Clinical Trial/Results Disclosure

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Goals of Clinical Trial Disclosure

**Provision of information on clinical trials to patients/health care providers (HCPs) to:**

- Raise patient/HCP awareness of ongoing clinical trials
- Enhance/contribute to transparency of clinical trial information:
  - ongoing/active/completed clinical trials
  - results of clinical trials

**Compliance with guidance recommendations/legal requirements relating to:**

- Registration
- Results disclosure
Registration/Results Disclosure: Current Laws & Guidance

**Registration:**
- Guidance:
  - ICMJE, IFPMA, WHO, PhRMA
- Law:
  - FDAMA 113
  - State of Maine

**Results Disclosure:**
- Guidance:
  - PhRMA, Registration
- Law:
  - State of Maine
History of Disclosure

- Concept of clinical trial registries was initially considered in the 1970s
- 1988 - Hope Act: registration of AIDS Studies
- 1997 – FDAMA 113 Law: registration of studies on serious, life threatening illnesses
- 2002 – PhRMA Principles: register all hypothesis-testing studies
- 2004 – ICMJE Editorial: register to publish
- 2005 – State of Maine law: website posting of trials/trial results, including adverse events
State Legal Requirements RE: Clinical Trial/Results Disclosure

State of Maine Law:

• Signed into law: June 2, 2005
• Effective date: October 15, 2005
• Information for disclosure:
  – “Beginning October 15, 2005, a manufacturer or labeler of prescription drugs dispensed in Maine that employs, directs or utilizes marketing representatives in Maine shall disclose its clinical trials and information concerning results of clinical trials on a publicly accessible website.”
• Applies to clinical trials conducted on or subsequent to October 15, 2002

14 states are considering legislation of this type
PhRMA Guidance
RE: Clinical Trial/Results Disclosure

Pharmaceutical Research and Manufacturers of America:

• Timing: for marketed products only, disclosure of results should be within 1 year of clinical trial completion
  – Post-marketing study results should be registered within 1 year of study/trial completion

• Definitions of disclosure:
  – results of clinical trials should be posted on a publicly accessible database, regardless of trial outcome
International Federation of Pharmaceutical Manufacturers and Associations:

• **Timing:** disclosure should be within 1 year after the drug is commercially available/marketed in at least 1 country
  – *but posting of results may be delayed up to 1 year subsequent to announcement of the intent to publish*

• **Definitions of disclosure:**
  – prefer peer reviewed publication
  – other venues (i.e., abstract/poster/presentation at scientific mtg.)
Clinical Trials: Protocol/Result Databases/Websites

- **Disease-specific websites:**
  - National Cancer Institute ([www.cancer.gov](http://www.cancer.gov))

- **National/country specific websites:**
  - [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov)
  - [www.ClinicalStudyResults.org](http://www.ClinicalStudyResults.org)

- **Individual company websites:**
  - [www.lillytrials.com](http://www.lillytrials.com)

- **Coordinating websites:**
  - [www.CenterWatch.com](http://www.CenterWatch.com)
Clinical Trials: Protocol/Result Databases/Websites

- There is no *single* global comprehensive registry
- Numerous clinical trial/protocol registries exist globally:
  - WHO International Clinical Trials Registry
  - International Federation of Pharmaceutical Manufacturers & Associations
- Pharmaceutical member companies of various national/international organizations have:
  - Committed to post data derived from completed clinical trials on all marketed products in an accessible clinical trials results database 1 year after last-patient-out or end of trial
  - If results are to be published, sponsoring companies have an additional year to complete the publication process
Goals/Outcomes: Clinical Trial Disclosure

- Provision of information on clinical trials to patients/health care providers (HCPs) to:
  - Raise patient/HCP awareness of ongoing clinical trials
  - Enhance/contribute to transparency of clinical trial information:
    - ongoing/active/completed clinical trials
    - results of clinical trials

- Compliance with guidance recommendations/legal requirements relating to:
  - Registration
  - Results disclosure

- How will disclosure of clinical trial data affect publication in peer-reviewed journals?
Journal Survey

200 Journals

31 Unusable 89 Responses

58 Useable

**Does journal have publication policy?**

- Top 100 Journals (30 journals):
  - Yes: 60%
  - No: 22%
  - N/A: 20%

- Lower 100 Journals (28 journals):
  - Yes: 43%
  - No: 29%
  - N/A: 19%

**Would the journal publish if data were posted?**

- Top 100 Journals (30 journals):
  - Yes: 72%
  - No: 8%
  - Case-by-case: 6%

- Lower 100 Journals (28 journals):
  - Yes: 75%
  - No: 8%
  - Case-by-case: 17%
Panel Discussion

To ask a question, please click the ‘Q&A’ icon at the top-left of your screen and type in your query. Every attempt will be made to answer each question.

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Authorship

Jeffrey E Fletcher PhD
Senior Clinical Publications Lead
AstraZeneca
Authorship

Authorship definition unclear long before pharmaceutical, biotechnology, and device industries started publishing data
- Publish or perish
- Chairman’s names added
- Influential others added
- Acknowledgments insufficient recognition
- I’ll pat your back, you pat mine

Some industry publications also based authorship on unclear definition
- External vs internal authors
- Selection of external authors

Need for clear definition of authorship
Authorship guidelines

Who should be an author?

- **ICMJE (II.A.1)** Authorship credit should be based on 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

- **PhRMA (p20)** Persons providing substantial contributions into study conception and design, OR data acquisition OR data analysis and interpretation AND writing/revising manuscript AND final approval of version to be published

- **COPE (p70)** Authorship should minimally imply responsibility for a section, balance intellectual contributions (conception, design, analysis, writing) against collection of data & other routine work, responsibility for content, professional writers (not clear whether they are authors or just acknowledged)

- **GPP (p153)** ICMJE guidelines are good starting point, respect requirements of journal, outline authorship policy in investigator’s agreement
External authors

- External authors optional, not required (internal authors may be sufficient if external expert advice not essential)

- **Right reason:** Experts’ insights bring value to study or publication, improving patient care
  - Improved study design
  - In-depth data analyses
  - Novel interpretation of results or clinical perspective

- **Wrong reason:** Expert author increases likelihood of acceptance by top-tier journal and community
  - Minimal author input
  - Restricted author access to full database
  - Marketing-driven interpretation of results
Who should be an author?

- Internal clinicians, biostatisticians, health economics experts involved in study design, data analyses, and review of manuscript
- Investigator assisting with experimental design and recruiting a significant number of patients
- Investigator having no involvement in study design, but recruited a significant number of patients and should provide considerable insight into data analysis and interpretation
- External expert having no involvement in study design, no recruited patients, but should provide considerable insight into data analysis and interpretation

Anyone meeting authorship criteria (eg, any of the above, whether internal or external individuals)
Who should be acknowledged?

- **ICJME (II.A.1)** Generally list nonauthor investigators, purely technical help, writing assistance, financial and material support (must give permission to be acknowledged)

- **PhRMA (p21)** Persons analyzing and interpreting data, or producing manuscripts and presentations must act in conjunction with author and should be recognized (author or acknowledgments, based on contribution)

- **COPE (p70)** Decide early in planning (no definition of those acknowledged)

- **GPP (p153)** People making significant contribution (but do not qualify as authors), funding, company involvement in data analysis or manuscript preparation (if not apparent in author list)
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Metrics

Lois E. Wehren, M.D.
Associate Director, Medical Communications
Merck Research Laboratories
Why Do We Publish?

- Share information on our studies with the scientific/medical/payer communities
- Fulfill regulatory/legal requirements to publish trial results
- Build relationships with authors/investigators management
- Compete effectively with other products
Need for Standardized Metrics

- Senior management must be able to evaluate productivity

- Want a metric or metrics that is (are)
  - Straightforward
  - Quantifiable
  - Able to be benchmarked
  - Applicable across franchises

- However, not all products are the same
  - Franchises are idiosyncratic
  - Products at different points in life cycle
Factors to Consider

- **Status in lifecycle**
  - Pre-launch communication needs – education, awareness
  - Clinical data heavy around submission/launch
  - Secondary analyses; pooled analyses; reviews
  - Late lifecycle products likely to have few new trials
  - New indications

- **Data availability**
  - Number of indications
  - When, what kind

- **Audience**
  - Specialty vs. primary care
  - Managed care
  - Multiple indications = multiple audiences
  - Global vs. regional

- **Company commitment**
  - Resources – money, FTEs

- **Competitive marketplace**
What Does the Company Want to Measure?

Impact of publications/presentations on audience(s), which is:

Change in behavior on part of prescribers
What is the Impact of Publications on Individual Practice? the Market?

- Next to no data on this
- No widely accepted measures
  - May be proprietary company information
- Possible techniques
  - Assess market in months following publication of key findings
    - Large number of confounders
  - Health care provider surveys
    - Identifying appropriate populations
  - Compare product history within company – Drug X launched with no Phase 3 papers published while Drug Y had 2
    - Confounders
What Can the Organization Measure?

- **Surrogate endpoints**
  - **Volume**
    - Number of publications/presentations
    - Number of publications/message
  - **Value**
    - Ability to address gaps
    - Addressing key audiences vs. all audiences
  - **Key publications**
  - **Keeping noise level up relative to competition**
  - **Team efficiency**
    - Average publication turnaround times
    - Percent acceptances on first submission
  - **Money**
    - ROI
The Hard Truth

- Trying to fit all products into a one-size-fits-all metric is often impractical and inappropriate.

- Financial measures may be more effective across products, but don’t yield meaningful information about publication value.
  - Planning costs not factored in.

- Need to adapt to changes in strategic imperatives over time.
  - Change in competitive landscape.
One Solution

- Establish key benchmarks for given time period
  - It doesn’t have to be annually
- Benchmarks must be linked to strategic needs of product
- Clearly communicate goals throughout the organization
  - Link to strategy
- Have clearly agreed upon time points to assess plan success, with clear accountability
- Ultimate objective is that plan meets its strategic imperatives
  - Inappropriate measures might give reassuring results but not truly assess value of publication plan
- Adaptation to changing environment can be important objective
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