Ethical Issues in the Publication of Clinical Trial Information

The International Pharmaceutical Compliance Summit on Medical Affairs, Clinical Trials, Safety and Publication

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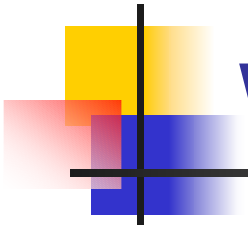
*The comments and opinions expressed herein are the author's only and should not be attributed to Purdue Pharma L.P.



What's the Plan?

- Introductions
- Research Goals/Reporting Goals
- Setting the Stage – How did we get here?
- What is the Difference Between a Clinical Trial Registry and a Clinical Trial Database?
- Open Access Issues
- Other Issues for Consideration
- Discussion

Goals – Conducting Research vs. Reporting Research Results

- The goal of research is: To generate scientific and clinical knowledge
- The goal of reporting is: To ensure that scientific and clinical knowledge gained from research will be listed and shared from study initiation to conclusion to ensure that positive and negative findings can be evaluated in the broad context of outcome possibilities
  - Both positive and negative results have intrinsic value

Who said it?

- "Results! Why, man, I have gotten a lot of results. I know several thousand things that won't work."
- "Just because something doesn't do what you planned it to do doesn't mean it's useless."
- "I have not failed. I've just found 10,000 ways that won't work."

Thomas A. Edison

(US inventor, 1847-1931)

Setting the Stage – Some Important Events

2002	PhRMA publishes "Principles of Conduct of Clinical Trials and Communication of Clinical Trial Results" (the "PhRMA Principles")
June 30, 2004	PhRMA Principles updated
Sept. 16, 2004	International Committee of Medical Journal Editors proposes comprehensive trials registration; 11 member journals adopt trials registration policy
Oct. 1, 2004	PhRMA website, www.clinicaltrialsresults.org, a clinical study results database becomes available to the public
January 6, 2005	PhRMA announces new voluntary disclosure policy
January 6, 2005	International Alliance on Clinical Trial Disclosures publishes "Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases" (the "Joint Position")
July 1, 2005	Deadline for posting all new studies (not just studies of serious or life-threatening diseases) to www.clinicaltrials.gov
Sept. 13, 2005	Deadline for posting all ongoing studies (not just studies of serious or life-threatening diseases) to www.clinicaltrials.gov

What is the difference between a Clinical Trial Registry and a Results Database?

- Clinical Trials Registry
  - "Provides patients and physicians with information about ongoing clinical trials that are open and recruiting patients."*
- Clinical Study Results Database
  - "Designed to improve accessibility to, and transparency of, the results of clinical studies. This electronic database is a central standardized repository for published and unpublished clinical studies that have already been completed. This industry-sponsored registry will provide access to the results of all hypothesis-testing clinical studies of marketed drugs – regardless of outcomes."*

* Descriptions taken from PhRMA website.

PhRMA Principles

- Pharmaceutical Research & Manufacturers of America (PhRMA) Principles of Conduct of Clinical Trials and Communication of Clinical Trial Results (the "Principles")
  - www.ClinicalStudyResults.org
  - Standardized format, including:
    - Results from all hypothesis testing clinical studies
    - Mainly Phase III and Phase IV studies
    - October 1, 2002 forward
    - For all drug products approved in the United States
    - Regardless of publication status
    - Companies urged to post unpublished study summaries within one year of completion

Journal Publication – Statement of the International Committee of Medical Journal Editors

- ICMJE member journals* require as a condition of consideration for publication, registration in a public clinical trials registry
  - Must register on or before onset of patient enrollment;
  - Applies to all trials enrolling after 7/1/05.
  - For trials enrolling before 7/1/05, registration required by 9/13/05 before journal will consider publishing trial data
- ICMJE does not advocate a particular registry but requires that the registry be:
  - Accessible to the public
  - Free of charge
  - Open to all prospective registrants
  - Managed by a non-profit organization
  - Valid
  - Electronically searchable
  - Contain standardized entries
- ICMJE states that the only registry meeting all requirements at time of policy publication (9/16/04) was www.clinicaltrials.gov, sponsored by the US National Library of Medicine.

* JAMA, NEJM, New Zealand Medical Journal, Norwegian Med. J., CMAJ, The Lancet, National Library of Medicine, Annals of Internal Med, Croatian Med. J., Dutch Journal of Med., J. of the Danish Med. Assoc., Annals of Internal Med., The Med. J. of Australia

Joint Position* on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases

- Desire to balance public health benefits associated with clinical trial publication with protections of individual privacy, intellectual property and contract rights
- Committed to transparency
- Two different methods of communication
  - Clinical Trials Registry
  - Clinical Trial Results Database
- Implementation Dates:
  - Trials initiated on/after 7/1/05 should be included in registry.
  - Ongoing trials should be included by 9/13/05.

* Industry groups include European Federation of Pharmaceutical Industries & Associations, International Federation of Pharmaceutical Manufacturers and Associations, Japanese pharmaceutical Manufacturers Association and Pharmaceutical Research & Manufacturers of America

Joint Position (cont.) – Registry v. Database

- Clinical Trials Registry – a repository of information on ongoing clinical trials
  - All non-exploratory clinical trials submitted for listing in a free publicly accessible registry within 21 days of initiation of patient enrollment, unless there are alternative national requirements
  - Registry contains basic information sufficient to inform interested subjects and practitioners about how to enroll in trial
  - Trials identified by unique identifier that permits users to track a trial through multiple databases, including results databases

Joint Position (cont.) – Registry v. Database

- Clinical Trials Results Database – a repository for the summary results of completed clinical trials
  - Results of all non-exploratory clinical trials conducted on a drug that is approved for marketing and is commercially available in at least one country should be disclosed on a free, publicly accessible clinical trial results database, regardless of outcome
  - Exploratory study results should be publicly disclosed if they have significant medical importance and may impact labeling
  - If results are published in a peer-reviewed medical journal, the database should include a citation or link to article or summary of results, posted in standardized format
  - All results should include the trial's unique identifier code
  - Results should be posted within one year after drug is first approved and commercially available within a country or, for trials completed after this initial phase, within one year of trial completion unless such posting would compromise publication in a peer-reviewed medical journal.

Transparency & Accountability

- With regard to the industry decision to publish summaries of clinical trial results to a results database, PhRMA president Billy Tauzin said that:

  "[The industry is] doing this because [it] recognizes that sometimes what the law requires doesn't give patients all they need. Patients – both those with manageable conditions and those who are gravely ill – need information about new drugs that are being tested."

- "PhRMA's goal is to provide scientific information in a format that is useful to practicing physicians."
  - "a clearinghouse of information"
  - "one-stop shop"

Some Final Thoughts – a.k.a. Questions We Will Ask And (Try To) Answer

- By reporting both positive and negative clinical trial results, are we flooding the medical literature and websites with data that is not necessarily useful? Does that present any ethical dilemmas?
- Could providing positive and negative clinical trial results on the internet negatively impact the doctor/patient relationship?
- Will mandatory clinical trial reporting make pharmaceutical companies more risk averse? Will this affect clinical trial design for your company? If so, how?
- What is the impact of reporting clinical trial information on competitive advantage when bringing a new drug to market?

Some Final Thoughts – a.k.a. Questions We Will Ask And (Try To) Answer

- Would you expect that reporting clinical trial data in a database or on a website would hamper an investigator's ability to publish findings in a medical journal?
- What kind of constraints do these reporting requirements place on your company?
  - Time constraints?
  - Financial constraints?
  - Staffing constraints?
- If a clinical trial focuses on an off-label use or is a head-to-head comparison with another product, how should results be reported to avoid being construed as promotion claims?

Some Final Thoughts – a.k.a. Questions We Will Ask And (Try To) Answer

- Advocates of clinical trial results reporting feel that the websites will increase transparency and accountability within the industry which will, in turn, enhance the public trust in pharmaceutical companies. Do you think this is the case?