

# Pharmaceutical Companies and Research Publications



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# Challenges and Tensions in Framing Good Publication Practices (GPPs)

- **Volume of studies for publication**
- **Time commitments of leading researchers**
- **Pressure to get data into publications**
- **Production of high-quality manuscripts**
- **Relative interest in negative studies**

# Challenges and Tensions in Framing Good Publication Practices (GPPs)

- Invalid or “failed” studies
- Proprietary concerns
- Timing of publication
- Role of medical writing companies
- Investigator-sponsored studies

# Focus on Pharmaceutical Company Publication Practices

- **Expansion of ClinicalTrials.gov post-FDA Amendments Act**
- **Scrutiny of Responses to Unsolicited Requests From Physicians**
- **Growing Importance of Compendia for Product Coverage (e.g., Oncology)**
- **Industry Payments to Physicians and Potential Conflicts of Interest**

## FDA and “Good Reprint Practices”

- **Food and Drug Administration (FDA) Draft Guidance on Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (GRR Draft Guidance)**
  - Published in peer-reviewed journals, and not including supplements or other publications paid for by the manufacturer
  - Not false or misleading
  - Not abridged or summarized by manufacturer
  - Accompanied by approved labeling, bibliography, and (if called into question by another study) a representative contrary article
  - Distributed separately from promotional materials
  - Accompanied by disclaimers and disclosures

# Congressional Scrutiny

- **Letter from Chairman Henry Waxman (D-CA), House Committee on Oversight and Government Reform (November 30, 2007) to FDA Objecting to GRR Draft Guidance**
  - Companies “can manipulate and selectively distribute studies in order to make their products appear safer and more effective than they truly are.”
    - **“Systematically suppressed studies”**
    - **Studies...were distorted...”**
    - **“Omitted important ...data”**
    - **Study “reported only six months of data despite having collected 12 months of data”**
    - **“Distribution of the early peer-reviewed journal articles could have led to many unnecessary deaths”**

# Congressional Scrutiny

- **Letter from Chairman Henry Waxman (D-CA), House Committee on Oversight and Government Reform (November 30, 2007) to FDA Objecting to GRR Draft Guidance (cont'd)**
  - False Claims Act settlements “reveal that use of publications to promote off-label uses is a concerted strategy”
  - “There is abundant evidence that industry-funded published studies are overwhelmingly more likely to show favorable results than independently-funded studies.”
  - “There are severe limitations inherent in the peer review process”
    - Lack of access to the study protocol or underlying data
    - Peer reviewers do not necessarily have the time or expertise in all aspects of the subject matter
    - Journals cannot guarantee the correctness or authenticity of the article, or detect fraudulent or flawed research

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions**
  - Ensure the accuracy and integrity of the entire study database
  - Exploratory Studies
    - “Sponsors do not commit to publish the results of every exploratory study performed, or to make the designs of clinical trial protocols available publicly at inception.”
    - “If information from an exploratory study is felt to be of significant medical importance, sponsors should work with the investigators to submit the data for publication”
  - “In all cases, the study results should be reported in an objective, accurate, balanced and complete manner, with a discussion of the strengths and limitations of the study.”



# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Authorship -- Consistent with International Committee of Medical Journal Editors and major journal guidelines
    - “Anyone who provides substantial contributions to the conception or design of a study, or data acquisition, or data analysis and interpretation; and writing or revising of the manuscript; and has final approval of the version to be published should receive appropriate recognition as an author or contributor when the manuscript is published.”

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Authorship
    - “Companies sometimes employs staff to help analyze and interpret data, and to produce manuscripts and presentations. Such personnel must act in conjunction with the investigator-author.”
      - Contributions should be recognized in publications – as named author, contributor, or acknowledgements depending upon level of contribution
    - “All authors, whether from within a sponsoring company or external, will be given the relevant statistical tables, figures, and reports needed to support the planned publication.”

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Related Publications
    - For a multi-site trials, analyses based on single-site data have significant statistical limitations, and frequently do not provide meaningful information
      - Such reports should not precede and should always reference the primary presentation of paper of the entire study

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Investigator Access to Data and Review of Results
    - As owners of the study database, sponsors have discretion to determine who will have access to the database
    - Generally, study databases are only made available to regulatory authorities – but subject to exceptions --

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Investigator Access to Data and Review of Results
    - Exceptions:
      - Individual investigators will have their own participants' data, and will be provided the randomization code after trial conclusion
      - Sponsors will make a summary of the study results available to investigators
      - Any investigator who participated in the conduct of a multi-site trial will be able to review relevant statistical tables, figures, and reports for the entire study at the sponsor's facilities, or other mutually agreeable location

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Sponsor Review
    - “Sponsors have a right to review any manuscripts, presentations, or abstracts that originate from [their] studies or that utilize [their] data before they are submitted for publication or other means of communication”

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Sponsor Review
    - “Sponsors commit to respond in a timely manner, and not to suppress or veto publications or other appropriate means of communication (in rare cases it may be necessary to delay publication and/or communication for a short time to protect intellectual property).”
    - “Where differences of opinion or interpretation of data exist, the parties should try to resolve them through appropriate scientific debate”

# Industry Principles

- **PhRMA Principles on the Conduct of Clinical Trials and Communication of Clinical Trial Results – Publications Provisions (cont'd.)**
  - Journal Review
    - “If requested by a medical journal when reviewing a submitted manuscript for publication, the clinical trial sponsor will provide a synopsis of the clinical trial protocol and/or pre-specified plan for data analysis with the understanding that such documents are confidential and should be returned to the sponsor.”



## Other Sources of GPP Guidance

- International Committee of Medical Journal Editors (ICMJE)
  - Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication; Publication Ethics: Sponsorship, Authorship, and Accountability (updated October 2008) at <http://www.icmje.org/>
- World Association of Medical Editors (WAME)
  - Policy statements at <http://www.wame.org/resources/policies>
- Committee on Publication Ethics (COPE)
  - Guidelines on Good Publication Practice at <http://www.publicationethics.org.uk/guidelines>

## Other Sources of GPP Guidance

- American Medical Writers Association Code of Ethics and Position Statement on the Contributions of Medical Writers to Scientific Publications ([www.amwa.org](http://www.amwa.org))
- Wager, Field & Grossman, “Good Publication Practice for Pharmaceutical Companies” *Current Medical Research and Opinions* (19:149-154 (2003))
- CONSORT (Consolidated Standards for Reporting Trials) Statement
  - <http://www.consort-statement.org/>
- CSE's White Paper on Promoting Integrity in Scientific Journal Publications (2006)
  - [http://www.councilscienceeditors.org/editorial\\_policies/white\\_paper.cfm](http://www.councilscienceeditors.org/editorial_policies/white_paper.cfm)

## Guidance From Settlement Provisions

- Recent Settlements Increasingly Focused on Ghostwriting, Dissemination of Reprints, and Unsolicited Request Processes
  - e.g., State settlements with:
    - Pfizer on Celebrex<sup>®</sup>/Bextra<sup>®</sup> (October 23, 2008)
    - Eli Lilly on Zyprexa<sup>®</sup> (October 6, 2008)
    - Merck on Vioxx<sup>®</sup> (May 20, 2008)

## Points to Consider in Developing and Refining Publication Policies

- Publication Plans
- Roles of Marketing, Medical Affairs, Product Team, Compliance, Legal, etc.

## Points to Consider in Developing and Refining Publication Policies

- Role of Medical Writers
- Agreements and Communications with Medical Writing Companies

## Points to Consider in Developing and Refining Publication Policies

- Authorship and “Ghostwriting”
- Investigator Agreements

## Points to Consider in Developing and Refining Publication Policies

- Disclosures
- Documenting Reasons for Delayed Publication
- Duplicate or Redundant Publications

## Points to Consider in Developing and Refining Publication Policies

- Risk Tolerance in Use of Reprints
- Unsolicited Request Controls



## Points to Consider in Developing and Refining Publication Policies

- Consistency of Application of Policies – SOPs
- Tracking, Monitoring and Auditing

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