PROJECT TITLE: REPRODUCIBILITY AND REPLICATION ISSUES IN SCIENCE: QUANTITATIVE ANALYSES OF BIASES IN EPIDEMIOLOGY AND ITS ROLE IN RISK ASSESSMENT **Date:** 04/16/2018

Preliminary List of Participating Agencies

(developed based on outreach to IRAC membership)

Agency	Representative(s)
Food and Drug Administration, Center for Biologics Evaluation and Research (CBER)	Richard Forshee*, Yun Lu, Hussein Ezzeldin
Food and Drug Administration, Center for Food Safety and Applied Nutrition (CFSAN)	Michael Bazaco
Environmental Protection Agency, Office of Pesticide Programs (OPP)	David Miller*, Aaron Niman
U.S. Department of Agriculture, Food Safety and Inspection Service (FSIS)	Janell Kause, Berhanu Tameru
U.S. Department of Agriculture, Office of Pest Management Policy	Alex Domesle
U.S. Department of Agriculture, APHIS/PPQ	Sunil Kumar
U.S. Department of Agriculture, AMS/S&T/MPD	Shanker P. Reddy
Food and Drug Administration, Center for Veterinary Medicine	Craig Lewis
Food and Drug Administration, Office of Foods and Veterinary Medicine	Mike Batz

*Lead/leads identified

Background

There is increasing interest and concern in the scientific community on the "replication crisis" in science. Specifically, scientists are finding that the results from scientific experiments can be difficult to reliably replicate on subsequent investigations. Some have gone so far as to assert—and provide rational support for—that most published research findings are false (Ioannidis, 2005). Others have pointed out that even the more modest goal of reproducing previous research -- demonstrating that others can calculate the same results using the same data and methods -- is frequently difficult or impossible (ASA, 2017).

A number of theories have been advanced with respect to the reasons for this increased difficulty in replicating scientific results. These have included publication bias, increased pressures to publish, "vibrational" effects which come from the multitude of choices in the way data are analyzed, the prevalence of and emphasis in research on null hypothesis significance testing, and low power studies and the consequent "truth inflation" associated with significant effect sizes and any 'discovered effects'. Several researchers, directly or indirectly, have at least partially ascribed the current replication issues in science in general—and epidemiology in particular—to a combination of an emphasis in research on testing of novel hypotheses, on a lack of power in the studies that are done, and on an over-emphasis on the part of researchers and publishers on p-values and "achieving (statistical) significance". In addition, there tends to be an under-appreciation of the role and potential magnitude of biases, an over-reliance on the epidemiological mantra that non-differential misclassification leads to biases toward the null, and an under-recognition that confidence intervals around epidemiological effect size estimates rely on the unlikely probability that all errors are random and none are systematic. One consequence of this is that statistically significant epidemiological studies appearing in the literature can be over-interpreted and their estimated error bounds can be under-estimated.

To address these challenges, various analytic approaches and corresponding tools have been deployed (e.g., sensitivity analyses and quantitative bias analyses) and a more holistic weight-of-evidence approach has been taken that more fully considers the Bradford Hill criteria. Researchers have also been encouraged to improve the transparency of their work by providing their underlying data and analysis code, whenever possible. The relevance of this topic to IRAC is to further enhance the rigor of risk assessments and decision-making by increasing awareness of approaches that address issues of reproducibility, biases, and interpretation of the underlying science.

Proposal

The goal of this effort is to increase awareness of federal personnel involved in risk assessment risk management and risk communication of issues associated with interpretation of epidemiological effect size findings and their associated biases. This would also include enhancing the technical communication of the underlying science behind, rationale for, and implications of a more quantitative treatment of these biases. A second goal is to provide information and background on the potential of more recently available techniques and software to better and more quantitatively evaluate biases in these estimates and their direction.

Expected Outcomes

This IRAC Work Group will hold a 1.5-2 hour workshop planned for September 2018 at a central DC-area IRAC member agency location. The workshop will provide a forum to educate IRAC member agencies on the types of scientific biases in epidemiology relevant to risk assessment, why this is important to consider, and types of analyses and currently available tools to evaluate the impact of these biases. This first workshop presentation is intended to be a more general introduction to the topic that would be of interest to those involved in risk assessment generally. A second follow-on webinar-only presentation is anticipated to follow about one to two months later in which more detailed information would be presented that would be intended for those that are more heavily involved in this area and have a deeper interest. The Work Group will post a list of the scientific literature reviewed, workshop agenda, presentation, and summary on Foodrisk.org.

Work Format/Logistics

The Work Group members would communicate and interact regularly in FY2018, mostly by email and conference calls. Depending on the physical location and availability of work group members, regular or semi-regular in-person meetings in Washington, DC, may be desirable. The workshop will be held at an IRAC member-agency location in the Washington, DC-area.

Budgetary Requirements

No expenses are expected during FY 2018, with the exception of work group members' time and salary. The September 2018 IRAC workshop is part of on-going cross-agency information sharing among federal agencies and will be held locally and not require travel expenses.

References

Ioannidis, JP. 2005. "Why most published research findings are false". PLoS Medicine 2(8). E124.doi:10.1371.pmed.0020124. [accessed 9 February 2018 at http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0020124]

American Statistical Association. 2017. "Recommendations to Funding Agencies for Supporting Reproducible Research." [accessed 9 February 2018 at https://www.amstat.org/asa/files/pdfs/POL-ReproducibleResearchRecommendations.pdf]