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March 23, 2015

Francis Collins, M.D.
Director
National Institutes of Health
6011 Executive Boulevard
Suite 601, MSC 7669
Rockville, MD 20852-7669

RE: **RIN 0925-AA52 & Docket Number NIH-2011-0003**

Dear Dr. Collins:

The American Thoracic Society (ATS) appreciates the opportunity to comment on the national Institute of Health (NIH)'s recent NPRM proposals to enhance transparency of clinical trial results.

**General Comments**

The ATS welcomes the proposed changes that aim to increase the transparency of clinical trial data reporting and to improve decision making by patients and clinicians by enhancing access to up-to-date clinical trial data. This is an important and necessary step towards correcting existing problems with the current clinicaltrials.gov website.

There are, however, certain ambiguities in terminology and formulation of these proposed regulations that may continue to allow or facilitate the registration of unregulated or poorly regulated clinical trials as well as stem-cell and other medical tourism types of activities to the ClinicalTrials.gov website. This may result in public dissemination and visibility of misleading information. For example, the use of various terms in the proposed new regulations such as "certain clinical trials", "applicable clinical trials", and "specified clinical trials" to stipulate what needs to be listed in the registry is a potential source of confusion. A well-defined terminology that would unequivocally identify the type of clinical trials to which the new regulations apply would be preferable.

Further clarification of what constitutes a well-conceived and designed clinical trial would also be a helpful and welcome step for both the final rule and practices for listing trials on the ClinicalTrials.gov website.

**Adverse Events Reporting**

With regards to the reporting of adverse events, we recommend that the NIH revisit the attribution requirements as the goal is to identify (as best as possible) what is attributable to the therapy and not the disease. We suggest that the same major category be kept, with two subcategories to delineate between the therapies versus disease. Stratification around the 5% threshold could be considered for expected versus unexpected adverse events.

**Section 11.60 of the proposed rule**

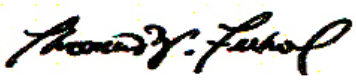
The ATS notes the voluntary submission of information is allowed for certain types of non-applicable clinical trials, such as Phase I trials under the proposed rule §11.60. This may include information on trials of unapproved, unlicensed, and unregulated products (http://www.nih.gov/news/health/nov2014/od-19.htm). We are concerned that this provision may dilute the reliability and integrity of the information submitted. In particular, the possibility remains that unproven stem cell and cell-based therapy interventions that lack solid preclinical data may be advertised to the public and clinicians under the guise of registered Phase I trials. The potential for abusing the mechanism of voluntary submission is illustrated by the observation that of the 182,821 trials listed on ClinicalTrials.gov only 34,413 trials (18.8%) are actively recruiting patients (information current as of January 27 2015). Of those, 52% are based outside of the U.S. and most likely voluntary submissions. A possible safeguard against the listing of medical tourism-like activities is the requirement of "U.S. FDA Approval, Licensure, or Clearance Status," or similar from Competent Authorities operating in countries to carry out clinical trials in compliance with ICH Clinical Trial for each intervention by rule §11.60. We believe that introducing a request for the name of the regulatory agencies who have already reviewed the preclinical data as part of an authorized clinical trial application and reference to peer-reviewed scientific publications may further protect patients and clinicians for promotional and deceptive information.

The proposal for inclusion of a lay (non-technical) summary of clinical trial results is a positive and welcome development as it will make understanding of complex information more accessible to the general public. By providing a tool that is patient-focused and public friendly, we believe that NIH can better inform patients, families and caregivers throughout the clinical trials process and improve recruitment in clinical trials in the U.S. through the creation of a more inclusive and transparent system. Although there are real risks of oversimplification of complex outcome measures or of inclusion of promotional and misleading material, as pointed out in the full text of the proposed rules, we strongly believe that both technical and non-technical summaries of the clinical trial results should be submitted for each trial. To ensure the veracity and integrity of these documents, stringent criteria and penalties should be established similar to the ones for noncompliance. We encourage NIH to consider developing a strategy to deter non-compliance.

Finally, the ATS recommends that the NIH establish and maintain a ClinicalTrials.gov public advisory committee consisting of researchers, industry representatives, and patient representatives. By including strong patient-focused engagement in this manner, we believe this advisory committee would ensure the long-term success of the ClinicalTrials.gov website.

The ATS thanks the committee for the opportunity to comment. If you have any questions, please Contact Nuala Moore, Associate Director of Government Relations at 202.296.9770 or Nmoore@thoracic.org.

Sincerely,



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