2009 Happenings in the World of Regulatory Compliance and Clinical Research Transparency

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The Events

- Fulfilling Post Marketing Requirements and Post Marketing Commitments – The Booz Allen Hamilton Report (April 10, 2009)

- Public Meeting on Expansion of the Clinical Trials Registry and Results Data Bank (April 20, 2009)

Regulatory Compliance

Sources of Post Marketing Requirements and Commitments

- Studies that were a condition of Accelerated Approval
- Studies in pediatric patients required under PREA
- Studies the FDA can require under FDAAA (ie. post-marketing requirements)
- Studies the sponsor committed in writing to conduct (ie. post-marketing commitments)

Tracking and Fulfilling Commitments
What You Heard in the Press

"Performance of postmarketing safety studies is virtually out of the FDA's control, with the majority of study commitments never initiated by the pharmaceutical industry and not pursued by FDA."

"1231 as yet unsatisfied commitments through September, 2005. Almost two thirds of them (n=797) were "pending" (i.e. not initiated)"

Furberg, et al.; Arch Intern Med 2006; 166:1938-1942

Bloomberg Article

- **Key Quotes**
  - "…860 post-approval studies that drugmakers haven't started even though they agreed to complete them, a Bloomberg News analysis of FDA database shows."
  - "It isn't clear whether the FDA or the drugmakers are more at fault. In some cases, the FDA's records on the status of studies appear to be wrong."
  - John Jenkins, Director, Office of New Drugs, CDER
    - "We have a huge workload, and we have to prioritize which things we devote resource to"
    - "The FDA has no reason to believe its database contains widespread errors"
  - "The FDA said it relies on information from companies to update the database and expects them to point out errors"

- **Other Information**
  - GSK Case Study
    - Searching the FDA database the reporter saw 31 unfulfilled (28 pending) postmarketing commitments for GSK products, 860 for industry overall BUT
    - GSK had submitted reports for 24 commitments
    - 1994-1996: 5; 2001-2004: 10; 2005-2006: 9

Booz-Allen-Hamilton Evaluation*

- Evaluation required by FDAAA
- Evaluation based on 1531 open PMRs/PMCs on Sept. 27, 2007

Key Findings

- FDA database status for PMR/PMCs
  - Accurate for 42% of studies
  - **INACCURATE FOR 51% OF STUDIES WITH UPDATES REQUIRED**
- Reasons for inaccuracies
  - Annual Status Reports not reviewed (47%)
  - FDA regulatory project managers unaware of final report submissions (44%)
- **"THE UPDATED STATUS DATA SHOW THAT MOST PMRs/PMCs HAVE BEEN INITIATED AND MORE THAN HALF OF THEM WERE EITHER SUBMITTED, FULFILLED OR RELEASED"**

Clinical Research Transparency: Highlights from Public Meeting

Study Results Posting: Lay Summaries

- Title VIII of the FDA Amendments Act stipulates that not more than 3 years after enactment the HHS Secretary will expand the NIH study results database by rulemaking to provide:

  "A summary of the clinical trial and its results that is written in non-technical, *understandable language for patients,* if the Secretary determines that such types of summary can be included *without being misleading or promotional.*"

- Public meeting held on April 20, 2009
  - Provide an update on clinicaltrials.gov database
  - Determine need for lay summaries
  - Identify a process for producing summaries

Items of General Interest

- Posting protocols to clinicaltrials.gov
  - 71,398 posted as of April 2009
    - 33% NIH, Industry and Academic
  - 300-350 posted per week at steady state

- Posting study results
  - General goal of providing information that would be informative to someone who was not part of the study
  - Results form 678 studies posted as of April 2009
    - 66% Industry, 33% other
  - 40/week at present, 150/wk at steady state

- New PhRMA commitments
  - All patient trials in scope
  - Results from terminated programs will be posted

Lay Summaries
Key Issues to be Addressed

- Determining need
  - NEJM was not supportive because of the authorship issues
  - Others (e.g. Consumer's Union) felt they were critical

- Authorship
  - Who will produce summaries that are viewed as unbiased and non-promotional?
    - Distinction between promotional and non-promotional is very subjective
    - PhRMA awaiting revision of FDA regulations to address lay summaries
    - Can FDA provide review support for these like they do for advertising?
    - What about independent writing groups?
  - Reading level?

Lay Summaries
Key Issues to be Addressed

- Content review
  - Who will provide oversight of accuracy?
  - How will disagreements on content be adjudicated?
  - What role can the lay public/patient advocacy groups play to assure comprehension?
- Financial support
  - Suggestion that this be covered by increased User Fees
    - User Fee Act only covers 1/3rd of results registrants
- Indemnification for authors