GUIDANCE FOR SPONSORS, INDUSTRY, RESEARCHERS, INVESTIGATORS, AND FOOD AND DRUG ADMINISTRATION STAFF

Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007

DRAFT GUIDANCE

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Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit electronic or written comments on the draft guidance by 60 days after the date of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For single copies of this draft guidance, please contact: Office of Policy, Food and Drug Administration, 5600 Fishers Lane, rm. 14-101, HF-11, Rockville, MD 20857, (301) 827-3360.

For questions regarding this draft document, contact Jarilyn Dupont, Office of Policy, Office of Commissioner, Food and Drug Administration, (301) 827-3360.

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Guidance for Sponsors, Industry, Researchers, Investigators, and Food and Drug Administration Staff

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I. Introduction

This guidance is intended to describe the Food and Drug Administration's (FDA or Agency) current thinking regarding whether some types of information and documents that sponsors, industry, researchers, and investigators submit to the Agency typically need not be accompanied by a certification under section 402(j)(5)(B) of the Public Health Service Act (PHS Act), 42 U.S.C. § 282(j)(5)(B). New section 402(j) of the PHS Act was added by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85).

FDA's guidance documents, including this draft guidance, do not establish legally enforceable rights or responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

Title VIII of FDAAA, Public Law 110-85, amended the PHS Act by adding new section 402(j), 42 U.S.C. § 282(j). The new provisions require that additional information be submitted to the clinical trials data bank (www.ClinicalTrials.gov) previously established by the National Institutes of Health (NIH)/National Library of Medicine (NLM), including expanded information on clinical trials and information regarding the results of clinical trials.

One new provision, 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act, requires that a certification accompany certain human drug, biological product, and device applications and submissions to FDA. The new provision reads as follows:

> (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.

The certification requirement went into effect on December 26, 2007. To assist sponsors, industry, researchers, and investigators in complying with the requirement, FDA created a certification form that is intended to accompany certain applications and submissions to satisfy the certification requirement. This form is FDA Form 3674, OMB Control No. 0910-0616. The form can be obtained at www.fda.gov/opacom/morechoices/fdaforms/default.html.

III. Purpose and Agency Recommendations

FDA has received numerous inquiries asking whether various kinds of information and documents that sponsors, industry, researchers, and investigators submit to the Agency are should be accompanied by the certification. The purpose of this guidance document is to provide FDA's current thinking regarding specific types of information and documents submitted to FDA under section 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act (the Act), or under section 351 of the PHS Act that typically need not be accompanied by the certification described in section 402(j)(5)(B), 42 U.S.C § 282(j)(5)(B). This guidance does not address all possible information and documents that sponsors, industry, researchers, and investigators may submit to FDA under those sections of the Act or the PHS Act. We intend to update this guidance document as appropriate to address additional information and documents that may be submitted under those sections and that typically may not need to be accompanied by a certification.

The purpose of Title VIII is to provide a means for ensuring that the public has access to information about certain clinical trials. Specifically, Title VIII is intended to provide a mechanism for the public to learn about certain clinical trials that are being conducted, as well as the results of those trials. In determining whether specific information or documents submitted under the statutory sections cited above typically need not be accompanied by the certification, FDA has focused on the role the certification plays in helping achieve the purposes of Title VIII of FDAAA.

One purpose of the certification is to require the submitter to confirm that it has complied with all applicable requirements of Title VIII, including the requirement to register applicable clinical trials.[1] Failure to submit a certification, knowingly submitting a false certification, failure to submit required clinical trial information, and submission of clinical trial information that is false or misleading are all newly added prohibited acts under section 301(jj) of the Act (21 U.S.C. § 331(jj)). Requiring a certification to accompany certain information and documents submitted to FDA is, therefore, one way of encouraging compliance with the provisions of the law.

The certification also serves the purpose of enabling FDA to exercise its responsibilities under the new law. For example, as stated previously, FDAAA created four new prohibited acts relating to compliance with the requirements of Title VIII, including compliance with the requirement to submit a certification. The certification requirement, therefore, is critical to the Agency's ability to determine whether the law has been complied with and whether an enforcement action is appropriate. In addition, section 402(j)(3)(F) of the PHS Act (42 U.S.C. § 282(j)(3)(F)) requires FDA to notify the Director of NIH of certain actions taken on applications and reports that were accompanied by a certification. That notification alerts NIH to the fact that the responsible party must submit the results of the trials within a certain period of time, thereby enabling NIH to exercise its responsibilities under Title VIII. The information in the certification form also will help FDA assist NIH in "linking" information posted on FDA's website regarding certain FDA regulatory actions to specific applicable clinical trials included in the registry and results databases. This linking, using the information in the certification form, eventually will allow FDA to help the public more easily correlate various reports, medical reviews, advisories, health alerts, advisory committee actions, and other materials with specific applicable clinical trials registered with ClinicalTrials.gov.

In determining whether the certification typically need not accompany a specific type of information or document that sponsors, industry, researchers, and investigators submit to the Agency under section 505, 515, 520(m), or 510(k) of the Act, or under section 351 of the PHS Act, we considered whether the information or document typically refers to, relates to, or includes information on an applicable clinical trial that the registry and results databases are intended to capture. Throughout the review cycle of a medical product, from the very first contact with FDA to postmarket activities, numerous documents are submitted to FDA. Certain

[1] "Applicable clinical trial" is defined at section 402(j)(1)(A)(i) of the PHS Act (42 U.S.C. § 282(j)(1)(A)(i)). For additional information, visit www.ClinicalTrials.gov.

information and documents submitted under the sections of the Act and the PHS Act cited above typically bear no relationship to the type of information that Title VIII is designed to capture. Consequently, submitting a certification with such information and documents would not serve the purposes of the legislation. Other information or documents submitted under the provisions cited above typically contain information on clinical trials regarding which the submitter has already provided a certification to the Agency. We believe that it would not further the purposes of the legislation if a certification were to accompany every type of information or document submitted to the Agency regarding a medical product regulated by FDA.

We recognize that there may be times that the types of submissions discussed above do, in fact, contain information that refers to, relates to, or includes information on an applicable clinical trial that the registry and results databases are intended to capture. In those cases, you should consider whether a certification is appropriate and contact us if you need additional guidance.

Based on these considerations, FDA recommends that a certification typically need not accompany the types of submissions of information or documents to the Agency listed below:

Investigational Applications/Submissions

- Chemistry and manufacturing amendments to Investigational New Drug Applications (INDs)
- Non-clinical pharmacology/toxicology amendments to INDs
- IND Safety Reports
- Single Patient INDs
- Meeting requests
- Investigational Device Exemption Applications (IDEs)

Marketing and Post-Marketing Applications/Submissions

- Chemistry and manufacturing amendments and supplements to Biologics License Applications (BLAs) and New Drug Applications (NDAs)
- Non-clinical pharmacology/toxicology amendments and supplements to BLAs and NDAs
- Humanitarian Device Exemptions (HDEs) and Premarket Approval Application (PMA) 30 Day Notices
- ANDA amendments and supplements that contain no in-vivo bioequivalence information
- ANDA, BLA, and NDA promotional materials
- BLA and NDA Safety Reports
- ANDA, BLA, NDA, HDE, and PMA mandatory and voluntary adverse event or medical device reports
- Meeting requests
- 510(k)s that contain no clinical data

IV. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. §§ 3501-3520). The collections of information have been approved under OMB Control No. 0910-0616.