Disclosure of Clinical Trial Results: Obligations and Industry Practices

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A Short History for Clinical Trial Disclosure

1980’s
1988 Hope Act (HIV/AIDS)

1990’s
1997 FDAMA Section 113
ClinicalTrials.gov v1.0

2000
ClinicalTrials.gov v2.0

2001
Celebrex®, Paxil®, Vioxx®, ICMJE editorial #1
(registration)

2004
WHO ICMJE editorial #2 (20 fields)
Maine law
Trasylol®

2005
TGN1412
WHO All clinical trials
Trasylol®
Maine Regs.

2006
FDAAA
ICMJE editorial #3 (all trials)
Avandia

2007
Maine AE reporting
Other US States Pending

2008
More Maine regs
More EU requirements

Increasing Foreign Registry Requirements
How Did We Get Here?

- Inconsistent reporting of protocols, results
- High-profile legal action against large pharma
- Lack of transparency of all stakeholders (industry, govt’ agencies, journals)
- Changing landscape of regulations
FDAAA Title 8 Basics (1)

- Registry milestones
  - Trials in serious, life-threatening conditions
    - Ongoing trials: 27 Dec 2007
    - New trials: within 21 days of FPFV
  - All other applicable trials
    - Ongoing trials: 27 Sept 2008
    - New trials: within 21 days of FPFV
FDAAA Title 8 Basics (2)

- Results milestones
  - Basic results required by 27 Sept 2008
    - Demographic, baseline characteristics
    - Primary, secondary outcomes
    - Point of scientific contact
    - Contractual restrictions of investigators ability to discuss results
  - Serious adverse event, frequent adverse event required by 27 Sept 2009
FDAAA Title 8 Basics (3)

- Expanded results rules expected by 27 Sept 2010
  - Lay and technical summary of results?
  - Posting trials of unapproved drugs?

- US Public Law 110-85 (FDAAA)
  - (http://prsinfo.clinicaltrials.gov/fdaaa.html)
Latest and Greatest: Maine

- Adopted revised regulations
  - Released 29 October 2009
  - Came into effect 02 November 2009

- Previous regulations different from FDAAA (e.g., adverse event reporting)

- New regulations more in line with FDAAA (i.e., similar field requirements)
New Maine Regulations (1)

- Applicable clinical trials
  - Phase II-IV
  - Off-label uses
  - Observational
  - Post hoc analyses
- Bioequivalency trials of a drug against the innovator drug or biological product, or against another drug or biological product
New Maine Regulations (2)

- Trial conducted outside the US that
  - have ≥1 sites within the US or its territories
  - results have been/are intended to be submitted to/held for inspection by FDA as part of research/marketing application
  - sponsor relies upon results for marketing/promotional claims or educational efforts/materials to prescribers/consumers in Maine
New Maine Regulations (3)

- Trials exempt from new regulations
  - Protocols registered before Jan. 1, 2010
  - Results submitted before Jan. 1, 2010
  - Observational trials completed before Jan. 1, 2010
New Maine Regulations (4)

- Any discontinued clinical trial
  - Must be registered by latest of
    • 21 days after patient enrollment begins
    • first date drug/bio product is dispensed, administered/delivered/promoted in Maine for any indication
  - Must post results by latest of
    • 1 year (+ applied extensions) after trial completion
    • first date drug/bio product is dispensed, administered/delivered/promoted in Maine for any indication
**New Maine Regulations (5)**

- All post hoc analyses with significant deviation/correction of previous results of interventional trials are subject to new regs

- Data field requirements now closely mirror FDAAA/ClinicalTrial.gov requirements

- Must complete all mandatory data elements and all other relevant (“optional”) data elements (if data available)
New Maine Regulations (6)

- Links/citations to all articles by any of the trial investigators published in peer-reviewed medical journals summarizing safety/efficacy
- Sponsors have 120 days after adoption of new regulations to post information
- Prescription Drug Clinical Trial Reporting - Final Rule
  (www.maine.gov/dhhs/boh/clinical-trials-reporting-final.doc)
Ex-US Clinical Trial Disclosure (1)

- Article 57(2) of Regulation (EC) No726/2004
  - Relates to Phase II-IV adult clinical trials in EudraCT

- Article 41 of Regulation (EC) No1901/2006
  - Relates to all paediatric clinical trials

- Submissions (sometime in 2010)
  - Both: protocol information submitted at CTA; made public immediately at CTA approval
  - Paediatric results submitted within 6 months of trial completion; adults within 1 year of trial completion; both: made public immediately after submission
Ex-US Clinical Trial Disclosure (2)

- Many registries/results databases are populated by the health authorities/ regulatory agencies
- 21+ mandated ex-US registers
- 13+ voluntary ex-US registers
  - Many now may require native languages
Where Do We Go From Here?

“Such other categories as the Secretary determines appropriate”? 
Information Resources

- DIA Clinical Trial Registry/Results Database Working Group
  - Meets ~1\textsuperscript{st} Tuesday every month
- NIH/ClinicalTrials.gov staff
Contact Information

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