



December 4, 2003

Dr. Margo Schwab
Office of Information and Regulatory Affairs
Office of Management and Budget
Executive Office of the President
725 17th St NW
New Executive Office Building
Room 10201
Washington, DC 20503
By email: OMB_peer_review@omb.eop.gov

Re: Proposed Bulletin on Peer Review and Information Quality, 68 FR 54023-29

Dear Dr. Schwab:

We are writing on behalf of the Association of American Medical Colleges (AAMC) and the Federation of American Societies for Experimental Biology (FASEB) to comment on the above-referenced notice of a proposed Bulletin seeking to standardize peer review requirements relating to significant federal regulatory actions. The AAMC represents the nation's 126 accredited medical schools, over 400 affiliated teaching hospitals, and 94 academic medical societies representing nearly 105,000 faculty members. FASEB is comprised of 22 societies with more than 60,000 members, making it the largest coalition of biomedical research associations in the United States. Together, our member organizations contribute extensively to and rely heavily upon research findings, data, and other information that may be incorporated in disseminations by the Public Health Service (PHS), and consequently take great interest in this notice.

The proposed Bulletin is intended to serve two goals: it would help further ensure that the quality of information released by federal agencies meets consistent standards and that major federal regulations and related actions are based upon sound science. The AAMC and FASEB fully support both goals. We nevertheless have profound concerns about the procrustean processes that the Bulletin would impose, especially from the perspective of the PHS agencies.

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First, the AAMC and FASEB believe that the proposed peer review standards are overly prescriptive and indifferent to generally respected, widely emulated practices of major Federal science agencies in determining scientific merit. Among these concerns:

(1.) The proposed peer review selection criteria that are intended to ensure an “independent” review would severely and unnecessarily restrict an agency’s access to the most qualified expertise. The proposed requirement for “especially significant” regulatory information would exclude from review panels individuals who currently receive or are seeking “substantial” funding from the agency conducting the review. This criterion would exclude leading scientists whose independent research may well rely on federal grants from the agency. Concerns about real or apparent conflicts of interest are appropriately managed through adequate disclosure and recusal mechanisms, which are the principal remedies called for by the medical journal commentaries cited in the OMB notice.¹ We cannot accept that receiving grants from a federal agency is per se cause to bar researchers from reviewing a proposed regulatory action, provided those researchers (or their close associates) have not contributed directly to the scientific underpinnings of the action under review.

(2.) The Bulletin also provides that, “if it is necessary to select a reviewer who is or appears to be biased in order to obtain a panel with appropriate expertise, the agency shall ensure that another reviewer with a contrary bias is appointed to balance the panel.” As written, this provision might imply that in some circumstances holding a contrary bias is itself a principal or sufficient basis for appointment to a review panel, or that a responsible agency official is required to make such an appointment subsequent to the selection process established within the agency.

The AAMC and FASEB urge that the final Bulletin reflect that diversity of views are an inherent strength in science, and are ubiquitous, and that the language be revised along the following lines: “It is incumbent upon the agency to identify and select candidates who reflect a range and balance in viewpoints and positions, consistent with requisite scientific and technical qualifications. The agency shall avoid constituting a review panel that is discernibly biased toward or against particular reasonable positions.”

(3.) The proposed Bulletin sets forth an extensive list of reporting requirements, intended to ensure transparency in peer review, but which could discourage candor or even participation in review panels. It would require that individually identified as well as group summaries of peer review discussions be reported to the agency and the public. In the PHS agencies and NSF, although the rosters of peer review committees and Councils are public, individual peer

¹ The notice cites Drazen JM, Curfman GD, *New England Journal of Medicine* 346:1901-2. (2002), and Campbell P., *Nature* 412:751 (2001). Notably, these commentaries have focused almost exclusively on researchers with financial ties to industry and not with government (or independent foundation) sponsorship, which has never been implicated among the concerns for bias addressed by these journals’ policies on conflicts of interest.

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reviewers' comments are never disclosed directly; rather, an applicant is provided with a detailed summary statement, anonymously incorporating the reviewers' and the committee's concerns and recommendations for improvement. This system is long established and works exceedingly well. With respect to scientific journals, peer reviewers' comments are typically transmitted to authors, but anonymously, along with an editor's synthesis and recommendations. The AAMC and FASEB recommend that the Bulletin require that only anonymized reports summarizing the consolidated findings and conclusions of the peer review panel be made public.

Our second major set of concerns focuses on the proposed requirements' likely interference with timely, responsible public health announcements to the detriment of the public weal. As was noted in earlier comments on the information quality guidelines², agencies of the Public Health Service must be acknowledged to have special prerogatives for evaluation and announcement of timely information important to the public health, even though such announcements may from time to time have impacts on the private sector that cross the "significant" threshold. These concerns have not diminished in the intervening years. Some notable recent examples of the exercise of the PHS prerogative include:

- The finding, from a terminated clinical trial, that treatment with anti-arrhythmic drugs of patients with history of myocardial infarction was not beneficial, as was then medical lore, but in fact dangerous;
- The announcement that hormone-replacement therapy for post-menopausal women was of minimal benefit and caused troubling adverse effects, again in contravention of medical lore;
- And most recently (October 10, 2003), and again based on information from a terminated trial, that a novel class of cancer drug appears significantly to reduce the rate of breast cancer recurrence.

All of these announcements have likely had and will have "especially significant" financial effects (as defined by OMB) on the manufacturers of the agents in question. All of them represent, in our opinion, appropriate agency responses to matters of high public health import on the basis of the best available and reliable contemporary information. It is likely that all of these announcements would have been delayed and may have been prevented under the most stringent, formulaic standards of "data quality," and we see no public benefit from mandating an additional layer of OMB interposition, peer review and public comment that, at best, would have delayed these announcements for untold months.

² AAMC comment letter to Brooke Dickson, August 13, 2001, responding to 66 FR 34489.

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The key point is that, in each of the above examples, there no doubt was and would always be robust debate and even disagreement within the scientific and patient communities about one or another element of the studies, as well as about the timing and wisdom of Data Safety and Monitoring Board decisions to interrupt two of the trials upon the appearance of statistically significant differences in outcomes in the experimental and control arms. This is the kind of healthy debate that appropriately occurs within the scientific community about all provocative new scientific findings until such time that new corroborative or negating data appear. In such a context, AAMC and FASEB argue that it is in the public interest to permit the leadership of the Public Health Service agencies, in concert with their established advisory processes, to exercise their professional experience and best judgment in meeting their statutory obligation to promote and protect the public's health. The imperative for timely, decisive review and announcement of important public health research findings is largely irreconcilable with the recursive procedures and other proposed requirements of the Bulletin.

The proposed Bulletin further mandates that:

Each agency shall provide, at least once a year: A summary description of any existing, ongoing, or contemplated scientific or technical studies that *might (in whole or in part)* constitute or support significant regulatory information the agency intends to disseminate within the next year; and the agency's plan for conducting a peer review of such studies under the requirements of this bulletin, including the identification of an agency contact to whom inquiries may be directed to learn about the specifics of the plan (emphasis added).

As evident in the examples given above, this reporting requirement would be extremely problematic in the circumstances of PHS responses to important, unanticipated, and more important, *unanticipatable* findings from ongoing research. The research agenda of PHS agencies is largely investigator driven, and it is typically impossible for an agency to predict the emergence of research findings that might merit broad dissemination. Notwithstanding OMB's concerns, the AAMC and FASEB believe that the PHS agencies' record of reliance on peer review is sufficiently well established and of sufficiently high caliber to provide the necessary credibility and assurance sought by the proposed Bulletin, and that these agencies should be exempted from the advanced reporting requirements in Section 6.

In conclusion, we believe strongly that federal regulatory agencies must be permitted to retain appropriate flexibility in the implementation of peer review standards for scientific and technical information relevant to new rulemaking or dissemination. As written, the Bulletin conveys a disconcerting view of the state of science in Federal regulatory agencies, effectively mandating a "receivership" regime for the evaluation of scientific information supporting especially significant regulatory actions. If certain regulatory agencies lack the appropriate capacity,

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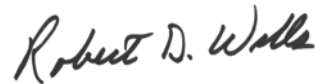
expertise, or will to perform credible evaluations of scientific and technical information, these deficiencies would be better addressed within those agencies themselves, or by direct intervention of the OMB or Congress as necessary. The superposition of one-size-fits-all, government-wide processes will inevitably have unintended adverse consequences and, in our opinion, absent a *demonstrable systemic problem* is not the optimal way to compensate for any specific agency's scientific failings.

The AAMC and FASEB appreciate the close attention that OMB afforded the research community's comments in its formulation and implementation of the earlier information quality guidelines mandated by the Information Quality Act of 2001,³ and is grateful for the consideration of these comments by OMB's Office of Information and Regulatory Affairs and the Office of Science and Technology Policy. We would be pleased to engage in further discussions about our concerns and possible remediation.

Sincerely,



Jordan J. Cohen, M.D.
President, AAMC



Robert D. Wells, Ph.D.
President, FASEB

Cc: The Hon. John Marburger, Ph.D., Director,
Office of Science and Technology Policy