



APR 13 2012

The Honorable Henry A. Waxman
Ranking Member
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515

Dear Representative Waxman:

Thank you for your February 14 letter regarding the January 3 issue of the *British Medical Journal (BMJ)* on compliance with mandatory reporting of results to ClinicalTrials.gov. Your interest in this matter is understandable, and I want to assure you that the National Institutes of Health (NIH) regards the submission of clinical trials results as critically important. An identical letter is being sent to Representatives Diana DeGette and Edward Markey.

Dissemination of clinical trial results is critical for scientific and public health reasons, and there is no question that Title VIII of the Food and Drug Administration Amendments Act (FDAAA) of 2007, which you and others helped enact, is improving the transparency of clinical trials. From a policy standpoint, the expansion of ClinicalTrials.gov furthers our longstanding commitment to the timely sharing of scientific knowledge and the rapid translation of research to improve human health.

As required by FDAAA, sponsors of certain applicable clinical trials are required to submit results and accomplishments of their activities to ClinicalTrials.gov, thus making this information available to the research community and public at large. In 2008, NIH launched the Results Data Bank to enable submission of the basic results information, and the module for accepting adverse event information became mandatory in September 2009. Additionally, the FDAAA requires that the Secretary of Health and Human Services issue regulations that will enhance compliance with both the registration and results components of the Act. Since the enactment of the FDAAA, NIH has worked closely with the Food and Drug Administration (FDA) to address the implementation and enforcement of all registration and results reporting provisions and to complete the Notice of Proposed Rulemaking (NPRM), the next step in completing implementation of the Act.

While the findings in the *BMJ* article are of concern to us because they suggest that compliance in reporting results on ClinicalTrials.gov is not what we would expect, we anticipate that once the proposed rule is published and final regulations are promulgated, compliance will be significantly improved. The NPRM currently in development will provide greater clarity about

the agency's thinking to sponsors of clinical trials in the business community and the academic research community about their obligations under FDAAA. The NPRM, when finalized, will further enhance understanding of what the agency requires of those who are subject to the law, particularly in terms of defining what is an 'applicable clinical trial,' timeframes for results submission, and penalties for noncompliance. NIH and FDA are working assiduously to complete the NPRM. We anticipate that the NPRM will be issued for public comment later this year.

Let me turn to your specific questions.

- 1) *Do the findings of the new study outlined above correspond with NIH's internal data on compliance with reporting requirements of section 801 of FDAAA? Please summarize NIH's internal compliance data.*

The FDA conducted a preliminary review of the data used by Prayle (made available by the authors on a public Web site) and identified a number of factors that influence the authors' analysis of results reporting, such as the inclusion of trials that did not meet the definition of 'applicable clinical trials' and trials that did not fall within the established timeframe, both provisions outlined in FDAAA. For example, uncontrolled trials and trials of unapproved products should not be included in such an analysis nor should trials where the responsible party submitted a nonpublic certification that it is seeking approval for a new indication, as such a certification provides for a potential delay in submitting the results for up to three years after the completion data of the trial. We also are aware that the authors may not have had access to some results that had been submitted on time but were in quality review prior to posting on ClinicalTrials.gov. These factors illustrate the complexity of accurately measuring compliance in the absence of a final regulation implementing FDAAA. Studies such as the Prayle analysis inform the NIH of the multifaceted issues surrounding mandatory reporting of results, highlighting areas where we can do a better job in terms of increasing compliance.

While the NPRM is under internal review, our focus continues to be on providing those who are subject to the requirements of the law with the information, tools, and assistance needed to understand and comply with the statute. Once the NPRM is issued, the responsible parties will have a better understanding of our interpretation of their obligation under FDAAA.

- 2) *Does NIH have adequate resources and authority to enforce reporting requirements?*

NIH has sufficient resources and authority to implement the reporting requirements.

- 3) *Does NIH believe additional statutory changes are necessary to address the issues of underreporting of clinical trial data and non-compliance with reporting requirements in Section 801 of FDAAA?*

We are confident that, when the regulations are in place, the clinical research community will be equipped to comply with the requirements, and the FDA will be able to enforce them more fully. At this juncture, it would be premature to conclude that statutory changes are needed to address any underreporting and noncompliance

In closing, I would again like to thank you for your interest in ensuring that the results of clinical trials are reported in a timely fashion and available to the public. NIH will continue to look into the data from the *BMJ* and other studies and do all we can to ensure further compliance.

Sincerely yours,

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Francis S. Collins, M.D., Ph.D.
Director



APR 13 2012

The Honorable Diana DeGette
Ranking Member, Subcommittee on
Oversight and Investigations
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515

Dear Representative DeGette:

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Director



APR 13 2012

The Honorable Edward J. Markey
Ranking Member
Committee on Natural Resources
U.S. House of Representatives
Washington, D.C. 20515

Dear Representative Markey:

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