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It's Final: Expanded Registration and Results Submission Requirements for ClinicalTrials.gov

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Pharmaceutical and Biotechnology Alert

On September 16, 2016, the Department of Health and Human Services (HHS) issued a final rule that "clarifies and expands" the requirements for clinical trial registration and results submission on the ClinicalTrials.gov website. Perhaps most notably, the final rule now requires submission of results information for completed clinical trials of unapproved, unlicensed, and uncleared drugs, biologics, and devices. The final rule also describes potential consequences of noncompliance, including civil and criminal actions and civil money penalties. Further, non-compliance also puts at risk grant funding by HHS. As discussed below, companies should review and revise their existing policies and procedures to ensure timely compliance.

Coming in at over 700 pages, we are in the process of digesting the final rule and preparing more detailed analyses. In the meantime, we provide this client alert to highlight some of the most important points regarding drug clinical trials:

- **"Applicable drug clinical trial" defined**. The final rule articulates a set of criteria for determining whether a trial is an "applicable drug clinical trial" subject to the registration and results submission requirements, which has previously been a source of confusion. Specifically, a trial with one or more arms and one or more prespecified outcomes measures is an "applicable drug clinical trial" if all of the following apply:
  - The study type is interventional;
  - The study phase is other than phase 1;
  - The clinical trial studies a drug product regulated by the Food and Drug Administration (FDA); and
  - One or more of the following applies:
    - At least one facility location for the clinical trial is within the United States or its territories;
    - A drug product (including a biological product) under investigation is a product manufactured in and exported from the United States or one of its territories for study in another country; or
    - The clinical trial has an investigational new drug application (IND) number.
- **Registration of clinical trials.** Applicable drug clinical trials must be registered no later

than 21 days after enrollment of the first human subject. The required registration information includes:

- *Descriptive information*, such as the study title, summary, design, and phase;
- *Recruitment information*, such as eligibility criteria, whether healthy volunteers are accepted, recruitment status, and availability of expanded access;
- *Location and contact information*, such as the name of the sponsor, responsible party, and facility information; and
- *Administrative information*, such as IND number and human subjects protection review board status.

- **Timing for submission of results information**. Unless certain exceptions apply, results information must be submitted for an applicable drug clinical trial, regardless of whether the studied drug is approved by FDA. As noted above, the requirement to submit results information for completed clinical trials of unapproved drugs is a significant new requirement added by the final rule.
  - In general, results information must be submitted no later than one year after the completion date of the applicable drug clinical trial. If seeking approval of a new use or initial approval of a drug, a certification for delayed submission of results may be obtained prior to the one-year results submission deadline. However, results submission cannot be delayed more than two years after the date the certification was submitted.
  - An extension to the deadline for submission of results information may be requested for "good cause." More than one extension for a given clinical trial may be requested.
  - A permanent waiver of the requirements for clinical trial results information submission may be granted under "extraordinary circumstances."

- **Results information.** The submission of results information for an applicable drug clinical trial requires the following elements:
  - *Participant flow.* Information on the progress of participants through the trial by arm, including the number of initial participants and the number completed.
  - *Demographic and baseline characteristics*. The age, sex/gender, and any other demographic measures of trial participants assessed at baseline and used in the analysis of the primary outcome measures, as well as baseline information on the race and ethnicity of participants in the clinical trial, if collected.
  - *Outcomes and statistical analyses.* Data for each primary and secondary outcome measure by arm or comparison group, along with their associated statistical analyses.
  - *Adverse event information*. Information for three groups of adverse events: (i) serious adverse events, grouped by organ system; (ii) all adverse events other than serious adverse events that exceed a frequency of five percent; and (iii) all-cause mortality.
  - *Protocol and statistical analysis plan*. Copies of the protocol and statistical analysis plan, including amendments (a significant new requirement added by the final rule).

- *Administrative information.* Administrative details, including the points of contact for scientific information about the clinical trial results and the disclosure of certain agreements between the principal investigator and the sponsor, such as whether the principal investigator is an employee of the sponsor.

- **Potential legal consequences of non-compliance**. Failure to comply with the applicable drug clinical trial registration and results reporting requirements is a prohibited act under the Federal Food, Drug, and Cosmetic Act, and may result in civil or criminal actions or civil monetary penalties of up to $10,000 per day. Non-compliance will also put at risk any remaining and future grant funding by HHS. The final rule also notes that other laws, such as those requiring submission of truthful information to the government, may be a basis for enforcing these requirements.

The final rule covers numerous points in addition to those highlighted above, including considerations for expanded access trials and transition provisions for results submission for trials that have already been completed or are ongoing.

The final rule will become effective on January 18, 2017, after which companies will have 90 days to come into compliance. Companies will need to update their policies and procedures by that time to ensure that they comply with the new requirements established by the final rule.

If you have any questions about the new requirements, please do not hesitate to contact one of the authors of this client alert or other lawyers you work with at Hogan Lovells.

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