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Ensuring Scientific Integrity: Guidelines for Managing Conflicts[1]

Summary

In the past decade or more there has been an important and ongoing public debate about the susceptibility of scientific research to biases of various kinds. This dialogue has been centered in the United States (US), Canada, and Europe, but is now increasingly escalating in other global regions and within international organizations. The discussion has extended to the peer-reviewed literature, scientific conferences, the mass media, government advisory bodies, and beyond. While biases can come from myriad sources, the overwhelming focus of the debate, to date, has been on industry-funded science. Given the critical role that industry has played and will continue to play in the research process, the International Life Sciences Institute North America (ILSI NA) Working Group on Guiding Principles, several years ago, set out proposed conflict-of-interest (COI) guidelines, regarding industry funding for protecting the integrity and credibility of the scientific record, particularly with respect to food, health, and nutrition science (Rowe 2009). Eight principles were enumerated, specifying ground rules for industry-sponsored research. The document was intended to be dynamic, prompting ongoing discussion and refinement and since its simultaneous publication in six scientific journals[1] the paper has been cited by more than 25 other articles. This present IUFoST Scientific Information Bulletin (SIB) is based on that original ILSI NA paper, "Funding food science and nutrition research: financial conflicts and scientific integrity." Although the issue of scientific integrity and the principles enumerated here clearly have global applicability, the context for their development was US-and-Canadian-focused. This SIB is consistent with and furthers the goals of IUFoST's "Ethical Guidelines on Professional Behaviour."

Introduction

A considerable and growing body of literature has evolved in recent times on the subject of conflicts of interest (COI) and their potential influence on the scientific record and the integrity of scientific research. In much of the literature, conflicts are treated as disqualifying factors in scientific papers and research; i.e., scientists with conflicts of interest are viewed as being at least partially integrity-compromised, and, even with complete and open disclosure, are regarded, at least to an extent, as of suspect scientific credibility. It is hoped that this paper will define and clarify the highly complex issues

[1] This article is based on the 2009 paper of the International Life Sciences Institute North America (ILSI NA) Working Group on Guiding Principles: Rowe S et al, "Funding Food Science and Nutrition Research: Financial Conflicts and Scientific Integrity," published simultaneously in early 2009 in six scientific journals, *Nutrition Reviews (Nutr Rev. 2009 May;67(5):264-72), American Journal of Clinical Nutrition, Journal of the American Dietetic Association, Journal of Nutrition, Nutrition Today, Food Science.*

involved in questions of conflict and scientific bias, particularly with regard to that portion of research funding originating with the food industry.

The focus here is confined to one very specific issue and its relationship to bias: financial conflicts of interest and, specifically, funding-based conflicts. As an aside, it must be pointed out that there is an inherent tendency for all funding, from whatever source, public or private, government or industry, to bias behavior, unconsciously or otherwise. The focus of the current article is on the management of potential bias from industry funding of science.

Why is There Industry Funding of Research?

The agricultural, food, and nutrition sciences have come to be a crucial part of evolving food, health, and nutrition research, which, in turn, plays an ever-growing role in improving the human condition. Yet, although regarded as important determinants of human health, agricultural practices, food processing and safety, and nutritional status do not receive the same attention and funding from the research agencies, globally, as do human diseases. For example in the United States, government funds allotted to agricultural, food, and nutrition research amount to approximately $2 billion annually (with most of this focusing on agricultural production) vs. the more than $30 billion appropriated to the US health agency, National Institutes of Health. (US NIH and US AAAS 2012). Internationally, the same disparity holds true: for example, while Sub-Saharan Africa received World Health Organization (WHO) disease funding of more than $3.6 billion in its 2012 budget (WHO 2012), only a third of that was allocated to agricultural research for the same general region (UK Government Office for Science 2011).

Industry-funded research projects, large and small, comprise a large proportion of all global food, health, and nutrition science research. The laws and regulations of many jurisdictions, including the US and the European Union, place on the manufacturer the responsibility for product safety and for the truthfulness of label claims. Most of this research falls outside of the mission of traditional government funding agencies and would simply not be undertaken if it were not for food industry support. Pursuant to an extensive web of laws and regulatory requirements concerning food and food ingredients that have evolved, especially in the western world over the past century, industry scientists and academic researchers who work with industry strive to enhance food quality, studying everything from the safety of ingredients to the evidence in support of health claims that appear on food packaging.

Historical Perspective

What follows is a short historical overview of industry participation in food and health research over the past several decades, during which lines separating public and private benefit have blurred.

From its beginning, the food industry has concerned itself with researching food products and ingredients from the perspective of safe and efficient delivery of food to a rapidly expanding population. Prior to World War II the overwhelming bulk of food research globally was funded and carried out by food industry scientists – there was little public funding of food safety and nutrition research. Of course, during the War, government involvement in the food sector was enormous among all combatants, not so much for nutrition research as for supply-related research. In the post-World War II period, with the development of proprietary technologies to enhance food preservation and safety, the

world continued to see a significant increase in the administrative challenges of research funding.

Especially in recent decades, the research community and those involved in health communications and public policy advocacy became increasingly concerned about the possibility that exogenous interests might influence published results of scientific research (Silverman 2002). By late 2000, this concern had become heightened around medical/pharmaceutical practice: a number of articles appeared in the major medical journals exploring the financial relationships of the pharmaceutical industry and physicians and their possible effect on physicians' decisions around patient treatment, researchers' decisions concerning study design, and companies' interference in publication, as well as on public health policy in general (Martin and Kasper 2000). Medical and other scientific journals began establishing rules for disclosure of financial conflicts, in an attempt to manage them.

In succeeding years, concern broadened to include other industries, more recently the food industry, with authorities questioning how financial conflicts might impinge on the outcomes of health, nutrition, and food safety research. It was generally acknowledged that the issue was complex and not susceptible to narrow or inflexible remedies, but that has not deterred some groups from concluding that industry-funded science is inherently biased (Yale 2007), demanding that all industry-funded research, whether conducted at contract research facilities or at universities, be denied consideration in the formulation of public policy, and also demanding that scientists who have conducted industry-funded research be barred from serving on public policy advisory committees (Center for Medical Consumers et al 2012).

In 2012, an independent audit of the European Food Safety Agency's (EFSA) conflict of interest practices reached the opposite conclusion, and recommended "against strengthening EFSA's conflict of interest policy, because doing so would introduce additional burdens on scientists participating in EFSA's expert panels and might make them hesitant to join (Vrieze 2012)." Similarly, it is this article's contention that industry funding, while a major component of the scientific landscape, is only one piece of an extremely complex research environment. The twin issues of financial conflict and bias demand a reasoned approach and skillful management.

What Are Biases and Conflicts?

Conflicts of interest are not, in themselves, determinants of bias. Even a massive multiplicity of conflicts, in and of itself, carries with it no certainty of bias. The definitions themselves make the distinction clear:

Conflict of interest: "… a situation in which a person has a private or personal interest sufficient to appear to influence the objective exercise of his or her official duties as, say, a public official, an employee, or a professional" (e.g., a scientific researcher) (Business Ethics 2012).

Bias: From a dictionary reference, bias is an "a preference or an inclination, especially one that inhibits impartial judgment… (TheFreeDictionary 2012)." A cognitive bias is "the human tendency to make systematic errors in judgment, knowledge, and reasoning" (especially as a result of filtering information through one's own likes and dislikes) (TheFreeDictionary 2012).

Or, more rigorously, *bias* is the "deviation of results or inferences from the truth, or processes leading to such systematic deviation. Any trend in the collection, analysis,

interpretation, publication, or review of data that can lead to conclusions that are systematically different from the truth (Green Facts 2012)."

For researchers, a *conflict* might describe a situation in which a funder has offered financial incentives for research and hopes for a particular research result; it might also describe a situation in which the researcher, for philosophical, religious, or professional reasons, wishes to achieve a certain result. Neither situation necessarily results in a *biased* result – which would rather depend on a measurable deviation of research results from "the truth" – or from what is, at the time, generally perceived as the true state of affairs. Of course, it amounts to an axiom that in science, and especially in food science, absolute "truth" is unattainable – as scientific inquiry continues, the hope is that truth is approached ever more closely. All that can be known is the best *approximation* to "truth" attainable with objective, unbiased evaluation of current relevant scientific knowledge.

Regrettably, much of the literature confounds *bias* and *conflict*. Even if all conflicts were banished forever, there would still be a myriad of sources for bias. There are, for example, the well-known forms of scientific and publication bias: sample-selection bias, sample-size bias, data-collection bias, data-quality bias, statistical-analysis bias, confounding-variable bias, and publication bias, to cite just a few of the more commonly encountered pitfalls leading to skewed research conclusions (Bulgar et al 2002).

These particular forms of scientific sources of bias may actually be easier to identify than other cognitive and emotional causes having nothing to do with the formal research process. Consider the following possible sources of bias:

- one's previous body of work
- one's desire for fame and respect among peers (or alternatively desire to achieve iconoclastic stature)
- religious bias
- ethical or values-based bias
- philosophical bias
- political bias
- one's nationality or ethnicity
- pressure to publish
- pressure to win prizes
- fear of losing one's job or position
- highly personal matters, e.g., one's physical or mental health issues, one's family's health, etc.
- the pernicious effect of pack behavior or "group think" facilitated by social or professional networks, either in the physical world or in cyberspace
- blogs, web sites, chat rooms, list serves, and other communication tools of the Web
- financial or funding bias – resulting from all kinds of financial incentives: gratuities, bribes, grants, free trips, gifts, cash prizes – the desire to please one's source of funding, either unconsciously or by deliberate arrangement

The multiplicity and variety of sources for bias in research and in public health communications generally are extensive, complex, and yet of major importance to scientific research, the integrity of individual study, and the body of scientific literature as a whole.

Current Management of Scientific Bias

For food, health, and nutrition research and science communications there are a number of checks and balances to guard against biased scientific conclusions and public

misunderstanding. First, there is a well-developed, time-tested system of peer review, built not only into journal publication but also into academic systems of promotion and tenure decisions. Universities have in place governance and review processes to exercise oversight, particularly on industry-funded research projects.

There is also peer *pressure* as a check on bias, the peer pressure of meetings, conferences, e-mail listservs and discussion boards run by scientific colleagues, as well as the peer pressure emanating through scientific societies and other organizations. For more than a century, peer review has served to provide a rigorous framework by which research papers and articles can be evaluated prior to their general dissemination – although not foolproof, scientists regard the process as a reliable safeguard against errors and biases, as well as scientific misconduct.

Proposed Guidelines to Ensure Scientific Integrity

In July 2010 the 230 participants of the 2nd World Conference on Research Integrity approved the Singapore Statement of globally-applicable principles and responsibilities related to research integrity and scientific conduct – the principles listed include honesty, accountability, professional courtesy and fairness, and good stewardship of research. Issuance of the consensus Statement, which was a major outcome of the conference, took place against a background of several high-profile cases of research misconduct – it is posted on the website of The International Council for Science (2nd World Conference on Research Integrity 2010).

Additionally, based on work commissioned by the International Life Sciences Institute North America (ILSI NA) Working Group on Guiding Principles, a series of proposals were developed to manage potential biases resulting from conflicts of interest between research investigators and companies wishing to fund their work. In the 2009 ILSI NA paper (Rowe et al 2009), disclosure was seen as an essential but no longer sufficient measure to safeguard research from undue influence exerted by funding organizations; the paper argued that managing conflicts, case by case, is the requisite step. Industry participation in the effort to disclose and manage financial conflicts of interest was seen as crucial.

The paper offered as one rationale for conflict management the following scenario: future university science students will find their way either into private sector research occupations or public sector careers; all need a set of principles to guide their interaction with funding organizations, whether public or private, and those organizations will need principles to guide them in their interactions with academic scientists. The ILSI NA Working Group proposed the guidelines to serve as a checklist in achieving unbiased research results from industry-funded activities – just as they might be useful guidance in public- or foundation-funded projects. The paper and the proposed guidelines were published simultaneously in six peer-reviewed scientific journals (Rowe et al 2009):

Industry and industry-funded researchers shall:

1. **Conduct or sponsor research that is factual, transparent, and designed objectively; according to the scientific process, the research design will generate an appropriately phrased hypothesis and the research will answer the appropriate questions, rather than favor a particular outcome;**
2. **Require control of both study design and research itself to remain with scientific investigators;**

3. **Not offer or accept remuneration geared to the outcome of a research project;**
4. ***Prior to the commencement of studies, ensure that there is a written agreement that the investigative team has the freedom and obligation to attempt to publish the findings within some specified time-frame;***
5. **Require, in publications and conference presentations, full signed disclosure of all financial interests;**
6. **Not participate in undisclosed paid authorship arrangements in industry-sponsored publications or presentations;**
7. **Guarantee accessibility to all data and control of statistical analysis by investigators and appropriate auditors/reviewers;**
8. **Require that academic researchers, when they work in contract research organizations (CRO), make clear statements of their affiliation; require that such researchers publish only under the auspices of the CRO.**

Importance of the Guidelines

Obviously, guidelines are not law, not mandates or regulation, but simply voluntary guidelines. But if the research community embraces them, or even embraces their spirit, there will surely be a profoundly beneficial effect on the quality and integrity of research – encouraging responsible oversight and stewardship of scientific research by all funding organizations. It must be stressed that each organization wishing to adopt the guidelines needs to develop its own quality control mechanism to ensure significant compliance.

A strong peer-review system coupled with open declaration of research sponsorship in all scientific communications is a mandatory pre-requisite for these guidelines to be effective. The second prerequisite is that university policies be promulgated to address the issues raised in guidelines 2, 3, 4, and 7 regarding control of the design and conduct of the research and its publication. It is the responsibility of both funding entity and the researcher(s) being funded to adhere to the guidelines; existing oversight structures are also encouraged to endorse and adhere to them. Furthermore, it should be understood that failure to embrace the guidelines would raise serious questions about any research project so conducted.

It has been suggested that industry-funded research in the past may have revealed a bias toward results favored by the food industry. The authors of one publicized study (Lesser et al 2007) reaching that conclusion proposed several explanations: (1) that food industry companies may wish to demonstrate the superiority of their products to those of competitors; (2) that investigators are influenced by their funding in formulating their research design and/or hypotheses; (3) that industry sponsors of research may suppress unfavorable results; (4) that authors of scientific reviews may deliberately bias their searches and interpretations to the benefit of their industry funders; (5) that scientific reviews may disproportionately represent studies "arising from industry-supported scientific symposia." Such critique overlooks the fact that most university research is basic in nature and that companies frequently enter into research agreements with university faculty at a point when preliminary experiments (whether conducted in the faculty member's or the company's laboratory) have established the proof of concept and therefore the likelihood that the research will have positive results is enhanced.

Notwithstanding the obvious observation that scientific reviews conducted by *non*-industry supported authors, are also subject to many potential biases, the eight principles articulated in the 2009 paper and in this SIB address virtually all possible sources of skewed research. Indeed, if these principles are vigorously adopted as the guidelines they are intended to be,

there would be virtually no reason to quarrel with a research conclusion except by disputing the science itself.

In fact, the eight articulated principles are intended to provide a clear statement of responsibility on all sides – those funding activities as well as those being funded – when academic institutions or academicians are recipients of industry funding for research, publication, or presentation. The principles are intended to offer guidance for the food industry and academic researchers who work with industry, when industry-funded research projects are involved. They may be thought of as a checklist to help ensure insulation of any research project from the provision of the resources enabling the project.

What's Been Left Out/Direction of Further Investigation

It is important to state explicitly what this SIB has excluded from consideration and to indicate areas for future exploration in terms of bias/COI. Substantial discussion of all of the following potential institutional sources of bias has been specifically excluded:

Foundation-funded research
Public-sector-funded research
Pro-bono work by academicians on:
- Advisory panels to industry;
- Grant panels;
- Government advisory panels;
- Non-governmental organization (NGO) panels;
- Voluntarism on behalf of professional societies.

This is a short list of organizational work and funding situations that routinely pose profound challenges to the independence and integrity of scientific research – the list could certainly be lengthened. All these potential sources of bias are outside and beyond the scope of this SIB.

Conclusion

The guidelines offered here may best be seen as a starting point for the development of a comprehensive set of principles useful for managing conflict-of-interest issues in research funding, globally. They may also be a useful starting point for organizations wishing to tailor more specific principles to address challenges specific to their industry, region, or research sector. The preceding discussion might also prove useful in stimulating additional COI research.

For example, future investigations of bias/conflict of interest issues might explore the ramifications for inappropriate influence of *organizational* bias on food, health, and nutrition research or on public policy. Furthermore, the role played by non-scientific and other institutions in communications involved in creating science-based public policy would be a fertile area of bias investigation.

A discussion of the differing public and policy-maker attitudes toward the global food industry versus the pharmaceutical and other industries, in funding scientific research, also falls outside of and beyond the scope of this article. The different ethical standards to which the food industry and other industries have been held in considering their support of research, particularly pharmaceutical-industry-funded science, would surely be a rich subject for further investigation.

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