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FDAAA One Year Later: Recent Developments in Clinical Trial Posting Requirements

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Game Plan

- Clinical Trial Results Databank
- New Certification Requirement
- Developments from Maine

CLINICAL TRIAL RESULTS DATABANK

Expanded Databank: Overview

- Food and Drug Administration Amendments Act of 2007 (FDAAA) expands existing NIH registry
  - More studies must be submitted
  - More information on each study must be submitted
- FDAAA creates a Clinical Trial Results Databank
  - Links to existing results information
  - Basic results databank
  - Expanded results databank

Basic Results Databank

- By September 27, 2008, NIH must establish a basic results databank

- Required Trials
  - "Applicable clinical trial" (i.e., controlled clinical trial other than a phase I study)
  - Initiated after September 27, 2007 or ongoing as of December 26, 2007;

  AND

  - Involves an approved drug product or a cleared or approved device

Basic Results Databank (cont'd)

- Required Information
  - Tables of patient demographic data
  - Tables of primary and secondary outcome measure data
  - Point of contact
  - Information on any agreements restricting ability of the principal investigator to publish or discuss results

- Adverse Event Information
  - By March 27, 2009, Secretary must issue regulations determining the best method for reporting adverse event information for approved drugs
  - If regulations are not issued, requirement becomes self-executing

Basic Results Databank (cont'd)

- Submission Deadline: 1 year after the estimated or actual completion date, whichever is earlier

- Extensions
  - Drug or device not yet approved or cleared for any use: 30 days after approval or clearance
  - Drug or device not yet approved or cleared for studied use: 30 days after approval or clearance, non-approval or NSE, or withdrawal without resubmission for 210 days
  - Good cause: as necessary

- *No explicit extension available for seeking publication in peer-reviewed journal (though "good cause" might apply)*

NIH/FDA Implementation

- Results databank is now operational and available for company postings
- Guidance Documents
  - NIH Draft Data Elements Definitions
  - FDA reportedly working on guidance document
- Adverse Event (AE) Information
  - NIH currently permitting adverse event (AE) information to be posted voluntarily
  - Failure to implement AE reporting through required rulemaking

Common Issues

- Do results need to be posted now?
  - Yes, but very few trials likely are subject to the new posting requirements immediately because
    - The results posting requirement applies only to studies initiated after 9/27/07 or ongoing as of 12/26/07; and
    - Posting deadline is one year from completion date
  - If you post results "voluntarily" (i.e., when not required), you may be subject to additional posting requirements under 42 USC 282(j)(4)(A)

Common Issues (cont'd)

- Are foreign clinical studies required to be submitted?
  - Does it matter if another company is conducting the studies?
  - FDA guidance should address this and other issues
- Are observational studies covered?
  - Is the trial controlled?
  - Does the study involve only the use of a marketed drug in the course of medical practice?

Common Issues (cont'd)

- What happens if study structure makes it impossible to meet deadlines (e.g., blind reads, longer term secondary outcomes)?

- Can posting be delayed if seeking publication in peer-reviewed journal?

Practice Tips

- Ensure that licensing, co-development, contract research organization (CRO) and investigator agreements specify who will be responsible for submitting clinical trial information to NIH
- Make “voluntary” submissions carefully and with full appreciation of the added obligations
- Adopt policies/SOPs for clinical trial reporting and follow them
- Request extensions when necessary
- Design trials with new posting requirements in mind

NEW FDAAA CERTIFICATION REQUIREMENT

Databank Compliance Provisions

- Certifications
- Pilot Quality Control Project
- Public Notice of Violations
- Prohibited Acts
- Civil Money Penalties

Certifications

- As of December 26, 2007, various applications (including NDAs, BLAs, INDs, PMAs, and 510(k)s) must include a certification that all applicable databank requirements have been met

- Form FDA-3674 implements the certification requirement

- FDA is requiring certifications for investigational new drug applications (INDs), despite industry objections and questionable legal authority

Certifications (cont'd)

- Arguments against certifications for INDs
  - INDs are not "applications" under section 505; they are "exemptions" from the need to file an application
  - IDEs clearly do not need to include certifications, and there is no good policy reason to distinguish between INDs and IDEs
  - Since INDs must be submitted before a trial starts, there would be nothing to certify
- FDA rejected these arguments
- FDA policy may still be challenged, either pre-enforcement or as part of enforcement action

FDA Draft Guidance

- FDA adopts extremely broad reading of scope of certification requirement
- FDA identifies certain exemptions
  - Safety reports
  - Meeting requests
  - Promotional materials
  - CMC amendments or supplements
  - Non-clinical pharmacology/toxicology submissions
  - ANDA amendments/supplements that do not contain bioequivalence data
  - 510(k)s without clinical data

Why does it matter?

- Failure to submit a required certification of compliance or the knowing submission of a false certification is a “prohibited act”

- A person who commits a “prohibited act” as specified above is subject to
  - Civil penalties (e.g., seizure, injunction)
  - Criminal penalties (imprisonment and fines); and
  - Civil money penalties (CMP) up to $10,000 per day with no statutory cap

MAINE CLINICAL TRIAL REPORTING UPDATE

Maine Results Posting

- Maine recently stated that, as of 12/8/08, companies must post results information under Maine law on ClinicalTrials.gov rather than on other publicly accessible internet sites

- Re-posting of studies previously posted on other sites (e.g., company, PhRMA) is not required

Maine Position - Issues

- Summary format (ICH E3) required under Maine law not supported by ClinicalTrials.gov
  - Maine states it will deem federal reporting as satisfying Maine requirements
- Many Maine submissions may be treated as "voluntary" submissions under federal law, triggering additional posting obligations
- Potentially makes federal AE reporting mandatory rather than voluntary in absence of required rule-making

Contact Information

Scott M. Lassman is a Partner and Co-Chair of the FDA Practice Group in the law firm of Wilmer, Cutler, Pickering, Hale & Dorr (WilmerHale), where he specializes in FDA legal, regulatory and policy issues. Prior to joining WilmerHale, Mr. Lassman served as Senior Assistant General Counsel for the Pharmaceutical Research and Manufacturers of America (PhRMA), where he was responsible for FDA regulatory and policy matters. Mr. Lassman played a leading role in negotiating the $400 million Prescription Drug User Fee Act (PDUFA) agreement with FDA, which recently was signed into law as FDAAA. Mr. Lassman's strong policy background at PhRMA is complemented by more than ten years of experience in private practice solving complex FDA legal and regulatory issues for pharmaceutical, biotechnology and medical device clients.

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Open Discussion/Audience Q&A

Next ISMPP U

- **Topic:** Richard A. Epstein, James Parker Hall Distinguished Service Professor of Law at the University of Chicago, and author of Overdose: How Excessive Government Regulation Stifles Pharmaceutical Innovation FDAAA Legislation Update
- **Date:** November 19th
- **Time:** 11am EST – "Brunch and Learn"

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