ACS Chemical Neuroscience

Editorial

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Elevating Standards for Discoveries Reported in *ACS Chemical Neuroscience*: New Criteria to Enhance Reproducibility, Experimental Transparency, Reliability, and the Value of Negative Data

Beginning in mid-2015, *ACS Chemical Neuroscience* will adopt and require researchers to follow new NIH guidelines pertaining to transparency, reliability, and reproducibility in preclinical research published in the journal.[1,2] The new guidelines will pertain to both *in vitro* and *in vivo* studies as well as chemical characterization of novel small molecules; all of these new guidelines are set forth to enable reported studies to be reproduced accurately and reliably.[1,2] Why is *ACS Chemical Neuroscience* and the broader scientific community, including every major publisher, modifying long-standing criteria for data reporting? There has been growing concern across industry and academia regarding a general inability to reproduce published data. A study published in *Nature Reviews Drug Discovery* in 2011, illustrated that the pharmaceutical industry cannot rely on published translational data related to drug targets.[3,4] Primarily from academic laboratories, they found that 65% of the published data was inconsistent and only 14% of published literature data could be repeated in-house.[3,4] These and other similar studies[5] initiated efforts within NIH to increase rigor, enhance reliability, and diminish bias in translational drug discovery and development research by NIH funded investigators.[1−5] The National Institute of Neurological Disorders and Stroke (NINDS) led the charge within NIH, establishing guidelines for funded researchers to improve the quality of their preclinical data by providing greater experimental details in the design, execution, and interpretation of studies.[1,2] In 2014, Francis Collins and other NIH staff have issued multiple commentaries and policy updates to restore "the self-correcting nature of preclinical research" and more recently to balance gender in cell and animal studies to avoid reliance on male-only models.[6] In essence, these guidelines aim to optimize the predictive value of preclinical research translating to heterogeneous populations. Clearly, elevating our standards requires a partnership between funding agencies, investigators, editors, and reviewers; in fact, this significantly increases the burden on editors and reviewers to ensure revised standards are met. Fortunately, *ACS Chemical Neuroscience* has never placed limitations on the Methods section of a manuscript or the contents of Supporting Information. We welcome your data, rationale, and interpretations!

What data should be included in order to be aligned with new reporting criteria? For *in vitro* studies, full descriptions of the assays, cell lines, and where key reagents were purchased and in what grade need to be included. When possible, commentary should be made regarding receptor reserve and protein expression levels of cell lines, so that other researchers can reproduce experimental conditions. All *in vitro* potency/efficacy data should be reported from an average of three independent experiments (n = 3) and reported with standard error measurement (i.e., EC_{50} = 130 nM, pEC_{50} = 6.90 ± 0.11). The Supporting Information (SI) should also contain the raw data and a supporting figure containing concentration−response-curves (CRCs) with error bars. Other types of cell based, *in vitro* assays should also display appropriate statistics with full explanation of the number of replicates for the data presented. Within the text, the statistical method should be discussed as well as a detailed explanation if any outliers where removed from the composite data presented. The same is true regarding Western blots and other basic biochemical and molecular pharmacology studies. When a manuscript describes novel molecules, we have always required full experimental details and tabular NMR data. In order to be aligned with NIH, we will require copies of NMR spectra, for any key compounds, be included in the SI, similar to the procedure at ACS organic chemistry journals. Moreover, overt statements need to be made regarding the purity and potency confirmation of scaled-up compound lots employed in *in vivo* animal studies.

The largest changes will center on preclinical *in vivo* studies, where authors will need to provide detailed information on species and strain, vendor and vendor location, sex (must be balance of males and females), and age. Moreover, per NIH guidelines,[1−5] the manuscript should discuss the rationale for the models employed and end points selected, as well as any exclusion criteria utilized (and how excluding outliers impacted significance/statistics). Studies must also include relevant positive/negative controls and adequate sample size to power the statistics. As with *in vitro* work, details of the statistics methods used must be well described. When pharmacological studies are performed *in vivo*, rationale for dose, route, and timing for dosing must be provided. While not required, rudimentary pharmacokinetic/pharmacodynamics (PK/PD) is also beneficial and powers the study, especially for CNS PD studies, CNS exposure for doses employed should be provided (satellite animal data is acceptable). Data interpretation is another major concern. Authors should comment on their approach for randomization and/or blinding as well as exclusion criteria. Most importantly, studies performed and reported as outlined above will empower negative results to impact the biomedical community. Authors should report both positive and negative results from well powered and well-controlled studies. While a manuscript of all negative data would not seem prudent, in the case of knockout (KO) animals, for example, characterizing KO phenotype with negative data is acceptable and has the potential for broad impact.

This editorial contains a great deal of new guidelines in a "mile high" overview format. I cited all the relevant NIH sites and references detailing the new guidelines set forth to enhance transparency, reliability, and reproducibility in preclinical research for those funded by NIH. Clearly, these come at a trying time for biomedical and translational scientists struggling to balance grant support, innovation, and the "publish or

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perish" dogma so prevalent in academia, along with overriding concerns regarding journal impact factors. At *ACS Chemical Neuroscience*, we are very concerned about the reliability of the data we publish and are excited to align ourselves with the larger initiative put forth by NIH and accepted by almost every major publisher. We will provide monthly updates as we approach 2015, and we will also launch a revised version of the Instructions for Authors with additional details. While the changes are significant, we will benefit as a community, and science will advance more rapidly by adherence to these new guidelines.

Craig W. Lindsley, Editor-in-Chief

AUTHOR INFORMATION

Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

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