11/09/07

FACT SHEET (Available at http://prsinfo.clinicaltrials.gov/)

Registration at ClinicalTrials.gov: As required by Public Law 110-85, Title VIII

On September 27, 2007, a U.S. law was enacted that expands the types of clinical trials that must be registered in ClinicalTrials.gov, increases the number of data elements that must be submitted, and also requires submission of results data. There are penalties for non-compliance with the law. This fact sheet addresses the new registration requirements, some of which have reporting deadlines beginning on **December 26, 2007.** Information about the requirement to submit results data will be forthcoming.

1. General Requirements for Registration

A. Clinical Trials That Must be Registered at ClinicalTrials.gov ("Applicable Clinical Trials")

- Trials of Drugs and Biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation [1]
- Trials of Devices: Controlled trials with heath outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric postmarket surveillance [2]

B. Who is Responsible for Trial Registration? ("Responsible Party") [3]

1. The sponsor of the clinical trial [4]; - *OR* -
2. The principal investigator (PI) of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the PI is responsible for conducting the trial and has sufficient data rights.

C. Required Data Elements -

The Responsible Party must submit descriptive, recruitment, location, contact, and administrative information when registering an applicable clinical trial [5]. More data elements are required than under prior U.S. law, and these new requirements include primary and secondary outcome measures, start date, and target number of subjects.

2. Timing of Registration at ClinicalTrials.gov

In general, the Responsible Party for an applicable clinical trial must submit required information by the later of 12/26/**2007** or 21 days after the first patient is enrolled [6].

Exceptions: (a) data for trials "ongoing" as of 9/27/2007 that do ***not*** involve a "serious or life threatening disease or condition" must be submitted by 9/27/**2008** [7], [8];
(b) trials that involve a "serious or life threatening disease or condition", are initiated before 9/27/07, and have a "completion date" prior to 12/26/2007 [9] are not subject to the new requirements, although they may be subject to other laws.

3. Penalties for Failure to Register

Penalties for responsible parties who fail to register applicable clinical trials are significant and may include civil monetary penalties [10] and, for federally-funded trials, the withholding or recovery of grant funds [11]. Starting December 26, 2007, any application or report submitted to FDA under sections 505, 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act or under section 351 of the Public Health Service Act will need to include certification of compliance with any applicable provisions [12].

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ENDNOTES

1. "`(iii) APPLICABLE DRUG CLINICAL TRIAL-

`(I) IN GENERAL- The term `applicable drug clinical trial' means a controlled clinical investigation, other than a phase I clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of this Act. [The Public Health Service Act]

`(II) CLINICAL INVESTIGATION- For purposes of subclause (I), the term `clinical investigation' has the meaning given that term in section 312.3 of title 21, Code of Federal Regulations (or any successor regulation).

`(III) PHASE I- For purposes of subclause (I), the term `phase I' has the meaning given that term in section 312.21 of title 21, Code of Federal Regulations (or any successor regulation)."

[PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(1)(A)(iii)]

2. "`(ii) APPLICABLE DEVICE CLINICAL TRIAL- The term `applicable device clinical trial' means--

`(I) a prospective clinical study of health outcomes comparing an intervention with a device subject to section 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act against a control in human subjects (other than a small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes); and

`(II) a pediatric postmarket surveillance as required under section 522 of the Federal Food, Drug, and Cosmetic Act."

[PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(1)(A)(ii)]

3. "`(ix) RESPONSIBLE PARTY- The term `responsible party', with respect to a clinical trial of a drug or device, means--

`(I) the sponsor of the clinical trial (as defined in section 50.3 of title 21, Code of Federal Regulations (or any successor regulation)); or

"`(II) the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements under this subsection for the submission of clinical trial information."

[PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(1)(A)(ix)]

4. Under 21 C.F.R. 50.3, "Sponsor" is defined as "a person who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators."

5. "`(ii) CONTENT- The clinical trial information required to be submitted under this paragraph for an applicable clinical trial shall include--

`(I) descriptive information, including--
`(aa) a brief title, intended for the lay public;
`(bb) a brief summary, intended for the lay public;
`(cc) the primary purpose;
`(dd) the study design;
`(ee) for an applicable drug clinical trial, the study phase;
`(ff) study type;
`(gg) the primary disease or condition being studied, or the focus of the study;
`(hh) the intervention name and intervention type;
`(ii) the study start date;
`(jj) the expected completion date;
`(kk) the target number of subjects; and
`(ll) outcomes, including primary and secondary outcome measures;

`(II) recruitment information, including--
`(aa) eligibility criteria;
`(bb) gender;
`(cc) age limits;
`(dd) whether the trial accepts healthy volunteers;
`(ee) overall recruitment status;
`(ff) individual site status; and
`(gg) in the case of an applicable drug clinical trial, if the drug is not approved under section 505 of the Federal Food, Drug, and Cosmetic Act or licensed under section 351 of this Act, specify whether or not there is expanded access to the drug under section 561 of the Federal Food, Drug, and Cosmetic Act for those who do not qualify for enrollment in the clinical trial and how to obtain information about such access;

`(III) location and contact information, including--
`(aa) the name of the sponsor;
`(bb) the responsible party, by official title; and
`(cc) the facility name and facility contact information (including the city, State, and zip code for each clinical trial location, or a toll-free number through which such location information may be accessed); and

`(IV) administrative data (which the Secretary may make publicly available as necessary), including--
`(aa) the unique protocol identification number;
`(bb) other protocol identification numbers, if any; and
`(cc) the Food and Drug Administration IND/IDE protocol number and the record verification date."

[PL 110-85, Section 801(a), (adding new 42 U.S.C. 282(j)(2)(A)(ii))]

6. "`(C) DATA SUBMISSION- The responsible party for an applicable clinical trial, including an applicable drug clinical trial for a serious or life-threatening disease or condition, that is initiated after, or is ongoing on the date that is 90 days after, the date of the enactment of the Food and Drug Administration Amendments Act of 2007, shall submit to the Director of NIH for inclusion in the registry data bank the clinical trial information described in of subparagraph (A)(ii) not later than the later of--

`(i) 90 days after such date of enactment;

`(ii) 21 days after the first patient is enrolled in such clinical trial; or

`(iii) in the case of a clinical trial that is not for a serious or life-threatening disease or condition and that is ongoing on such date of enactment, 1 year after such date of enactment."

[PL 110-85, Section 801(a), (adding new 42 U.S.C. 282(j)(2)(C))]

7. "`(viii) ONGOING.—The term 'ongoing' means, with respect to a clinical trial of a drug or a device and to a date, that—

`(I) 1 or more patients is enrolled in the clinical trial; and

`(II) the date is before the completion date of the clinical trial.

[PL 110-85, Section 801(a), (adding new 42 U.S.C. 282(j)(1)(A)(viii))]

8. Consistent with current FDA and ClinicalTrials.gov guidance, the NIH interprets "serious and life-threatening disease or condition to mean: (1) diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and (2) diseases or conditions with potentially fatal outcomes, where the endpoint of clinical trial analysis is survival.

The seriousness of a disease is a matter of judgment, but generally is based on such factors as survival, day-to-day functioning, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. For example, acquired immunodeficiency syndrome (AIDS), all other stages of human immunodeficiency virus (HIV) infection, Alzheimer's disease, angina pectoris, heart failure, cancer, and many other diseases are clearly serious in their full manifestations. Furthermore, many chronic illnesses that are generally well managed by available therapy can have serious outcomes. For example, inflammatory bowel disease, asthma, rheumatoid arthritis, diabetes mellitus, systemic lupus erythematosus, depression, psychoses, and many other diseases can be serious in some or all of their phases or for certain populations.

Any investigational drug that has received fast track designation by the FDA is considered a drug to treat a serious disease or condition.

9. "(v) COMPLETION DATE.—The term 'completion date' means, with respect to an applicable clinical trial, the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the prespecified protocol or was terminated.

[PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(1)(A)(v)]

10. "`(1) PROHIBITED ACTS- Section 301 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331) is amended by adding at the end the following:

`(jj)(1) The failure to submit the certification required by section 402(j)(5)(B) of the Public Health Service Act, or knowingly submitting a false certification under such section.

`(2) The failure to submit clinical trial information required under subsection (j) of section 402 of the Public Health Service Act.

`(3) The submission of clinical trial information under subsection (j) of section 402 of the Public Health Service Act that is false or misleading in any particular under paragraph (5)(D) of such subsection (j).'

(2) CIVIL MONEY PENALTIES- Subsection (f) of section 303 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 333), as redesignated by section 226, is amended--

(A) by redesignating paragraphs (3), (4), and (5) as paragraphs (5), (6), and (7), respectively;

(B) by inserting after paragraph (2) the following:

`(3)(A) Any person who violates section 301(jj) shall be subject to a civil monetary penalty of not more than $10,000 for all violations adjudicated in a single proceeding.

`(B) If a violation of section 301(jj) is not corrected within the 30-day period following notification under section 402(j)(5)(C)(ii), the person shall, in addition to any penalty under subparagraph (A), be subject to a civil monetary penalty of not more than $10,000 for each day of the violation after such period until the violation is corrected.';

(C) in paragraph (2)(C), by striking `paragraph (3)(A)' and inserting `paragraph (5)(A)';

(D) in paragraph (5), as so redesignated, by striking `paragraph (1) or (2)' each place it appears and inserting `paragraph (1), (2),or (3)';

(E) in paragraph (6), as so redesignated, by striking `paragraph (3)(A)' and inserting `paragraph (5)(A)'; and

(F) in paragraph (7), as so redesignated, by striking `paragraph (4)' each place it appears and inserting `paragraph (6)'.

[PL 110-85, Section 801(b), adding new section 21 U.S.C. 331(jj)]

11. `(i) GRANTS FROM CERTAIN FEDERAL AGENCIES- If an applicable clinical trial is funded in whole or in part by a grant from any agency of the Department of Health and Human Services, including the Food and Drug Administration, the National Institutes of Health, or the Agency for Healthcare Research and Quality, any grant or progress report forms required under such grant shall include a certification that the responsible party has made all required submissions to the Director of NIH under paragraph (2) and (3).

`(ii) VERIFICATION BY FEDERAL AGENCIES- The heads of the agencies referred to in clause (i), as applicable, shall verify that the clinical trial information for each applicable clinical trial for which a grantee is the responsible party has been submitted under paragraph (2) and (3) before releasing any remaining funding for a grant or funding for a future grant to such grantee.

[PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(5)(A)(i) and (ii)]

12. ‘‘(B) CERTIFICATION TO ACCOMPANY DRUG, BIOLOGICAL PRODUCT, AND DEVICE SUBMISSIONS.—At the time of submission of an application under section 505 of the Federal Food, Drug, and Cosmetic Act, section 515 of such Act, section 520(m) of such Act, or section 351 of this Act, or submission of a report under section 510(k) of such Act, such application or submission shall be accompanied by a certification that all applicable requirements of this subsection have been met. Where available, such certification shall include the appropriate National Clinical Trial control numbers.

[PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(5)(B)]