INDUSTRY SUPPORT FOR AUTHORS AND PUBLICATIONS: WHAT GOOD LOOKS LIKE

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Presentation Overview

- Define the Issue
- Risks/Perceptions
- Compliance Principles
  - Transparency
  - Totality
  - Timeliness
- Emerging Issues

Defining the Issue

- Companies fund a variety of data generating activities for investigational and marketed products:
  - Primary clinical research that is either sponsored by the company or investigator-initiated studies
  - Outcomes research based on economic models or epidemiologic data
  - Review analyses that synthesize prior data collections
- To manage the public disclosure of these activities, companies have established publication planning units that undertake such activities as:
  - Identifying and selecting authors
  - Establishing deadlines for manuscript/abstract development
  - Assisting in manuscript/abstract development
  - Identifying appropriate peer-reviewed journals or professional conferences for publication/release of the data and
  - Coordinating submission of materials to journals or conferences

Defining the Issue

- Publication planning often is linked to product promotion/education, but they are distinct activities:
  - Publication planning is about the development of manuscripts/abstracts and the initial placement of that material in the public domain
  - That initial placement, usually in the form of a reprint, then may be disseminated and its impact amplified by a sales force as part of product promotion or may be the subject of CME as part of product education
- Focus will be on the initial publication planning role, not the subsequent dissemination activities

The Current Perception

- From the New York Times, October 2, 2010—
  - "According to government investigators and plaintiffs' lawyers, many of the studies of antipsychotics were conceived in marketing departments of pharmaceutical companies, written by ghostwriters and then signed by prominent physicians — giving the illusion that the doctors were undertaking their studies independently. Such practices continue. 'The content is preplanned,' said one doctor who has worked as an uncredited medical writer for antipsychotic studies. Data is used selectively and interpreted for company benefit, said the doctor, who still works in medical writing and spoke on the condition of anonymity to preserve future job prospects. Such papers influence medicine in many ways, as sales representatives show them to doctors and future research builds upon them. 'Review articles and original research articles have advertising messages in them,' the doctor said. 'That's part of the plan.'"

Challenges to the Activity

- Inherent in the activity—perceived disconnect between company management of publications and the unbiased integrity of scientific research
- Kickbacks in payments to HCP authors
- Bias in the research/lack of independence
  - Work with authors to “massage the data”
- Manipulation in the timing and disclosure of data
  - Emphasize good data/minimize bad data
  - Rush publication of good data/“slow walk” bad data
  - Fail to publish all data

Independence of IIRs

- Key to Investigator-Initiated Research is independence:
  - Research and publication controlled by the investigator, not the company
  - Company should not manage IIRs after selection and funding
- Company should insist upon a timely deliverable—manuscript or abstract—with budget hold-back to create an incentive
- Selection of IIR should include consideration as to whether investigator can meet deliverable requirement
- Budget for deliverable, including any funding for statistical analysis, medical writer and placement assistance, should be contained and agreed upon as part of IIR proposal

Key Principle: Transparency

- There is still lingering “confusion” as to company’s role in funding research and in assisting in the writing and publication of study reports
- The only way to alleviate this confusion is through full disclosure of funding related to a study and listing of authors who meeting neutral authorship criteria and acknowledgment of others who supported the manuscript/abstract

Author Transparency: Ghostwriting

- Sen. Charles Grassley's definition of "ghostwriting":
  - Payment from companies to marketing /medical education companies to draft review articles on the drug or device
  - Draft articles are then presented to prominent academics/physicians to sign on as authors, whether or not they are intimately familiar with the underlying data and relevant documentation
  - Listed authors have minimal or limited input in the development and/or writing of the article – when published, the actual involvement of listed "authors" is not always clear

Prevalence of Ghostwriting

- Rates of ghostwriting at major publications (JAMA 2009):
  - 10.9% NEJM
  - 7.9 % in JAMA
  - 7.6 % in The Lancet
  - 7.6 % in PLoS Medicine
  - 4.9 % in The Annals of Internal Medicine
  - 2 % in Nature Medicine
- According to a 2009 study released by editors of JAMA, among authors of 630 articles who responded anonymously to an online questionnaire created for the study, 7.8% acknowledged contributions to their articles by people whose work should have qualified them to be named as authors on the papers but who were not listed

Sources of Disclosure Guidelines

- Codes of practice have been developed by a myriad of institutions
  - International Committee of Medical Journal Editors
  - Pharmaceutical Research and Manufacturers of America International Society for Medical Publication Professionals
  - Association of American Medical Colleges
  - American Medical Writers Association
  - Institute of Medicine
  - World Association of Medical Editors
  - Journals have their own internal standards as well which must be complied with to submit an article for publication

ICJME Requirements

- International Committee of Medical Journal Editors - Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (Updated April 2010)
  - Hundreds of medical journals follow the ICMJE's Uniform Requirements including Annals of Internal Medicine, British Medical Journal, JAMA, NEJM and The Lancet

Authorship and Research Contributors (ICJME/PhRMA)

- Authorship criteria:
  - substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
  - drafting the article or revising it critically for important intellectual content; and
  - final approval of the version to be published
- Acquisition of funding, collection of data, or general supervision of the research alone does not constitute authorship
- Contributors who do not meet the criteria should be listed in the acknowledgments

Guidelines on Author Conflicts of Interest (ICJME)

- Authors must state explicitly whether potential conflicts do or do not exist
- Authors should identify individuals who provide writing or other assistance and disclose the funding source for this assistance
- Editors must decide whether to publish information disclosed by authors about potential conflicts

Guidelines on Author Conflicts of Interest

- ICJME Disclosure Form requests specific financial information:
  - Associations with commercial entities that provided support for the work reported in the submitted manuscript
  - Associations with commercial entities that could be viewed as having an interest in the general area of the submitted manuscript
  - Any similar financial associations involving their spouse or their children under 18 years of age
  - Some journals go further - JAMA requires information about all relevant financial interests, relationships or financial conflicts within the past 5 years and for the foreseeable future

Industry Sponsored Research (ICJME)

- Authors should describe the role of the study sponsor, if any, in study design; collection, analysis, and interpretation of data; writing the report; and the decision to submit the report for publication
- Editors may request that authors of a study funded by an entity with a financial interest sign a statement, such as “I had full access to all of the data in this study and I take complete responsibility for the integrity of the data and the accuracy of the data analysis.”

Industry Sponsored Research (ICJME):Peer-review Process

- Editors should be encouraged to review copies of the protocol/contracts associated with project-specific studies before accepting such studies for publication
- Editors may request a statistical analysis of all data by an independent biostatistician
- Editors may choose not to consider an article if a sponsor has asserted control over the authors' right to publish
- Some journals impose much stricter standards

Key Principle: Totality

- Companies must take steps to avoid the charge that they are “burying” data
- Assumption has to be that if the company sponsored or funded the research, the results of that research should be placed in the public domain
- This becomes an even more pressing issue with registration of trials under including www.ClinicalTrials.gov web site

Key Principle: Timeliness

- A variation on the concern of “burying” data is the timeliness of the release of data
- Assumption has to be that release of neutral or negative data should similar to the time frame for positive data
- There are no hard and fast publication rules here, but unless there are complications in assessing the data that can be explained, goal should be to release data publicly within 12-18 months from the end of the study

PhRMA Code on Clinical Trials Registration/Summary of Results

- Under section 4 of PhRMA Code companies commit to
  - Register clinical trials and posting results on a publicly available web site, including www.ClinicalTrials.gov
  - Submit, in a timely manner, summary information about all clinical trials that involve the use of our marketed or investigational products in patients
  - Post summary results of all clinical trials conducted in patients involving the use of products that are approved for marketing, or that are investigational products whose development programs are discontinued regardless of outcome

PhRMA Code on Investigators' Access to Clinical Trial Data

- PhRMA Code requires that
  - Individual investigators in multi-site clinical trials have their own research participants' data, and be provided the randomization code after conclusion of the trial
  - Sponsors make a summary of the study results available to the investigators and any investigator who participated in a multi-site clinical trial will be able to review relevant statistical tables, figures, and reports for the entire study
  - Sponsors provide all investigators with a full summary of the study results regardless of whether the investigator is an author

Emerging Issues: Clinical Trial Registration/Summary of Results

- Proposed Rule - Expanded Registration and Results Reporting at ClinicalTrials.gov
- NIH to issue regulations that will prescribe procedures reporting the results, including adverse events
- Intended to provide more complete results information and to enhance patient access to and understanding of the results of clinical trials

Emerging Issues: Clinical Trial Registration/Summary of Results

- Proposed Rule will also consider
  - whether results information should be required to be submitted for applicable clinical trials of drugs, biological products, or devices that have not been approved, licensed, or cleared by FDA
  - whether narrative summaries of clinical trials and their results can be included in the data bank without being misleading or promotional
  - Final Rule was expected at the end of September 2010

Conclusion/Recommendations

- Document how publications are initiated and developed and implement policies that facilitate such documentation. For example,
  - Written Agreements between the sponsor and authors which clearly delineate rights and responsibilities
  - Documentation of intellectual and substantive comments and revisions
  - Documentation of all individuals who were permitted to review, and comment on the manuscript
- Establish policies to ensure that non-exploratory data are not withheld from the public domain and are released in a timely manner
- Understand that trial registration, originally intended to inform potential research subjects, can now be a tool to monitor data release and publications