

## **Yale University Open Data Access (YODA) Project Public Comment Response to NPRM Proposed Rule**

The Yale University Open Data Access (YODA) Project at the Yale-New Haven Hospital Center for Outcomes Research and Evaluation (CORE) supports and applauds the Notice of Proposed Rule Making that introduces regulations for submitting clinical trial registration and summary results information to ClinicalTrials.gov in compliance with the FDA Amendments Act (FDAAA) of 2007. While the NPRM is an important step forward in promoting the responsible and comprehensive dissemination of clinical research findings, we believe that further steps can, and should be, taken to heighten the likelihood that the NPRM will successfully promote open science and facilitate the sharing of clinical research data. We suggest the following:

- The scope of these changes should be expanded to also include the availability of detailed summary results, such as Clinical Study Reports, as well as de-identified individual patient-level data, in addition to summary results. [Section III.C.1]
- The availability of summary results and de-identified patient-level data should also apply to phase 1 trials of drugs and biological products and small feasibility studies of medical devices. [Section III.C.1]
- The rule should include a definition of “small feasibility” for device trials (for example: “A small feasibility device trial is defined as a trial with less than x patients). [Section III.C.1]
- The rule should include a definition of “controlled” for single-arm studies as those looking at changes from historical controls or baseline. A comparison is needed. Alternatively, the term “controlled” can be removed so that all single-arm trials are included (as often occurs in trials of medical devices). [Section III.C.1]
- Consistent with the recent *JAMA Internal Medicine* article (Seife, 2015), ClinicalTrials.gov should note any inspections of trial sites that were classified as “official action indicated” during an FDA audit. [Section III.C.1]
- The national clinical trials database should link clinical trial registration numbers (NCT #s) to FDA documents, especially New Drug Applications, Supplemental New Drug Applications for new drug indications, Biologic Licensing Applications, Premarket Approval pathway clearances for medical devices, and so forth in order to increase transparency and better serve public health. Similarly, FDA documents should be required to include NCT#s for straightforward interoperability between the two sources of clinical trial information. [Section III.C.1]
- As suggested by the recent “Sharing Clinical Trial Data” report from the Institute of Medicine, the YODA Project supports publicly sharing summaries of results for clinical research and patient registries and lay-language summaries with participants immediately after publication of an article, presentation at a professional meeting, issuance of a press release, or disclosure to the Securities and Exchange Commission, or no later than 1 year after completion of the trial. In addition, as suggested above, data from clinical research and patient registries should be made available through data sharing initiatives to external investigators to promote open science. [Section III.C.8]
- Related to the prior point, mention of either an ongoing or completed clinical trial in a Securities and Exchange Commission filing should trigger trial registration on ClinicalTrials.gov within 30 days. [Section III.C.8]
- In regards to the proposed regulations to “require the submission of non-technical and technical narrative summaries if such summaries can be produced in such a way that they will not be misleading or promotional to potential users of the data bank, should a peer-review or editorial process be required for these?”, it would be helpful to expand on how these lay summaries can be written so that they are unbiased. The YODA Project would suggest that a medical writer

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external to the study sponsor be given the authority to prepare these summaries for all registered trials to ensure that summaries are unbiased and objective. An alternative would be to have these summaries peer-reviewed by a public health scientist external to the study sponsor. [Section III.C.6]

- Submission of full proposals to ClinicalTrials.gov should be required to assist in interpreting results information. The full proposals should include the informed consent template. [Section III.C.7]
- Quality control of results submitted to ClinicalTrials.gov is currently required to be completed within 30 days; however, oftentimes the review requires more time. Rather than publicly posting the submission as incomplete, alternative language should be posted in the interim that notifies readers that the results reported are preliminary. This would ensure that results are reported as soon as practicable. [Section III.C.12]
- The YODA Project supports the proposal to require the submission of additional types of information related to adverse events and feels that the benefit to society outweighs the burden to investigators. This includes an all-cause mortality table and submission of information related to adverse event collection approach and time frame. [Section III.C.15]
- The YODA Project supports the potential mechanism (1) to allow a responsible party to voluntarily give the NIH permission to release clinical trial registration information for an applicable device clinical trial of a device that previously has not been approved or cleared for public posting in the data bank. [Section III.C.3]

Through rigorous clinical trial policies set forth by the HHS, we can increase the availability and use of clinical research data to generate new knowledge that will benefit society.