

Authentication of Key Biological Resources: A guide to the new NIH requirement

As part of its efforts to improve transparency and reproducibility the NIH now requires a one page statement regarding the “Authentication of Key Biological Resources.” Grants evaluated in early 2016 were required to include this section but it did not impact scoring. Reviewers were asked to identify which proposals did the most effective job at completing this section. Based on information gained from CHHE members who participated in these discussions some tips and suggestions are listed below. Importantly this section is for *established* resources. NIH specifically emphasizes that “For applications proposing to establish a new biological resource, such as a cell line, animal model, antibody or probe, the research activities to be conducted in pursuit of the resource development, including plans for validating the resource, should be described in the Research Strategy section of the application and will be subject to scoring.”

The most effective statements broke down the information by category beginning with a general one elaborating on broad themes. Here are some suggested sections:

General: Discuss or highlight any published guidelines to which the studies will adhere, how risk of bias will be handled, the degree to which the research team will be blinded to treatment groups, the level of experimental detail that will be included in published methods, the long term storage plan for experiments records/data, and if/how raw data files can be obtained. Here is an example sentence:

For the specialty chemicals that we propose to synthesize, we will structurally authenticate each using guidelines provided by the Society for XXX for new compounds (published in the Journal of XXX and in YYY).

Antibodies: This is a big issue, even for commercially available antibodies. You have to prove in this section that you can and will run all appropriate controls. If you can cite a regularly reviewed list of “validated” antibodies (such as the one maintained by the Journal of Comparative Neurology) that is helpful but insufficient on its own to be convincing. Explain how you will test new batches/lots and properly preserve existing stocks. Here is an example sentence:

The requirements and recommendations detailed in the seminal publication XXXX by XXXX and colleagues on antibody validation will be followed here [CITATION]. These efforts include....

Verification of Cell Lines: This is also a big issue. Convince the reviewers that you can unequivocally demonstrate that the cells you are working on are what you think they are (not contaminated with HeLa or anything else). Include information about how you will demonstrate purity and sex, keep track of passages, store all lines, and control for phenotypic and genomic changes over time. Simply saying you’ll adhere to ATCC guidelines is not enough. Be specific about what will be done and the type of environment the cells will be used/maintained in. Citations of prior or model work in this area salient to your proposal are a big help. For primary cells/cultures, those made in house do not need to be mentioned in this section but an authentication plan for those obtained from another laboratory should be provided. Also state what you’ll do if you find the cell line to be contaminated. As an example:

If testing reveals that any of the commercially obtained cell lines are misidentified, stocks will be discarded and any colleagues who have other stocks will be informed along with

the manufacturer. If any novel incidence of cross-contamination is discovered we will publish that finding to alert others in the scientific community. We will also notify XXX of journal XXX run by the Society of YYY for information dissemination and inclusion on their database of known contaminated lines.

Transgenic Animals: Explain how the successful generation of the line will be validated and cite any experience the lab has with these techniques (including the validation techniques). As an example:

As a first confirmation step, when floxing out GENE X or GENE Y from XX neurons in Aim II, we will do double label ISH for these receptors in XX neurons to show that GENE X or GENE Y mRNA is no longer expressed in XX neurons but is still expressed in other neurons (see Figure X in the proposal). Note that our lab routinely does these validation steps already with every transgenic mouse line we generate (e.g., CITATION)

Drugs/Chemicals: Discuss how purity of the compounds will be assured. This is particularly important for toxicants (and their metabolites), chemical standards and any chemicals synthesized for the study by an outside vendor (or collaborator). Validation of anything synthesized in house should be described in the main proposal. There was some confusion about what to do about pharmaceuticals. Verifying their “purity” should not fall upon the researcher. Stating where they would be obtained and stored, however, was considered important. Also explain how potential effects of lots/batches will be controlled for. An example of language with an appropriate level of detail for new chemicals:

Synthesized compounds will be stored neat or in stock solution batches at –20°C or –80°C as appropriate, and subjected only to a single freeze-thaw cycle. Quality assurance over time will be established by subjecting each batch of material to repeat HPLC, GC-MS, LC-MS, and 1H NMR prior to use and upon completion of use.

Other reagents/resources which may also warrant inclusion those for PCR, microarray, RNAseq, and histological staining. More information is available on the NIH Extramural News website at <https://nexus.od.nih.gov/all/2016/01/29/authentication-of-key-biological-andor-chemical-resources-in-nih-grant-applications/>