

**NLM Board of Regents Working Group on Clinical Trials**  
**Teleconference, July 1, 2009**

**Participants:** Thomas Bradley, Robert Califf, Jordan Cohen, Sherrilynne Fuller, Donald Kennedy, Barbara McNeil, Cynthia Morton, James Powell, Frank Rockhold, Louis Rossiter, Alastair Wood NLM Staff, Jerry Sheehan, Tony Tse, Becky Williams, Deborah Zarin.

I want to follow-up on the key discussion items from last week's call. I would appreciate comments on any topic, but items #1 and #2 are of most immediate interest due to upcoming meetings here.

**1. Should we expand the requirements to report results for trials of unapproved products?**

- a. During the discussion, the following issues were discussed:
  - i. There was support for mandating results reporting for trials of the unapproved drugs or devices; specific proposals varied. Alastair Wood's NEJM article (attached) includes recommendations, with which some others on the call agreed.
  - ii. Some suggested that results of Phase 1 trials should be considered (e.g., issues surrounding the TGN 1412 trial).
  - iii. Optimal scope and timing remained an open question.
- b. To continue the discussion and to elucidate specific aspects of a policy, please send me comments on the following proposal, which I will attempt to summarize and circulate back to the group:

Results must be reported for all trials that meet the requirements set forth in the law, regardless of the approval status of the drug or devices used in the study, within 12 months of the "primary completion date" (i.e., date of final data collection for the primary outcome measure(s)).

Note the following about this proposal:

- i. Broader than the one proposed by Alastair
- ii. Consistent in scope with the proposed EMEA rule for drug trials
- iii. Standardizes timeframe for approved and unapproved drugs and devices

**2. Discussion of acceptable reasons for allowing "Extensions" to the "Due Date" for results reporting**

- a. Natural and other "disasters" is one category of acceptable reason.
- b. Circumstances in which ongoing data collection might legitimately block the ability to report results for the primary outcome measure(s) were discussed as another category.
- c. There was some support for the notion of requiring all pre-specified outcomes to be reported 12 months after data collection for the primary outcome measure.
- d. Some also suggested that, for studies with more than one primary outcome measure (e.g., co-endpoints) with different data collection time points, the latest time frame would be used to determine the "primary completion date" (rather than the earliest, as currently drafted).
- e. Extensions could be considered if, at the time of the due date, data are being collected for a secondary outcome measure only if the pre-specified analysis plan for that measure meets certain requirements. (I am hoping that Frank Rockhold will draft such criteria for discussion by the WG.)

**3. Non-Serious Adverse Event Reporting**

- a. The scientific rationale for moving the frequency threshold from 5% to zero (i.e., all

- adverse events) was discussed.
- b. In a related discussion, the default public view of non-serious adverse events could be modified in different ways (e.g., enable the user to control how much data would be displayed; not displaying AE data directly on the default page, requiring users to explicitly request AE information).
- c. The importance of understanding whether data were collected systematically or reported spontaneously was also discussed.

#### **4. Reporting Deaths in a Single All-Cause Table**

- a. The importance of reporting all deaths from all causes in a single table, possibly only in the "academic view," was discussed.
- b. There was some concern that some deaths might be counted multiple times, if sufficient instructions are not provided.