Memorandum on measures to include data on the costs of trials in ClinicalTrials.Gov

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From: Luis Gil Abinader and James Love
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Re: Expanding ClinicalTrials.Gov to include data on the costs of trials

This memo provides a request that the Department of Health and Human Services (HHS), working through the National Institutes of Health (NIH), use its rulemaking authority for ClinicalTrials.Gov to include data on the costs of human subject clinical trials.

The Secretary of Health and Human Services (HHS) can initiate a rulemaking process to expand the scope of the information disclosure requirements set forth in 42 U.S. Code § 282(j) to include the budget and actual amount spent on each clinical trial. This obligation can apply to any trial or subset of trials, such as trials funded in part by the federal government, interventional trials (instead of observational trials) that involve pharmaceutical drugs or therapies, trials used by the FDA in their medical reviews to approve products, trials that qualify for the U.S. Orphan Drug Tax Credit or trials that are undertaken to qualify for the FDA's 505A Pediatric Extension.

The authority to promote this process is provided under 42 U.S. Code § 282 (j)(2)(A)(iii).

Additionally, and in the shorter term, the NIH can amend its own policy on the dissemination of NIH-funded clinical trial information, issued on September 16, 2016, to require that awardees or investigators of clinical trials funded in whole or in part through the NIH extramural and intramural programs report to http://ClinicalTrials.gov the budget or actual amount spent, in addition to the information currently subject to reporting requirement. The 2016 NIH clinical trials policy went beyond the core requirements of 42 U.S. Code § 282(j) and 42 CFR § 11.22 in other aspects, such as the types of studies subject to reporting requirements, and nothing impedes the NIH from expanding its own policy to also include clinical trials costs of NIH-funded trials.

Having detailed information about clinical trial costs disaggregated by trial is essential for providing estimates of development costs that can be adjusted for risks and other factors, using data on trial failure/success rates by phase, which is available now, and fairly transparent.

42 U.S. Code § 282(j)[1], inserted by Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA)[2], creates the core standard for the registration of certain clinical trials on http://ClinicalTrials.gov. The information subject to reporting requirements is specified under 42 U.S. Code § 282(j)(2)(A)(ii), and comprises: a) descriptive information, such as a brief summary and study design; b) recruitment information, including eligibility criteria and recruitment status; c) location and contact information, such as the name of the sponsor; and d) administrative data, including an unique protocol identification number. Currently, 42 U.S. Code § 282(j)(2)(A)(ii) does not require reporting information on the cost of the clinical trials.

42 CFR § 11 is the regulation implementing 42 U.S.C. 282(j), and provides requirements and procedures for the submission of clinical trial information.[3] 42 CFR § 11.22 defines the "applicable drug clinical trial" that are subject to registration requirements as follows.

> "(2) Applicable drug clinical trial. A clinical trial with one or more arms that meets the following conditions is an applicable drug clinical trial:
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> (i) Study Type is interventional;
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> (ii) Study Phase is other than phase 1;
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> (iii) The clinical trial Studies a U.S. FDA-regulated Drug Product; and
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> (iv) One or more of the following applies:
>
> > (A) At least one Facility Location for the clinical trial is within the United States or one of its territories,
> >
> > (B) A drug product (including a biological product) under investigation is a Product Manufactured in and Exported from the U.S. or one of its territories for study in another country, or
> >
> > (C) The clinical trial has a U.S. Food and Drug Administration IND Number."[4]

42 CFR § 11.28 describes the type of information that is subject to the reporting requirements, which also comprises: a) descriptive information, b) recruitment information, c) location and contact information, and d) administrative data. Currently, 42 CFR § 11.28 does not impose requirements for reporting information on the cost of the clinical trials.

(1) Expanding the information requirements through regulation

42 U.S. Code § 282 (j)(2)(A)(iii) states that the HHS Secretary can modify the clinical trial information requirements if it provides "a rationale for why such a modification improves and does

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[1] https://www.govinfo.gov/content/pkg/USCODE-2011-title42/html/USCODE-2011-title42-chap6A-subchapIII-partA-sec282.htm

[2] https://www.govinfo.gov/content/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf

[3] https://www.govinfo.gov/content/pkg/CFR-2017-title42-vol1/xml/CFR-2017-title42-vol1-part11.xml

[4] 42 CFR § 11.22

not reduce such clinical trial information." An amendment to include information regarding the budget or actual money spent on clinical trials will clearly expand the information available.

> "MODIFICATIONS.—The Secretary may by regulation modify the requirements for clinical trial information under this paragraph, if the Secretary provides a rationale for why such a modification improves and does not reduce such clinical trial information."[5]

(2) Expanding the information requirements through internal policies

Notwithstanding 42 U.S. Code § 282(j) and 42 CFR § 11.22, U.S. Federal agencies have legal authority to adopt broader clinical trial reporting requirements, if they chose to do so. On September 16, 2016, the NIH issued a policy "to promote broad and responsible dissemination of information from NIH-funded clinical trials through ClinicalTrials.gov."[6] That policy "applies to all NIH-funded clinical trials **regardless of study phase, type of intervention, or whether they are subject to [42 CFR § 11]**."[7] [Emphasis added] Since the scope of 42 U.S. Code § 282(j) and 42 CFR § 11.22 only covers certain clinical trials based on its phase, type and other eligibility criterias, while the 2016 NIH policy applies to all trials as long as they are funded by the NIH, the NIH policy is broader than the statue and the regulation. The 2016 NIH policy applies to clinical trials funded in whole or in part through the NIH extramural and intramural programs.

Although the 2016 NIH policy does not adopt broader requirements with regards to the content of the information reported, there are no impediments to do so. The policy states that the term "registration information" "has the same meaning as the term 'registration information' in [42 CFR § 11]" and covers "descriptive information, recruitment information, location and contact information, and administrative data." The NIH could add more items to this provision and require information relating to the budget or actual money spent on clinical trials.

Other Federal agencies have adopted clinical trial reporting policies that expand upon 42 U.S. Code § 282(j) and 42 CFR § 11.22. On January 28, 2015, the National Cancer Institute (NCI) issued a clinical trial reporting policy "aimed at ensuring public availability of results from NCI-supported clinical trials."[8] The trials covered in this policy are "all initiated or commenced NCI-Supported Interventional Clinical Trials whether extramural or intramural." This includes "research grants, cooperative agreements, and contracts to conduct Interventional Clinical Trials in all phases and disciplines." This policy also goes beyond the core statutory standard with regards to the applicable trials, although not with regards to the content of the disclosure. The NCI or other agencies can expand this policy to include budget or actual money spent on clinical trials.

We note that there is a very significant public interest in having more transparent, reliable and useful information on trial costs. In implementing a rule, HHS could also benefit from the efforts to create standards for reporting R&D costs associated with the Medical pricing negotiations, although

[5] 42 U.S. Code § 282 (j)(2)(A)(iii)
[6] https://grants.nih.gov/grants/guide/notice-files/not-od-16-149.html
[7] https://s3.amazonaws.com/public-inspection.federalregister.gov/2016-22379.pdf
[8] https://grants.nih.gov/grants/guide/notice-files/NOT-CA-15-011.html

the issue of standards for reporting R&D costs are not settled, and will benefit from more input from the community of stakeholders who are expected to use the data, including academic and policy researchers.

We note that the California Institute for Regenerative Medicine (CIRM) provides an example of routine disclosures of that government's outlays on clinical trials, which is more useful in many respects than the current data available from the NIH RePORT or RePORTER as regards understanding the costs of trials. For each trial it funds, the CIRM provides the ClincialTrials.Gov ID, the enrollment and CIRM grant award, among other information. Publishing of the data on the web increases transparency and gives the taxpayers who fund the trials a deeper understanding of the agency's work and the costs associated with product development.