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Ten Recommendations for Closing the Credibility Gap in Reporting Industry-Sponsored Clinical Research: A Joint Journal and Pharmaceutical Industry Perspective

Bernadette A. Mansi, BA; Juli Clark, PharmD; Frank S. David, MD, PhD; Thomas M. Gesell, PharmD; Susan Glasser, PhD; John Gonzalez, PhD; Daniel G. Haller, MD; Christine Laine, MD, MPH; Charles L. Miller, MA; LaVerne A. Mooney, DrPH; and Maja Zecevic, PhD, MPH

From GlaxoSmithKline, King of Prussia, PA (B.A.M., C.L.M.); Amgen, Thousand Oaks, CA (J.C.); Leerink Swann Consulting, LLC, Boston, MA (F.S.D.); Novartis Pharmaceuticals Corporation, East Hanover, NJ (T.M.G.); International Society for Medical Publication Professionals, Briarcliff Manor, NY (T.M.G.); Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ (S.G.); AstraZeneca, Macclesfield, United Kingdom (J.G.); *Journal of Clinical Oncology*, Alexandria, VA (D.G.H.); *Annals of Internal Medicine*, Philadelphia, PA (C.L.); Pfizer Medical, New York, NY (L.A.M.); and *The Lancet*, Elsevier, New York, NY (M.Z.). Dr Gesell is currently with United BioSource–Envision Group, Franklin Lakes, NJ. Dr Haller is currently with *Gastrointestinal Cancer Research*, Melville, NY.

The credibility of industry-sponsored clinical research has suffered in recent years, undercut by reports of selective or biased disclosure of research results, ghostwriting and guest authorship, and inaccurate or incomplete reporting of potential conflicts of interest.[1,2] In response, many pharmaceutical companies have integrated best practices and recommendations from groups such as the International Committee of Medical Journal Editors (ICMJE), the Good Publication Practice guidelines, the Committee on Publication Ethics, the EQUATOR (Enhancing the QUAlity and Transparency Of health Resources) Network, and the Medical Publishing Insights and Practices (MPIP) initiative into their internal policies and standard operating procedures.[3-10] However, a credibility gap remains: some observers, including some journal editors and academic reviewers, maintain a persistent negative view of industry-sponsored studies.[11] Given industry's pivotal role in the development of new therapies, further improvements in research conduct and disclosure are needed across the industry-investigator-editor enterprise to restore confidence in industry-sponsored biomedical research.

In 2008, the MPIP was founded by members of the pharmaceutical industry and the International Society for Medical Publication Professionals to elevate trust, transparency, and integrity in publishing industry–sponsored studies through education and creation of a discussion forum among industry research sponsors and biomedical journals.[12,13] In 2010, the MPIP convened a roundtable of 23 journal editors and industry representatives (see the "Acknowledgments" section for a list of MPIP participants) to characterize the persistent and perceived credibility gap in industry-sponsored research and identify approaches to resolve it. Attendees agreed that there have been important improvements in the conduct and reporting of industry-sponsored studies during the past 5 years, but several opportunities remain for additional improvement. Attendees reached consensus on a top 10 list of recommendations (Table), intended to serve as a call to action for all stakeholders—authors, journal editors, research sponsors, and others—to enhance the quality and transparency of industry-sponsored clinical research reporting. Although framed in the context of industry sponsorship, many of these recommendations would enhance the credibility of clinical research publications in general, regardless of the funding source.

Recommendation 1: Ensure Clinical Studies and Publications Address Clinically Important Questions

Many perceive a mismatch between the research hypotheses of some industry-sponsored studies and the needs of the public and practicing clinicians to improve patient health. The best way to elevate the credibility of industry-sponsored clinical research is to ensure that such research is designed to answer important clinical and scientific questions while respecting regulatory requirements that may influence certain aspects of study design. Credibility is compromised when clinical research is intended for marketing purposes rather than advancing scientific and medical knowledge. Sponsors could enhance transparency and credibility by better explaining to journals,[14] the biomedical community, and the public the decision-making process underlying the research endeavor. For example, sponsors could be more transparent in describing how external input and involvement from the academic community were obtained to inform study design (eg, by acknowledging participants in protocol development, advisory boards, and other roles).

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TABLE. Top 10 Recommendations for Closing the Credibility Gap in Reporting Industry-Sponsored Clinical Research

1. Ensure clinical studies and publications address clinically important questions
2. Make public all results, including negative or unfavorable ones, in a timely fashion, while avoiding redundancy
3. Improve understanding and disclosure of authors' potential conflicts of interest
4. Educate authors on how to develop quality manuscripts and meet journal expectations
5. Improve disclosure of authorship contributions and writing assistance and continue education on best publication practices to end ghostwriting and guest authorship
6. Report adverse event data more transparently and in a more clinically meaningful manner
7. Provide access to more complete protocol information
8. Transparently report statistical methods used in analysis
9. Ensure authors can access complete study data, know how to do so, and can attest to this
10. Support the sharing of prior reviews from other journals

Recommendation 2: Make Public All Results, Including Negative or Unfavorable Ones, in a Timely Fashion, While Avoiding Redundancy

Many industry sponsors have committed to disclosing the results of all clinical studies through recognized trial registries. Complete and transparent disclosure is required by law in many regions, fulfills the ethical obligation to trial participants, and is critical to the advancement of science. The ability to cross-reference trial registries, results databases, and all related publications informs the scientific community whether studies are completed or are under way and discourages selective reporting. Several recent articles have highlighted that there is a persistent need for better disclosure of clinical trial results, irrespective of study sponsorship.[15-17]

Whereas results from well-designed studies that are negative, confirmatory, inconclusive, or less immediately relevant to practicing clinicians can be particularly challenging to publish, these manuscripts can contribute toward the progress of science, may open the door for future research, and can prevent redundancy. Sponsors and authors should strive to disseminate them in appropriate venues, provided the data are put in context and the study limitations are clearly stated. This may require editors and publishers to explore and implement novel publication approaches well suited to these sorts of reports. Some possible approaches could include journals dedicated to these studies (perhaps in open-access format), abridged article formats more suitable to them, and/or specific reviewing mechanisms focused on scientific validity as opposed to "impact." Many of these potential solutions are currently being explored and developed by journals and publishers.[12] Finally, sponsors and authors should avoid redundant or duplicate publications. As part of this effort, sponsors could support editors' educational efforts to combat plagiarism.[18]

Recommendation 3: Improve Understanding and Disclosure of Authors' Potential Conflicts of Interest

Recent advances by academia, journals, and organizations such as the Institute of Medicine and ICMJE have improved processes for disclosing authors' potential conflicts of interest. Consensus among journal editors remains elusive on some specifics, such as the time frame for the reporting period and minimum amounts for financial reporting. These debates notwithstanding, however, editors and sponsors should support the use of the updated ICMJE Conflict of Interest Reporting Form[19] and continue dialogue regarding its improvement. Furthermore, the same conflict of interest reporting standards should be applied uniformly to all authors, regardless of the source of research funding.[20]

To further enhance disclosure transparency and reduce the administrative burden on authors, all parties should also explore the feasibility of developing a centralized, publicly accessible disclosure database.[21] Specific issues that need to be addressed include responsibility for quality control and maintenance, privacy/public data access issues, data ownership, and database funding. If these issues could be resolved, a digital database would provide an efficient and effective means of promoting transparent reporting.

Recommendation 4: Educate Authors on How to Develop Quality Manuscripts and Meet Journal Expectations

Ineffective or inappropriate reporting can diminish the value and credibility of clinical research. Authors who are well versed in study design, conduct, and analysis may lack formal writing training or knowledge of reporting guidelines such as the Consolidated Standards of Reporting Trials (CONSORT) requirements.[22] The experiences of editors and industry publication professionals suggest there is a large

"information gap" in this regard, particularly related to authors' knowledge of key aspects of authorship that directly affect the quality and credibility of submitted manuscripts.

Journals and research sponsors should collaborate to educate researchers and other groups who conduct or contribute to publication development, whether they work in industry, academia, or other venues. Best practice guides should be widely disseminated to industry and academic authors. For example, the MPIP's Authors' Submission Toolkit[23] can help authors navigate the manuscript development and submission process, and EQUATOR's author resource library can provide guidance on research reporting.[24] On the basis of author and editor feedback, additional materials or educational programs may be needed to supplement existing guidelines; editors and industry representatives should collaborate to identify specific areas of unmet need and develop educational resources to address them. Finally, editors have an additional opportunity and responsibility to expand their academic educational efforts and drive education within and among journals to encourage the harmonization of editorial policies and reviewer standards in line with evolving best practices.

Recommendation 5: Improve Disclosure of Authorship Contributions and Writing Assistance and Continue Education on Best Publication Practices to End Ghostwriting and Guest Authorship

Research sponsors have improved their credibility significantly by incorporating into their policies and standard practices[5-10] definitions of authorship and contributorship developed by ICMJE, the American Medical Writers Association, the European Medical Writers Association, and other professional bodies. Importantly, these definitions explicitly recognize the positive role that professional writers can play in manuscript development, provided they are appropriately acknowledged as authors or contributors (in accordance with ICMJE guidelines) and their names, affiliations, and potential conflicts of interest are disclosed.[25]

All parties must continue to work toward zero tolerance of ghostwriting (defined as failure to acknowledge individuals who helped write the paper) and guest authorship (defined as inclusion of individuals as authors who do not qualify because they do no meet ICMJE or journal criteria for authorship). Sponsors should ensure that employees' contributions are fully disclosed, using the same standards for employees and nonemployees. Such disclosure should be done without applying quotas of the maximum number of industry-employed authors or prespecified ratios of industry-employed to independent authors that would inappropriately exclude individuals who qualify for authorship or acknowledgment. For their part, journals need to eliminate any biases against manuscripts that have industry authors. Finally, sponsors, academic institutions, and editors should reinforce collaboratively the unacceptability of ghostwriting and guest authorship.

Recommendation 6: Report Adverse Event Data More Transparently and in a More Clinically Meaningful Manner

There is an unmet need for better and more uniform reporting of adverse events. Although "no clinically significant adverse events" and "no unexpected adverse events" are common shorthand in journal articles, such phrases lack clinical relevance, particularly regarding rare adverse events that may be important for agents used over a long period in large populations. Editors, sponsors, and clinicians would benefit from consensus on more uniform reporting guidelines that clearly specify the type and format of adverse event data provided in the manuscript and/or supplemental material.[26] In addition, journals may need to revisit their manuscript length policies if they wish this information to be present in the main document.

Finally, editors and sponsors must educate authors on the need to balance the strength of adverse event claims vs the features and limitations of trial design appropriately. In a study that is not powered to assess rare adverse events, it is more appropriate to qualify the findings (eg, "additional severe adverse events were not detected in this short, small trial") than to make broad statements that could mislead readers (eg, "generally safe and well tolerated").

Recommendation 7: Provide Access to More Complete Protocol Information

Some journals request submission of a clinical study protocol to validate methods and end points used in submitted manuscripts, screen for analysis or reporting errors, confirm that the manuscript matches the protocol, and verify that any protocol amendments do not affect study conduct or integrity inappropriately.[27] In addition, several journals post online complete protocols or excerpts together with the published manuscript to provide greater transparency and additional context to readers. Journals should describe their protocol submission requirements and publication policies in their instructions for authors and apply them irrespective of study sponsorship.

Public dissemination of protocols by journals raises several practical issues that require further

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discussion. To foster development of effective policies on protocol disclosure, sponsors should engage with journals on the appropriate format and organization and the extent and legitimacy of redactions to protect proprietary intellectual property or other concerns. In addition, because study protocols are frequently amended as research progresses, disclosure of different versions in multiple public venues may create confusion and redundancy. Stakeholders should explore whether a single repository is feasible and meets the objective of transparency.

Recommendation 8: Transparently Report Statistical Methods Used in Analysis

Most journals assess statistical methods as a routine part of the peer review process, often relying on established reporting guidelines such as CONSORT.[22] Sponsors should ensure that authors provide adequate information about the chosen methods based on the prespecified study design and parameters, and how they were applied to the final data set. To enhance credibility, authors need to adhere to existing reporting standards, and editors have a responsibility to uniformly enforce these requirements at their journals.

The issue of statistical analysis credibility warrants further discussion among editors, authors, and research sponsors to explore how journals can develop policies that raise standards for all clinical publications, independent of the financial support or authorship. Singling out industry-sponsored trials for additional statistical validation[28] unfairly implies that these studies' analyses are inherently deficient and deserve heightened scrutiny.

Recommendation 9: Ensure Authors Can Access Complete Study Data, Know How to Do So, and Can Attest to This

The credibility of industry-sponsored research is threatened when authors cannot explain or defend key details of study design and analysis or verify access to raw data. Sponsors' letters of agreements with authors should clearly define authors' data access rights and expectations and their responsibility to understand and attest to them if required by journals. Industry sponsors need internal policies and procedures that facilitate data access for investigators and authors, and journals should unambiguously state their submission and publication policies on data access. Journals and sponsors should consider that data access needs may also differ, depending on study type. For example, the level of data access expected and feasible for all authors may not be the same for a noninterventional study as for a multicenter interventional trial.

Recommendation 10: Support the Sharing of Prior Reviews From Other Journals

The MPIP's Authors' Submission Toolkit advises authors, when submitting a rejected manuscript to another journal, to explore the possibility of providing a copy of the prior manuscript version and reviewers' comments to demonstrate that suggestions have been incorporated.[23] Although the practice is not uniformly accepted at this time, some journals encourage the sharing of prior reviews on the grounds that it elevates transparency, avoids duplicated efforts, and increases the quality of subsequent submissions.

Given that there is no consensus among editors on whether to accept prior reviews, this decision should be made by individual journals. Those journals that accept prior reviews must articulate their policies clearly and instruct their peer reviewers on how best to use them, and authors must be educated about how journals integrate prior reviews into their decision-making processes.

Conclusion

These top 10 recommendations outline several opportunities to enhance the transparency and credibility of industry-sponsored clinical research. Sponsors must continue to promote best practice guidelines, incorporate them into their policies and processes, and work with other biopharmaceutical and medical device companies and professional organizations to ensure uniform adoption. They should also drive author education efforts by disseminating guidelines and materials. Editors must ensure their policies are clear, transparent, well publicized, and uniformly applied irrespective of author affiliation or study sponsorship, and should increase their collaboration and overall role in promoting best practices.

The MPIP roundtable participants identified several areas of potential collaboration between journals and sponsors. Joint educational activities, such as guideline development (eg, the MPIP's Authors' Submission Toolkit and this document), exemplify collaboration toward the shared goal of reporting high-quality clinical research. Sponsors and editors can also collaborate in ongoing educational activities for authors of sponsored research and should jointly discuss areas of persistent ambiguity to exchange ideas and align on key issues for mutual benefit. Finally, all parties should take the opportunity to extend these efforts toward raising the standards for all research activities, irrespective of industry sponsorship. Such efforts are vital to closing the credibility gap in reporting industry-sponsored clinical research.

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Abbreviations and Acronyms: **CONSORT** = Consolidated Standards of Reporting Trials; **ICMJE** = International Committee of Medical Journal Editors; **MPIP** = Medical Publishing Insights and Practices

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Correspondence: Address to Maja Zecevic, PhD, MPH, 360 Park Ave S, New York, NY 10010 (M.Zecevic@Lancet.com).

REFERENCES

1. Bruyere O, Kanis JA, Ibar-Abadie ME, et al. The need for a transparent, ethical, and successful relationship between academic scientists and the pharmaceutical industry: a view of the Group for the Rest of Ethics and Excellent in Science (GREES). *Osteopor Int*. 2010;21(5):713-722.
2. Pyke S, Julious SA, Day S, et al. The potential for bias in reporting of industry-sponsored clinical trials. *Pharm Stats*. 2011;10(1):74-79.
3. Strahlman E, Rockhold F, Freeman A. Public disclosure of clinical research. *Lancet*. 2009;373(9672):1319-1320.
4. PhRMA Principles on Conduct of Clinical Trials: Communication of Clinical Trial Results. PhRMA Web site. http://www.phrma.org/sites/default/files/105/042009_clinical_trial_principles_final.pdf. Accessed January 31, 2012.
5. Amgen. Amgen Guidelines for Publications. Amgen Web site. http://www.amgen.com/about/amgen_guidelines_for_publications.html. Accessed January 31, 2012.
6. AstraZeneca. Transparency of Trial Information. AstraZeneca Web site. http://www.astrazeneca.com/Responsibility/Research-ethics/Clinical-trials/Transparency-of-trial-information. Accessed January 31, 2012.
7. GlaxoSmithKline. Reports and publications, Public policies, Disclosure of Clinical Trial Information. GlaxoSmithKline Web site. http://www.gsk.com/reportsandpublications-policies.htm. Accessed January 31, 2012.
8. Johnson & Johnson. Transparency in Our Business Activities. Johnson & Johnson Web site. http://www.jnj.com/connect/about-jnj/our-citizenship/transparency-in-our-business-activities/transparency+in+our+business+activities. Accessed January 31, 2012.
9. Merck. Merck Guidelines for Publication of Clinical Trials and Related Works. Merck Web site. http://www.merck.com/research/discovery-and-development/clinical-development/

Merck-Guidelines-for-Publication-of-Clinical-Trials-and-Related-Works.pdf. Accessed January 31, 2012.

10. Pfizer. Conducting Ethical Research – Registration, Disclosure, and Authorship. Pfizer Web site. http://www.pfizer.com/research/research_clinical_trials/registration_disclosure_authorship.jsp. Accessed January 31, 2012.
11. Angell M. Industry-sponsored clinical research: a broken system. *JAMA*. 2008;300(9):1069-1071.
12. Clark J, Gonzalez J, Mansi B, et al. Enhancing transparency and efficiency in reporting industry-sponsored clinical research: report from the Medical Publishing Insights and Practices initiative. *Int J Clin Pract*. 2010;64(8):1028-1033.
13. MPIP Web site. www.mpip-initiative.org. Accessed January 31, 2012.
14. Clark S, Horton R. Putting research into context – revisited. *Lancet*. 2010;376(9734):10-11.
15. Lehman R, Loder E. Missing clinical trial data. *BMJ*. 2012;344:d8158.
16. Prayle AP, Hurley MN, Smyth AR. Compliance with mandatory reporting of clinical trial results on ClinicalTrials.gov: cross sectional study. *BMJ*. 2011;344:d7373.
17. Ross JS, Tse T, Zarin DA, et al. Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. *BMJ*. 2011;344:d7292.
18. Fighting plagiarism [editorial]. *Lancet*. 2008:371(9631):2146.
19. ICMJE. Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Ethical Considerations in the Conduct and Reporting of Research: Conflicts of Interest. ICMJE Web site. www.icmje.org/ethical_4conflicts.html. Accessed January 31, 2012.
20. Lanier WL. Bidirectional conflicts of interest involving industry and medical journals: who will champion integrity? *Mayo Clinic Proc*. 2009;84(9):771-775.
21. Steinbrook R. Online disclosure of physician-industry relationships. *N Engl J Med*. 2009;360(4):325-327.
22. CONSORT. The CONSORT statement. CONSORT Web site. www.consort-statement.org/consort-statement. Accessed January 31, 2012.
23. Chipperfield L, Citrome L, Clark J, et al. Authors' Submission Toolkit: a practical guide to getting your research published. *Curr Med Res Opin*. 2010;26(8):1967-1982.
24. EQUATOR. Resources for authors of research reports. EQUATOR Network Web site. www.equator-network.org/resource-centre/authors-of-research-reports/authors-of-research-reports. Accessed January 31, 2012.
25. Norris R, Bowman A, Fagan JM, et al. International Society for Medical Publication Professionals (ISMPP) position statement: the role of the professional medical writer. *Curr Med Res Opin*. 2007;23(8):1837-1840.
26. Ioannidis JPA, Evans SJW, Gøtzsche PC, et al. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med*. 2004;141(10):781-788.
27. Chan AW. Bias, spin and misreporting: time for full access to trial protocols and results. *PLoS Med*. 2008;5(11):e230.
28. Fontanarosa PB, Flanagin A, DeAngelis CD. Reporting conflicts of interest, financial aspects of research, and role of sponsors in funded studies. *JAMA*. 2005;294(1):110-111.