Final Rule: HHS and NIH's New Information Requirements for Clinical Trials: Is More Information Beneficial and For Whom?

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INTRODUCTION

On September 16, 2016, the U.S. Department of Health and Human Services (HHS) presented a final rule, in conjunction with a complementary policy of the National Institutes of Health (NIH), amending Tile 42, Chapter 1 of the Code of Federal Regulations[1]. This final rule will bring about a new era for the different stakeholders in the health care industry: patients, providers, researchers and our government[2]. It represents a big step toward increased access to information about certain clinical trials, a topic that affects subjects' informed consent directly. The regulation's aim is to specify "how data that were collected and analyzed in accordance with a clinical trial's protocol are submitted to *ClinicalTrials.gov*". As such, it does not create new requirements on data, design, or conduct of clinical trials[3].

All stakeholders in the field of research ethics have engaged in continuous debate regarding the need for "increased access to information about clinical trials"[4]. The lack of publications[5] (researchers that don't publish their findings for a variety of reasons such as that their data won't be of benefit to the whole community) of clinical trials and biased literature[6],[7] (when researchers publish positive rather than negative findings) concerning clinical trials outcomes are major concerns. The problems previously mentioned are what this regulation tackles.

ANALYSIS

First, Section 11.22 of the final rule explains which clinical trials must be registered in the webpage. It states that all clinical trials initiated after September 27, 2007, or any clinical trial initiated before or continued after such date, must figure in ClinicalTrials.gov[8]. Therefore, all clinical trials initiated after January 18, 2017 –the ruling's official effective date– must meet certain criteria to enter the site. For device clinical trials, they must be a pediatric postmarket surveillance of a device product or an interventional, non-feasibility study with one or more subjects[9]. For drug clinical trials, they must be an interventional, non-phase 1 study with one or more subjects[10]. As the Comments and Response Section of the Final Rule suggests, this Sections aims to broaden the spectrum of clinical trials that enter the site while specifying what kind of trial they are. Revealingly, this poses problems, because not all clinical trials can fit into the categories that the NIH has created; and thus, will become a major procedural problem for sponsors during registration. In addition, this undermines the Final Rule's spirit, because it anticipates that the information on the site will not necessarily be correct or accurate; undermining subjects' access to information and, ultimately, their informed consent.

Second, the most notable section of the new ruling is Section 11.28. It contains all the information that must be disclosed for each clinical trial. Studies that started before January 18, 2017 will submit the information required by section 402(j)(2)(A)(ii) of the Public Health Service Act[11] as usual[12]. This means that this ruling's information requirement won't affect them directly. However, for studies after the effective date, a plethora of information must be disclosed. Some of these requirements include: when stating the *primary purpose* of the study, the study's sponsor must select, as to clarify, what is the study's aim. They can be for future treatment, prevention, diagnosis, supportive care, screening, health services research, basic science, device feasibility or other aim[13]. In addition, when stating *study type*, the party must declare if it's an interventional, observational, or expanded access program study[14] (even though the HHS understands that these three criteria don't reflect the nature of all studies). Finally, the *study completion date*[15] and specification of primary and secondary outcomes[16] are also in the final rule.

The HHS, NIH, and JAMA[17] see in this new regulation a better way for potential research subjects to access information about trials. They argue four points: (a) there is more access to information about clinical trials[18]; (b) there are better references about clinical trials for investigators and IRBs[19]; (c) there is more information about unapproved products; and (d) for people looking into certain trials, there is more information about similar marketed products[20]. Again, they argue that this will help patients and researchers in knowing more in general about the clinical trials that affect them.

CONCLUSION

Although this may seem like we are a entering "new era" of clinical trial disclosure, several questions remain: will more information be beneficial for subjects? Will subjects be able to understand this new information? Will parties in a subject trial explain the new rule to their subjects? I think that this new rule lacks the subject's voice, their understanding. It falls short on what information they need to give an informed consent. As noted by the BMJ in 2012, there hasn't been a lot studies about what subjects want to know about clinical trials and in the limited studies conducted, it has been showed that subjects have different information needs[21]. Nonetheless, the 2012 study demonstrated that most were interested in information, among other things, about investigators' conflicts of interest and subjects' voluntariness and confidentiality –all missing in this final rule.

Certainly, this will pave the way for data exchange and greater transparency in the scientific community. But again, the question lingers: will it be of benefit for subjects? And if it does benefit subjects, how exactly? As STAT investigated[22] last year, there's a widespread behavior towards non-compliance and non-penalization, will it be different this time?

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[1] Clinical Trials Registration and Results Information Submission, 81 FR 64981 (September 21, 2016).

[2] Collins, Francis S. and Kathy L. Hudson "Clinical Trials: Sharing of Data and Living Up to Our End of the Bargain." National Institutes of Health. September 16, 2016. Accessed September 29, 2016. https://directorsblog.nih.gov/2016/09/16/clinical-trials-sharing-of-data-and-living-up-to-our-end-of-the-bargain/.

[3] 81 FR 64982.

[4] Steinbrook R. "Registration of clinical trials—voluntary or mandatory?" N Engl J Med. 2004 Oct 28;351(18):1820–2.

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[8] 81 FR 65143; §11.22(a)(1) & §11.22(a)(2).

[9] 81 FR 65143; §11.22(b)(1).

[10] 81 FR 65143; §11.22(b)(2).

[11] Codified as 42 U.S.C. 282(j)(2)(A)(ii).

[12] 81 FR 65143-65144; §11.28(a)(1).

[13] 81 FR 65144; §11.28 (a)(2)(D).

[14] 81 FR 65144; §11.28 (a)(2)(E).

[15] 81 FR 65144; §11.28 (a)(2)(T).

[16] 81 FR 65144; §11.28 (a)(2)(W) & 81 FR 65144; §11.28 (a)(2)(X).

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[20] Rogawski MA, Federoff HJ. "Disclosure of clinical trial results when product development is abandoned." Sci Transl Med. 2011 Sep 28;3(102):102cm29.

[21] See Kirkby HM, Calvert M, Draper H, et al. What potential research participants want to know about research: a systematic review. BMJ Open 2012;2: e000509. doi:10.1136/ bmjopen-2011-000509.

[22] Piller, Charles "Law ignored, patients at risk." STAT. December 13, 2015. Accessed September 30, 2016. https://www.statnews.com/2015/12/13/clinical-trials-investigation/.