JOURNAL OF BONE AND MINERAL RESEARCH
Volume 22, Number 11, 2007
Published online on October 1, 2007; doi: 10.1359/JBMR.07090A

Editorial

Challenges in Science and Academic–Industry Interactions

This issue of *JBMR* addresses some of the challenges inherent in the different perspectives of academic scientists and industry sponsors. Scientific "truth" is the primary aim that all should pursue in the jungle of academic–industry interactions. Potential competing interests in this area were brought into sharp focus by concerns raised about the presentation of data in a paper published in *JBMR* in June 2003[1] about the role of the pharmaceutical sponsor's statistician in that presentation and about limited access to the raw data for the academic scientists. The ASBMR-convened Task Force position paper[2] on Scientific Publishing of Industry-Supported Clinical Trials addresses academic–industry interactions and defines new criteria designed to strengthen the position of academic investigators in such interactions. The Letter of Response,[3] from the authors of the challenged paper, includes a statistical reanalysis of the original data that had been obtained from the sponsor pharmaceutical company. A brief timeline to this matter, signaled last year in *JBMR-Online,*[4] is provided in this Editorial, which notes aspects of the reanalysis and highlights procedural changes to limit the risk of similar problems in the future.

In November 2004, *JBMR* received a letter from Dr Blumsohn of Sheffield University alleging deficiencies in the data and reporting of the paper[1] published 18 mo earlier in June 2003 by Dr Eastell and co-authors, who included a Procter & Gamble statistician. Dr Blumsohn also raised similar concerns about two abstracts, related to the same data, presented at the ASBMR Annual Meeting in 2003 and of which he was a co-author with the authors of the June 2003 paper. Teleconferences, including the Editor-in-Chief of *JBMR*, the Chair of the ASBMR Publications Committee, and the ASBMR Director of Publications, took place in December 2005 to clarify Dr Blumsohn's concerns, and subsequently, Dr Eastell's position. *JBMR* did not and does not view itself as an investigative body; hence, Dr Blumsohn was asked then and subsequently to submit a letter in publishable form with sufficient information to permit a response from the authors. At that time, Dr Eastell stated that the authors of the *JBMR* paper had had sufficient confidence in the statistical analysis performed by their Proctor & Gamble statistician and co-author that they had felt comfortable signing a letter indicating "they had full access to the data," although in fact they did not have access to the raw data. He proposed and *JBMR* strongly supported that an independent statistical review be performed and, given the 30 months since publication of the original paper, *JBMR* asked that this be expedited.

During 2005 and 2006, *JBMR* received inquires from media representatives seeking clarification of what was happening, criticizing the influence of pharmaceutical funding on independent academic researchers, and critical of the lack of transparency on conflict of interests of authors in many major clinical journals. Hamstrung by the lack of a "publishable" letter of concern or any written response from the authors and with the desire not to influence the outcome of the statistical review, *JBMR* consistently indicated that the matter was in process and that the media would be advised of the outcome as soon as possible. Early in 2006, Dr Eastell notified *JBMR* that Proctor & Gamble had agreed to provide the raw data for a new analysis, that a statistician who was not a previous collaborator but was on the faculty of Sheffield University would perform the reanalysis after consultation with Dr Eastell and his colleagues, and that a second independent statistician, not on the faculty of Sheffield University, would review the reanalysis. Proctor & Gamble scientists would not be involved. Concerned at the slow progress of the resolution of this matter and relying largely on the lay media reports, *JBMR* published a statement of concern[4] in May 2006.

We refer readers to Dr Eastell and colleagues' Letter of Response[3] with the statistical reanalysis. Finally received in February 2007, it was accepted after scientific review and revision in September 2007. Their original paper[1] was a posthoc analysis of data from the pivotal risedronate efficacy studies and investigated the relationship between the degree of suppression of two urinary markers of bone resorption (C-telopeptide or CTX and N-telopeptide or NTX) and subsequent osteoporotic fracture incidence. From those analyses, the authors reached three specific conclusions:

- baseline levels of bone resorption predicted subsequent fracture risk in untreated individuals
- reduction in bone resorption partly explained the reduction in fracture incidence
- there was a "threshold" below which further suppression of bone resorption markers had no further benefit in terms of fracture risk reduction

The reanalyses[3] confirmed the first two conclusions, consistent with earlier studies. However, with regard to the third conclusion, they noted that both extremes of the original graphs[1] had been cropped, and thus did not show the more extreme resorption marker values. In the reanalysis, there was still a level (T-score = 0) below which further reduction of CTX was not associated with greater reductions in fracture incidence. However, this was not the case for the other resorption marker, NTX. Rather, the reanalysis indicated, as in their original paper,[1] that the lower the NTX T-score achieved, the greater was the reduction in fracture incidence. The difference between these two bone resorption markers, thought to measure the same phenomenon, is yet to be explained or fully explored clinically.

Dr Eisman has participated in multicenter international studies and received research funding and/or served as a consultant for Amgen, deCode, Eli Lilly (Australia), GE-LUNAR, Interleukin-Genetics, Merck, Sharp and Dohme, Novartis, NPS Pharmaceuticals, Organon, Roche-GSK (Australia), sanofi-aventis (Australia), and Servier. Dr Lorenzo receives research funding and serves as a consultant for Aastrom, Amgen, and Ariad.

Several procedural changes have developed alongside this process. In October 2005, an Editorial,[5] raising many of the issues related to this process, noted that the *Journal* does not have investigative powers and relies on academic institutions to address such matters. That Editorial stressed that *JBMR* depends on authors to be open and forthright in pursing and writing up their science and in declaring their conflicts of or competing interests. It is similarly noted that the *Journal* depends on reviewers in their reviewing of others' science to declare their conflicts of or competing interests, but it is clear that reviewers cannot verify any underlying data collection or analyses. The Editorial also advised all authors that, as of September 2005, the *Journal*'s "Instructions to Authors" required that any clinical trial for publication in *JBMR* must have registered with clinicaltrials.gov or similar public database before first subject entry.

In January 2006, the ASBMR leadership, which had been kept apprised of this matter, published an Editorial[6] addressing the issue of academic–scientific interactions and independence. In this, it advised membership that it had convened a Task Force on Scientific Publishing of Industry-Supported Clinical Trials to work with other interested scientific societies and journals to examine the role of industry in scientific publishing and to develop clearer criteria to protect academic investigators' status and independence in such studies. The ASBMR Task Force worked on gaining broad agreement from journals publishing bone and bone-related papers. The majority of societies and journals that participated agreed on a Statement of Principles, based on those summarized in the Association of American Medical Colleges (AAMC) Principles for Protecting Integrity in the Conduct and Reporting of Clinical Trials,[7] that recommend criteria with respect to publication of industry-supported academic research. The ASBMR Task Force report in this issue[3] strongly supports the AAMC Principles and thus the role and independence of academic scientists in academic–industry collaborations, such as in industry-supported/sponsored clinical studies.

No one doubts the importance to the advancement of science and health of collaborations between industry and academic medicine. However, there is also little doubt that the interests of science and industry are not always congruent. The outcomes of this process and the ASBMR Task Force should help reinforce the independent role of the academic researcher in these interactions, and we hope it will help to ensure the highest scientific standards in the performance and reporting of such studies. It is important to recognize that *JBMR* and ASBMR do not have nor seek any formal capacity to investigate allegations of scientific misconduct. We depend on parent universities and institutions or, as needed, national authorities including funding bodies to investigate allegations of scientific misconduct. Similarly, neither *JBMR* nor ASBMR has any mechanism to discipline, apart from declining to consider future manuscripts from authors found to have engaged in scientific fraud. The international medical journal editor groups support the position that scientific journals are not appropriate bodies to investigate claims of scientific misconduct.[8,9]

To limit similar problems in the future, *JBMR* had already required specific listing (and publication) of any and all potential conflicts of interest by all authors and that all authors sign that they have had full access to the underlying data for all manuscripts. All clinical trials are required to be listed before enrollment of the first subject. We are now adding the requirement that the authors must confirm that they are not aware of any disagreement about the content, analyses, or conclusions of their manuscript by anyone who has made a contribution to the work contained.

There are several lessons that can be learned from the realities and limitations surrounding the difficult and challenging process related to dealing with allegations of impropriety in scientific publishing.

1. The ultimate protection to science is open discussion and resolution of allegations such as those discussed here.
2. *JBMR* primarily depends on scientists being open and forthright in their publications, in their reviewing and in full disclosure of conflicts of interest and competing interests, to avoid claims of potential and hidden bias.
3. The actions of *JBMR*, ASBMR, and the Scientific Publishing of Industry-Supported Clinical Trials Task Force will, we hope, help support academic scientists in their interactions with industry.

The *Journal* has put in place procedures designed to identify and ideally prevent potential problems at the time of manuscript submission. The *Journal* needed and has also put in place more efficient operational procedures that will expedite the consideration of any such allegations in the future. We hope they will not be needed.

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John A Eisman, MBBS, PhD
Editor-in-Chief, JBMR

Joseph A Lorenzo, MD
Chair, ASBMR Publications Committee