Improving the Quality of NINDS-Supported Preclinical and Clinical Research through Rigorous Study Design and Transparent Reporting

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to reduce the burden of neurological disease. In support of this mission, NINDS funds basic, translational, and clinical research. There is growing recognition that the quality and reproducibility of both preclinical and clinical research depend on the rigor with which researchers conduct studies, control for potential bias, and report essential methodological details. The clinical research community has developed principles to improve the design, implementation, review, and reporting of clinical trials by attention to these issues (see, for example, the CONSORT statement[1]). NINDS believes that the same fundamental principles should also apply to the *in vitro* and animal studies that form the foundation for such clinical research.

Rigor, control of bias, and transparency of reporting are important for all research, and can significantly affect the quality of studies that provide the basis for large-scale therapy development programs and ultimately for clinical trials. Several disease-focused groups have provided guidance for preclinical studies involving specific neurological diseases[2-4]. However, given the range of diseases within the NINDS mission and the breadth of methods used in discovery science, early translational research, and trial-enabling safety and efficacy studies, no single set of criteria can apply to all studies. Nevertheless, attention to principles of good study design and reporting transparency are essential to enable the scientific community to assess the quality of scientific findings and for peer reviewers to advise NINDS appropriately on funding decisions.

For this reason, NINDS believes that it is important for investigators to consider the following points in their study design and to address those that are appropriate when describing preliminary studies in support of their applications:

Experimental design:

- Rationale for the selected models and endpoints (animal and/or cellular)
- Adequacy of the controls
- Route & timing of intervention delivery / dosing
- Justification of sample size, including power calculation
- Statistical methods used in analysis and interpretation of results

Minimizing bias:

- Methods of blinding (allocation concealment and blinded assessment of outcome)
- Strategies for randomization and/or stratification
- Reporting of data missing due to attrition or exclusion
- Reporting of all results (negative and positive)

Results:

- Independent validation/replication, if available
- Robustness and reproducibility of the observed results
- Dose-response results
- Verification that interventional drug or biologic reached and engaged the target

Interpretation of results:

- Alternative interpretations of the experimental data
- Relevant literature in support or in disagreement with the results
- Discussion of effect size in relation to potential clinical impact
- Potential conflicts of interest

References*

1. CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomised Trials. PLoS Medicine Volume 7 Issue 3 e1000251.
2. Update of the Stroke Therapy Academic Industry Roundtable Preclinical Recommendations. *Stroke 2009, 40:2244-2250*.
3. Guidelines for Preclinical Animal Research in ALS/MND: A Consensus Meeting. *ALS 2010, 11:38-45*.
4. Accelerating Drug Discovery for Alzheimer's Disease: Best Practices for Preclinical Animal Studies. http://www.alzdiscovery.org/wp-content/uploads/2011/01/alzheimersbestpracticesguidelines.pdf.

* These are selected, illustrative examples. Additional references relating to other diseases/disorders can be found in the literature.