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COMMENTARY

NIH Publishes New Clinical Disclosure Rules: Changing Scope of "Publicly Accessible" Information

On September 16, 2016, the Department of Health and Human Services ("HHS") published a new rule ("Final Rule") expanding the clinical trial information published to the ClinicalTrials.gov database. ClinicalTrials.gov is a public registry for clinical trial information maintained by the National Institutes of Health ("NIH").[1] The Final Rule clarifies certain requirements for registration and disclosure. Further, it expands the clinical trial disclosure requirements by:

- Requiring the submission of results information for *unapproved* drugs, biologics, and device products;
- Requiring the submission of the full protocol and a statistical analysis plan (although some redaction is permitted)[2]; and
- Expanding the requirements for submission of adverse event information.

These rule changes increase the amount and type of information that will be made accessible to the public. This poses the risk of placing otherwise patentable subject matter in the public domain, and/or making it available as prior art that may be cited by an examiner during prosecution of a patent application and/or used as a basis for alleging invalidity of patent claims in the context of a litigation or post-grant proceeding. This *Commentary* provides a summary of some of the key new requirements under the Final Rule.

Prior Art and Public Accessibility

The Patent Act provides that: "A person shall be entitled to a patent unless … the invention was patented or described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention." 35 U.S.C. § 102(a)(1) (AIA). This statutory "bar is grounded on the principle that once an invention is in the public domain, it is no longer patentable by anyone." *SRI Int'l, Inc. v. Internet Sec. Sys.*, 511 F.3d 1186, 1194 (Fed. Cir. 2008) (citation and internal quotation marks omitted). 35 U.S.C. § 102 "serves as a limiting provision, both excluding ideas that are in the public domain from patent protection and confining the duration of the monopoly to the statutory term." *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 64 (1998).

In order for a reference to qualify as a "printed publication" under Section 102, it must be accessible to the public. See *In re Wyer,* 655 F.2d 221 (CCPA 1981) (citation omitted). "Accessibility goes to the issue of whether interested members of the relevant public could obtain the information if they wanted to."

Constant v. Advanced Micro-Devices, Inc., 848 F.2d 1560, 1568 (Fed. Cir. 1988). A reference may be deemed "publicly accessible" if it:

> has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it and recognize and comprehend therefrom the essentials of the claimed invention without need of further research or experimentation.

In re Wyer, 655 F.2d at 226; *see Bruckelmyer v. Ground Heaters, Inc.*, 445 F.3d 1374, 1378 (Fed. Cir. 2006).[3]

The Final Rule

The Final Rule will become effective on January 18, 2017.[4] Responsible Parties will have 90 days after the effective date to come into compliance with the Final Rule.[5] It requires that certain "Responsible Parties" register and submit results for certain clinical trials. A "Responsible Party" is the sponsor of the clinical trial or a designated principal investigator.[6] Generally, a Responsible Party must register a clinical trial within 21 days of enrolling the first human subject[7] and submit results information within one year of the primary completion date of the trial.[8]

On the date the Final Rule was published, the NIH issued a complementary final policy, where a broad range of NIH-funded awardees and investigators conducting clinical trials will be expected to submit registration and results information to ClinicalTrials.gov, even if those clinical trials would not otherwise be covered by the Final Rule.[9]

Applicable Clinical Trials

In general, the Final Rule requires the submission of clinical trial information for a drug clinical trial that meets the following criteria:

- The trial is interventional;
- The trial phase is other than Phase 1;
- The clinical trial studies a U.S. FDA-regulated drug product; and
- One or more of the following applies: (i) there is at least one clinical trial site located in the United States; (ii) the product is manufactured in the United States or its territories and is exported for use in a clinical trial outside the United States; or (iii) the trial is conducted under an FDA investigational new drug application ("IND") or investigational device exemption ("IDE").[10]

Notably, the Final Rule does not require registration for Phase 1 trials of drugs and biological products, or feasibility studies of device products, unless funded by the NIH.[11] To provide more objective, structured criteria for evaluating whether study information must be disclosed, a checklist-based tool will be made available. However, the checklist tool is external to and separate from the registration process.[12]

Registration Requirements

Previously optional registration information, such as the primary purpose of the study, number of arms, and intervention descriptions, are now mandatory.[13] Moreover, the Final Rule includes new registration elements, for example, information regarding whether the product is manufactured in and exported from the United States.[14]

Results Information Submissions

The Final Rule changes the scope of clinical trial results information that must be disclosed. Previously, results information for unapproved drugs, biologics, or device products did not need to be submitted. The Final Rule requires registration and submission of results information for drugs, biologics, or device products regardless of whether the product is approved, licensed, or cleared for marketing by the FDA.[15] Similarly, the Final Rule now requires the reporting of some previously optional data as well as added new data elements to the required disclosure list.[16] For example, Responsible Parties will now be required to provide race and ethnicity information or indicate that the information was not collected.[17]

The Final Rule requires Responsible Parties to submit tables of information summarizing: (i) participant flow information; (ii) demographics and baseline characteristics of the enrolled participants; (iii) primary and secondary outcomes, including

results of any scientifically appropriate statistical tests; and (iv) adverse events.[18] Previous adverse events submissions required two tables—one table that summarized all serious adverse events experienced by participants enrolled in the clinical trial and a second table that summarized other adverse events that exceeded a frequency of 5 percent in any arm of the clinical trial. The Final Rule requires the addition of a third table summarizing all-cause mortality, with the number and frequency of deaths due to any cause.[19] Information describing data collection methods for adverse event data must also be submitted.[20]

It should be noted the Final Rule does not require the submission of technical or nontechnical narrative summaries of clinical studies. As stated in the preamble to the Final Rule, this is due to a lack of evidence that narrative summaries would not be misleading or promotional.[21]

The Final Rule will also require submission of the full protocol and a statistical analysis plan (if a separate document) at the time results are submitted. Responsible Parties will have some opportunity to redact the documents if confidential commercial information, personal identifying information, and/or trade secrets are included.[22]

Protocols from clinical trials and study results have been used in the past to support allegations of invalidity of patent claims in litigations and post-grant proceedings.[23] Consequently, it may be increasingly important to carefully review protocols and results submitted to ClinicalTrials.gov to understand the risk of public disclosure of what otherwise might be patentable subject matter.[24]

Timing of Disclosure

The Responsible Party can delay submission of results information for up to two additional years if a certification is submitted that either: (i) a drug, biological, or device product studied in the clinical trial is not yet approved, licensed, or cleared for marketing by the FDA and is still under development by the manufacturer; or (ii) the manufacturer is the sponsor of the clinical trial and has sought or will seek approval, licensure, or clearance for a new use of a product studied in the trial within one year.[25] Additionally, the Final Rule allows the Responsible Party to request extensions to the submission deadline for "good cause."[26] It remains to be seen what will be considered "good cause," but HHS intends to issue guidance after gaining more experience with extension requests.[27]

Conclusion

The Final Rule expands the scope of clinical trial information that will have to be disclosed to HHS and ultimately published on ClinicalTrials.gov. Notably, the submission of results information for *unapproved* drugs, biologics, and device products is now required. Furthermore, the Final Rule expands the requirements for results submission by making previously optional data elements now mandatory, including the requirement to submit full protocols.

This will increase the potential for the public disclosure of otherwise patentable subject matter under U.S.C. § 102(a)(1) (AIA). Since this information must be submitted within 21 days of enrollment of the first human subject, the one-year bar on patentability should be carefully considered prior to the start of the clinical trial, and appropriate steps to protect potential intellectual property rights should be considered at the very early stages of clinical trial program development.

Lawyer Contacts

For further information, please contact your principal Firm representative or one of the lawyers listed below. General email messages may be sent using our "Contact Us" form, which can be found at www.jonesday.com/contactus/.

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Endnotes

1 A similar policy was recently released by the European Medicines Agency ("EMA"), whereby clinical data submitted by pharmaceutical companies in their request for market authorization are published.

2 Clinical Trials Registration and Results Information Submission, 81 Fed. Reg. 64981, 64982 (Sept. 21, 2016) (to be codified at 42 C.F.R. Part 11), § 11.48(a)(5) .

3 Publication of data and protocols on ClinicalTrials.gov and by the EMA may also present similar prior art and validity issues for patents and patent applications filed outside the United States.

4 Clinical Trials Registration and Results Information Submission, to be codified at 42 C.F.R

5 *Supra* note 2 at 65018

6 *Id*. at § 11.4(c).

7 *Id.* at § 11.24(a)).

8 *Id*. at § 11.44(a)). The term "completion date" means the date that the final subject was examined and received intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated. 42 U.S.C. § 282(j)(1)(A)(v).

9 National Institutes of Health Policy on Dissemination of NIH-Funded Clinical Trial Information, pages 21-22.

10 *Id*. at §11.22(b)(2). Similar rules apply to device clinical trials.

11 *See id.* at §11.22.

12 *Supra* note 2 at 65030.

13 Clinical Trials Registration and Results Information Submission, to be codified at 42 C.F.R § 11.28(a)(i).

14 *Id. at* § 11.28(a)(2)(i)(R).

15 *Id*. at §11.42(b).

16 *Id*. at §11.48(a)

17 *Supra* note 2, at 65081.

18 Clinical Trials Registration and Results Information Submission, to be codified at 42 C.F.R. §11.48.

19 *Supra* note 2, at 65094.

20 *Supra* note 15, at §11.48(a)(4)(i).

21 *Supra* note 2 at 64988.

22 *Id.* at § 11.48(a)(5).

23 *See, e.g., In re Montgomery*, 677 F.3d 1375, 1382 (Fed. Cir. 2012) (finding anticipation based on study protocol that did not disclose any clinical study results).

24 For pediatric postmarket surveillance of a device product that is not a clinical trial, the Responsible Party must submit a copy of any final report that is submitted to the FDA. *Supra* note 15, at § 11.48(b).

25 *Id.* at § 11.44(b).

26 *Id*. at § 11.44(e).

27 *Supra* note 9, at 65076.