JOURNAL OF CLINICAL RESEARCH BEST PRACTICES

Vol. 4, No. 11, November 2008 "Can You Handle the Truth?"

What's New in GCP?

FDA Rejects Claims That Clinical Trial Registry Certification Does Not Apply to INDs, Other Reports

Reprinted from the Guide to Good Clinical Practice with permission of Thompson Publishing Group, 805 15th. St., Washington, D.C. 20005; www.thompson.com. To learn more about the Guide to Good Clinical Practice, visit: www.firstclinical.com/gcpguide.

The FDA rejected claims that mandatory certification by medical product developers does not extend to Investigational New Drug (IND) applications or supplements, annual reports, or adverse event reports.

The FDA Amendments Act of 2007 (FDAAA) requires sponsors submitting information to the FDA to include a certification that they had met the FDAAA trial registration requirements. The FDA developed Form FDA 3674 for medical product developers to use to certify trial registration with their submissions.

Comments to the agency contended IND submissions are not "applications" under the Food, Drug and Cosmetics (FD&C) Act. Some of the comments cited an earlier version of the legislation, which they said supported a contention that Congress "understood the distinction between 'applications' and 'submissions'." Other comments said submitting the certification for an IND was "illogical because an IND must be submitted to the FDA prior to enrolling subjects in clinical trials, yet registration in the clinical trials data bank is not generally required until 21 days after the first subject is enrolled."

The agency agreed that the word "application" is not contained in the FD&C Act regarding INDs, however, the regulations required by the law "define an IND as 'an investigational new drug application.'… These regulations repeatedly use the term 'application' in reference to an IND," the agency said.

FDA Considers IND an Application

"Therefore, the FDA considers an IND to be an application under section 505 of the FD&C Act. Congress is familiar with the FDA regulations and could have specifically exempted INDs from the certification process by directly excluding" INDs, the agency said.

The FDA cited the "numerous" requirements in FDAAA to update clinical trial registry data, to add a new clinical trials results database, and to provide new enforcement tools indicating that "Congress intended that the clinical trials data bank include information about clinical trials throughout the product development lifecycle. Clearly, the IND phase is an extremely important phase of this process."

The agency noted information needed to be submitted to the registry "well before a [new drug application (NDA)] is ever filed with the FDA. If the certification did not accompany INDs, there would be no means of ensuring that information is submitted to the registry data bank during the investigational stage, which would be inconsistent with the statute's intent to have such information available."

The FDA added that submission of the certification with INDs "helps to ensure that the clinical trial information is submitted to the registry for trials that are never submitted in an NDA" or a biologics license application.

As to the issue that the IND is filed before sponsors are required to register trials, this "does not require the conclusion that certifications were intended to be inapplicable to INDs," the agency said.

"Throughout the life of an IND, there are numerous opportunities for filing IND amendments, many of which will be filed after the trial is required to be registered."

Certification Requirement for Other Reports, Supplements Defended

As to the contention that the term "application" does not refer to supplements, annual reports, or adverse event reports, the agency noted supplements, annual reports and other submissions "are all characterized as 'applications' by the FDA" throughout its regulations. In addition the form (Form FDA 356h) that sponsors use to submit most IND-, NDA- and BLA-related submissions "includes check boxes for submitting annual reports, efficacy supplements, labeling supplements, and chemistry manufacturing and controls supplements."

The agency added that it recognized "the burden associated with submitting certifications with all of these filings" and is working to identify filings that will not require the certification.

The FDA also received a suggestion that the certification be incorporated into existing forms. The agency said the law requires the certification to "accompany" an application or submission. "We infer from this wording that the certification is not intended to be part of that application or submission." However the agency promised that as its information technology systems improve and more forms and submissions are filed electronically, "there will be a means to transfer information from an application onto the certification form."

Other comments said the certification should apply only to trials sponsored by the applicant. The FDA noted the law does not make a distinction between trials conducted by a sponsor and studies conducted by other entities that are used in an application.

"The FDA is aware that sponsors or applicants will be required to certify as to trials they did not conduct or register in the clinical trials data bank. The FDA has addressed this concern by requiring the submitter to declare that the information submitted is accurate, true and complete 'to the best of her/his knowledge.'"

The agency estimated more than 56,000 submissions per year will require the certification, which will take sponsors nearly 28,000 hours to complete.

The submissions include 29,480 drug and biologics investigational applications, including 1,837 new drug applications, 206 biologics license applications, 20,969 drug amendments, 826 biologics amendments, 4,764 drug annual reports, and 878 biologics annual reports.

The FDA also estimates 27,165 marketing applications, including 214 drug/biologics new applications/resubmissions, 424 new device applications, 4,451 drug/biologics amendments, 2,267 device amendments, 259 drug/biologics efficacy supplements/resubmissions, 1,273 drug/biologics labeling supplements, 2,526 device supplements, 7,753 drug annual reports, 629 biologics annual reports, 433 device annual reports, 5,173 generic drug annual reports, 563 generic drug originals, 477 generic drug amendments/supplements, and 723 generic drug labeling supplements.

To Find Out More

The FDA announcement detailing the agency's decisions and estimates is available at http://www.fda.gov/OHRMS/DOCKETS/98fr/E8-19625.pdf.

Other Recent GCP Developments in the Guide to Good Clinical Practice

Court requires company to provide Phase 2 drug to non-study patient

Trial master file can reduce document headaches in inspections