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Press Highlights

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NIH Aims to Increase Reproducibility in Preclinical Research

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Mounting evidence for the irreproducibility of a substantial number of biomedical research publications demands immediate and substantive action, say Francis S. Collins, director of the US National Institutes of Health (NIH), and Lawrence A. Tabak, the NIH's principal deputy director.

Francis Collins

In a Nature Comment article published January 27, the authors discuss interventions that the agency is exploring to restore the self-correcting nature of preclinical research, warning that "success will come only with the full engagement of the entire biomedical research enterprise". Collins and Tabak urge scientific publishers, universities, industry, and others to join them in taking the necessary steps.

"Preclinical research, especially work that uses animal models, seems to be the area that is currently most susceptible to reproducibility issues," say Collins and Tabak.

One report has suggested that "as many as two-thirds of studies related to preclinical animal trials were not able to be reproduced," Tabak told *MedPage Today*. "The truth is we don't really know what the full scope of the problem is," he added.

To address the situation, Collins and Tabak announced that the NIH will require its intramural postdoctoral fellows to receive training in responsible conduct of research. The authors are also considering a checklist for reviewers that ensures a more systematic evaluation of grant applications, and ways to anonymize the peer-review process, to reduce the effect of unconscious bias.

Other proposed changes include modification of the biographical sketch that grant applicants complete, to emphasize the significance of advances resulting from work in which the applicant participated, and to delineate the applicant's role in it.

The NIH is considering flexible or longer grants, to provide greater stability for investigators at certain career stages.

Collins and Tabak go on to request that journals provide more space for articles conducted in an exemplary manner, for that report negative findings, and for papers that correct earlier publications.

The authors explain that there is a growing chorus of concern, from scientists and laypeople, that the system to insure the integrity of biomedical research is failing and needs restructuring. They add that they have no evidence that irreproducibility is caused by scientific misconduct. In 2011, the Office of Research Integrity of the US Department of Health and Human Services pursued only 12 such cases. Collins and Tabak write that fraudulent papers are vastly outnumbered by the hundreds of thousands published each year in good faith.

Instead, they say, a complex array of factors contribute to lack of reproducibility. These include poor training of researchers in experimental design, increased emphasis on making provocative statements rather than presenting technical details, and publications that do not report basic elements of experimental design. The design elements that Collins and Tabak believe to be frequently ignored include blinding, randomization, replication, sample-size calculation and the effect of sex differences.

The problem is compounded by funding agencies that overvalue research published in high-profile journals, and academic centres that provide incentives for publications in such journals. Furthermore, there are few venues for researchers to publish negative data or papers that point out scientific flaws in previously published work.

On a positive note, Collins and Tabak state that human studies seem to be less at risk because they are governed by various regulations that stipulate rigorous design and independent oversight, including randomization, blinding, power estimates, pre-registration of outcome measures in standardized, public databases, and oversight by institutional review boards and data safety monitoring boards.

The authors feel that preclinical research—especially work that uses animal models— seems to be the area that is currently most susceptible to reproducibility issues.

In an attempt to provide greater transparency for data that are the basis of published manuscripts, the NIH has requested grant applications for development of a Data Discovery Index, which would allow investigators to locate and access unpublished, primary data. These grants will last for up to 3 years and will start to be awarded in September 2014.
Last December, the NIH launched an online forum called PubMed Commons, which allows authors and readers to share opinions and information about scientific publications. Authors can join and rate articles or contribute comments.