivo Experiments) Guidelines that were originally proposed in 2010,[5] which include an extensive checklist of information related to animal experiments that is considered essential to provide. However, it seems that the reporting standards may not have improved very much since initial presentation and acceptance of the guidelines by multiple journals.[6] Several reasons may account for the observed 'noncompliance' with the ARRIVE guidelines,[6] including difficulty ensuring that reviewers and editors carefully assess whether the guidelines have been followed, and the possibility that some authors may indicate that the guidelines have been followed (based on author interpretation and not because of any malintent) when in reality not all components have been pursued. Reviewers and editors frequently ask authors to expand on some of these necessary details, but the reviewers often focus on separate important issues while the specifics that are related to the mouse work may be overlooked. Another barrier might be the extensive nature of the ARRIVE checklist, which may not apply fully to many submitted manuscripts. This is relevant, because scientists (and physicians) are now facing an increasing barrage of regulatory documentation paperwork that is limiting their time for scientific investigation (or for their patients). Notwithstanding this limitation, we are uniting from different journals to highlight the importance of documenting what we consider to be the minimum list of information to improve transparency and the quality of data reporting. Our purpose is not to legislate a "one size fits all" philosophy, but rather to maximize the possibility of other researchers reproducing study findings from the same wild-type or mutant mouse strains. Our respective journals will be highlighting the criteria listed below in our Instructions to Authors, and some of our journals will also introduce an author-friendly checklist that will need to accompany manuscripts that use mice and other in vivo experimental models.

The criteria that will be expected of authors include the following information (Figure 1):

- Sex and age of mice (or other in vivo experimental models) for all the experiments;
- The genetic background(s) of the mice or other experimental in vivo models;
- For transgenic or genetic mouse models, whether the controls were sibling littermates or were purchased separately (if purchased separately, were the animals cohoused to minimize potential microbiome effects);
- Specifics of the animal diet composition;
- Whether mice were fasted (and for how long) or not before a challenge or assessment is carried out;
- Type of bedding, caging system, and enrichment used for housing the mice; and
- If interventions were done, were they done during the light or dark cycle.

Power analyses can be useful to estimate appropriate sample sizes; however, the standard deviations for relevant dependent variables are often not known a priori. Therefore, it is critical that the number of animals for each experimental arm or condition is reported together with biological replication of statistically significant results derived from independent groups of animals.

There are also other variables that may need to be considered that we have not included as primary expectations, particularly those related to behavior, stress, and growth conditions. These variables include acclimation to a new environment (eg, when animals are shipped by the vendor or moved from the animal facility to a procedure room), other environment effects (eg, temperature, humidity, noise), littermate size, and pheromone effects. These additional variables can be very important depending on the biologic readout. Moreover, environment effects, such as avoidance of large temperature changes unless approved as part of an animal protocol, are expected to be part of the normal procedures of humane treatment of animals.

What can journals and research institutions do moving forward toward a path to implementation?[7] Certainly all stakeholders need to be engaged and many funding agencies now expect that applicants pay closer attention to this important issue, as exemplified by the recent requirement from the National Institutes of Health to include a section titled *Authentication of Key Biological and/or Chemical Resources* in grant applications.[8] For journals, setting and enforcing clear expectations to authors, reviewers, and editors will be essential, because a checklist alone will not be sufficient, while making the process as user-friendly as possible. For institutions, several approaches can be considered and implemented, that are aimed at investigators and trainees. For example, the curricula for students who are enrolled in bioscience-related undergraduate and graduate programs should include training not only in the ethics in conducting research, but also in the basic tenets of conducting and designing animal experiments. It is important for this to start early and to be reinforced as training advances. Similarly, postdoctoral fellows in biomedical disciplines should be expected to enroll in similar workshops that would be offered by their home institutions. For such workshops, centralized (rather than department- or unit-specific) oversight and administration will more likely ensure uniformity and implementation. We look forward to working together on this important effort and to receiving feedback from our authors, reviewers and readers.

M. BISHR OMARY Gastroenterology
DAVID E. COHEN Hepatology
EMAD M. EL-OMAR Gut
RAJIV JALAN Journal of Hepatology
MALCOLM J. LOW Gastroenterology
MICHAEL H. NATHANSON Hepatology
RICHARD M. PEEK JR. Gastroenterology
JERROLD R. TURNER Cellular and Molecular Gastroenterology and Hepatology

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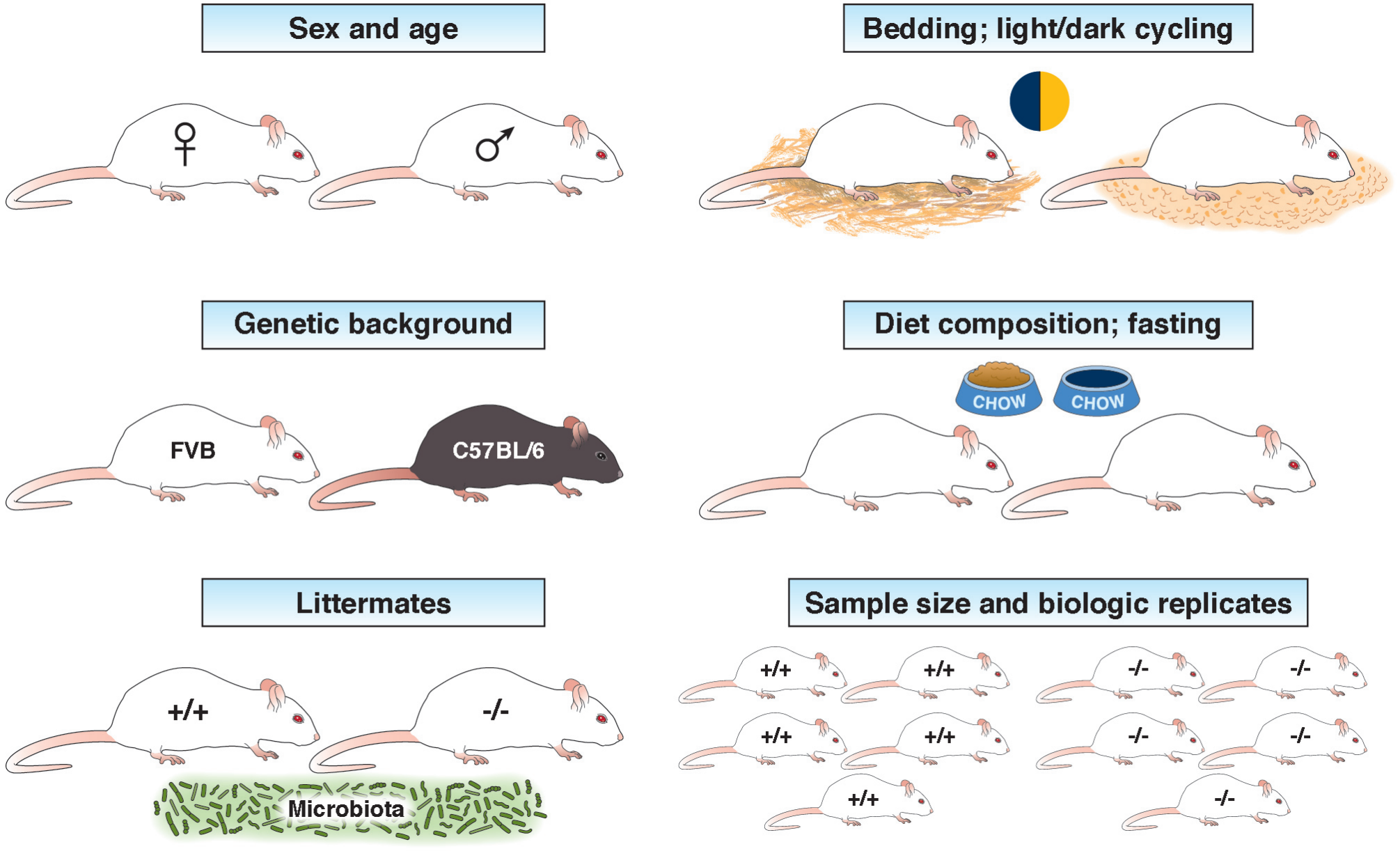
Acknowledgments
The authors thank the managing editors of our journals for helping facilitate the joint publication of this commentary. All authors contributed equally to this effort.

This commentary is being jointly published by *Cellular and Molecular Gastroenterology and Hepatology, Gastroenterology, Gut, Hepatology, and Journal of Hepatology*.

Conflicts of Interest
The authors disclose no conflicts.

Figure 1.Key elements to consider and highlight for mouse related studies. The schematic shows several important criteria that need to be considered when planning mouse (and other animal) experiments, and when submitting work for publication. FVB and C57BL/6 represent, as examples, commonly used mouse strains. Of note, vendor sources can also be important (eg, FVB/NJ from The Jackson Laboratory vs FVB/NTac from Taconic). Other considerations not displayed in the schematic, such as environment conditions, are highlighted in the text. +/+, wild-type littermate mice; -/-, knockout littermate mice.


Sex and age
♀
♂
Bedding; light/dark cycling
Genetic background
FVB
C57BL/6
Diet composition; fasting
CHOW
CHOW
Littermates
+/+
-/-
Microbiota
Sample size and biologic replicates
+/+
+/+
+/+
+/+
+/+
-/-
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