Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank

Guidance for Responsible Parties, Submitters of Certain Applications and Submissions to FDA, and FDA Staff

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Good Clinical Practice (OGCP)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiologic Health (CDRH)
Office of Regulatory Affairs (ORA)

August 2020

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Contains Nonbinding Recommendations

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Guidance for Responsible Parties, Submitters of Certain Applications and Submissions to FDA, and FDA Staff[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. This guidance does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the second title page of this guidance.

I. INTRODUCTION

This guidance document is intended to describe the current thinking of FDA's Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), and Center for Devices and Radiological Health (CDRH) (hereafter, "Center" or collectively, "the Centers"), regarding civil money penalties under section 303(f)(3) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).[2] That section authorizes FDA to assess civil money penalties against responsible parties and/or submitters of certain applications and submissions to FDA regarding drug products, biological products, and device products (hereafter, "submitters") who violate applicable FD&C Act prohibitions relating to requirements under section 402(j) of the Public Health Service Act (PHS Act),[3] including its implementing regulations in 42 CFR part 11, to submit clinical trial registration and/or results information to the ClinicalTrials.gov data bank and/or certain certifications to FDA.

The guidance document addresses the following questions:

- How do the Centers intend to identify whether responsible parties have failed to submit required clinical trial registration and/or results information to the ClinicalTrials.gov data bank or submitted false or misleading information to the data bank, or whether submitters

[1] This guidance has been prepared by the Office of Good Clinical Practice in cooperation with FDA's Center for Biologics Evaluation and Research, Center for Drug Evaluation and Research, Center for Devices and Radiological Health, and Office of Regulatory Affairs.
[2] 21 U.S.C. 333(f)(3).
[3] 42 U.S.C. 282(j).

have failed to submit to FDA the certification required by section 402(j)(5)(B) of the PHS Act[4] or knowingly submitted a false certification to FDA?
- Under what circumstances may a Center decide to seek civil money penalties against a responsible party or submitter?
- What procedures apply when a Center seeks civil money penalties?
- What civil money penalty amounts may be assessed for (1) failing to submit required clinical trial registration and/or results information to the ClinicalTrials.gov data bank, (2) submitting false or misleading information to the data bank, (3) failing to submit the required certification to FDA, or (4) knowingly submitting a false certification to FDA?

In general, FDA's guidance documents do not establish legally enforceable 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

Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended section 402(j) of the PHS Act[5] to require that a "responsible party" submit clinical trial registration and results information to the ClinicalTrials.gov data bank for certain "applicable clinical trials." The section also requires a submitter to certify to FDA that all requirements of section 402(j) have been met when submitting certain applications and submissions to FDA regarding drug products, biological products, and device products. FDAAA also directed the Secretary of Health and Human Services (Secretary) to promulgate regulations expanding the requirements for submission of clinical trial registration and results information for certain "applicable clinical trials" to the ClinicalTrials.gov data bank. On September 21, 2016, the National Institutes of Health (NIH) and the Department of Health and Human Services published the Final Rule for Clinical Trials Registration and Results Information Submission, 81 Fed. Reg. 64,982 (Sept. 21, 2016),[6] which implements the provisions of section 402(j) of the PHS Act by clarifying and expanding the clinical trial registration and results information requirements. The regulations are codified at 42 CFR part 11 and were effective January 18, 2017, with a compliance date of April 18, 2017.

FDAAA also amended the FD&C Act to add section 301(jj),[7] which includes the following prohibited acts:

1. Failing to submit or knowingly submitting a false certification to FDA under section 402(j)(5)(B) of the PHS Act;

[4] 42 U.S.C. 282(j)(5)(B).
[5] 42 U.S.C. 282(j).
[6] https://www.regulations.gov/document?D=NIH-2011-0003-0907.
[7] 21 U.S.C. 331(jj).

2. Failing to submit required clinical trial information under section 402(j) of the PHS Act; and

3. Submitting clinical trial information under section 402(j) to the ClinicalTrials.gov data bank that is false or misleading under 402(j)(5)(D).

FDAAA further amended section 303(f)(3) of the FD&C Act[8] to authorize FDA to assess civil money penalties against a person that commits these prohibited acts. The maximum penalty amounts and factors considered when seeking civil money penalties are discussed in Section III.E.

III. DISCUSSION

A. Definitions

The Centers intend to use the following definitions in implementing the FD&C Act's civil money penalty provisions relating to the submission of registration and results information to the ClinicalTrials.gov data bank and certain certifications to FDA.

1. **Civil money penalty or civil monetary penalty**: The terms "civil money penalty" and "civil monetary penalty" are used interchangeably and mean a monetary penalty assessed under section 303(f)(3) of the FD&C Act[9] for prohibited acts (found in section 301(jj) of the FD&C Act[10]) relating to the submission of clinical trial registration and results information to the ClinicalTrials.gov data bank and certain certifications to FDA.

2. **Applicable clinical trial**: The term "applicable clinical trial" refers to an applicable device clinical trial or an applicable drug clinical trial as defined in 42 CFR 11.10(a).

3. **Responsible party**: The term "responsible party" means the individual or entity required to submit clinical trial information for an applicable clinical trial, as defined in 42 CFR 11.10(a).

4. **Clinical trial information**: The term "clinical trial information" means the clinical trial registration and/or results information required to be submitted to the ClinicalTrials.gov data bank for an applicable clinical trial, as defined in 42 CFR 11.10(a).

[8] 21 U.S.C. 333(f)(3).
[9] 21 U.S.C. 333(f)(3).
[10] 21 U.S.C. 331(jj).

5. **Certification to FDA:** The phrase "certification to FDA" means the certification required under section 402(j)(5)(B) of the PHS Act[11] that must accompany an application or submission under sections 505, 510(k), 515, and 520(m) of the FD&C Act[12] and section 351 of the PHS Act.[13] Form FDA 3674 is used to certify that all applicable requirements of section 402(j) of the PHS Act, including its implementing regulations in 42 CFR part 11, have been met for all of the applicable clinical trials included in, relied upon, or otherwise referred to in the application or submission.[14]

6. **Submitter:** The term "submitter" means the individual or entity that submits certain applications and submissions to FDA regarding drug products, biological products, and device products and who provides a certification to FDA under section 402(j)(5)(B) of the PHS Act.[15] In some cases, the submitter may be someone other than the responsible party for an applicable clinical trial identified in the certification.

B. How do the Centers intend to identify whether someone has: failed to submit required clinical trial registration and/or results information to the ClinicalTrials.gov data bank; submitted false or misleading information to the data bank; or failed to submit or knowingly submitted a false certification to FDA?

The Centers generally intend to identify violations of the FD&C Act's requirements relating to the ClinicalTrials.gov data bank through evidence collected during inspections conducted as part of FDA's Bioresearch Monitoring Program (BIMO). How FDA will collect information to assess compliance with these requirements is described in FDA's Bioresearch Monitoring Compliance Program for Sponsors, Contract Research Organizations and Monitors.[16]

In general, the Centers may also identify violations based on the evaluation of complaints received by the Agency. The Centers intend to handle complaints in accordance with their existing processes for handling complaints about potential violations of FDA requirements. In evaluating complaints, the Centers may review any public and non-public information available to FDA, including, but not limited to, information submitted to the ClinicalTrials.gov data bank and to FDA.

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[11] 42 U.S.C. 282(j)(5)(B).
[12] 21 U.S.C. 355, 360(k), 360e, 360j(m).
[13] 42 U.S.C. 262.
[14] *See Form FDA 3674 - Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions*, available at https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM562439.pdf.
[15] 42 U.S.C. 282(j)(5)(B).
[16] *See* FDA Compliance Program 7348.810 Sponsors, Contract Research Organizations and Monitors.

C. Under what circumstances may a Center decide to seek civil money penalties?

When a Center believes that a responsible party for an applicable clinical trial may have committed a prohibited act under section 301(jj) of the FD&C Act[17] by failing to comply with the PHS Act's clinical trial registration and results information submission requirements, including the regulations found in 42 CFR part 11, the Center generally intends to send the responsible party a Preliminary Notice of Noncompliance (Pre-Notice) Letter, which describes the potential violation and requests that the responsible party take any necessary actions to address the potential violation within 30 calendar days after receiving the letter. The Centers also generally intend to send a Pre-Notice Letter to submitters who may have violated FDAAA's certification requirements in section 402(j)(5)(B) of the PHS Act.[18] Pre-Notice Letters notify the recipient that, beginning 30 calendar days after the date a Pre-Notice Letter is received, FDA will conduct a further review and assessment of the clinical trial information submitted to ClinicalTrials.gov and any other relevant information available to FDA and that failure to comply with the requirements relating to applicable clinical trials may result in further FDA regulatory action, including the issuance of a Notice of Noncompliance, civil money penalties, injunction, and/or criminal prosecution.

As discussed above, the Centers intend to identify potential violations of the FD&C Act's requirements relating to the ClinicalTrials.gov data bank in part through evidence collected during inspections conducted as part of FDA's BIMO program.[19] Generally, FDA's BIMO activities are associated with the submission of a research or marketing application or are a part of the Agency's investigation of a complaint. When evaluating potential violations identified during these activities, FDA intends to utilize a risk-based approach to determine the situations in which Pre-Notice Letters will be issued, consistent with FDA's public health mission and how the Agency approaches its other compliance programs. In applying this risk-based approach to evaluating potential violations of the FD&C Act's requirements relating to the ClinicalTrials.gov data bank, the Centers intend to focus their enforcement and regulatory attention in the following areas:

- Responsible parties who have failed to submit required clinical trial registration and/or results information under section 402(j) of the PHS Act, including its implementing regulations in 42 CFR part 11, for applicable clinical trials of products that potentially may pose a higher risk to human subjects or applicable clinical trials of products intended to address significant public health need. Examples may include, but are not limited to, applicable clinical trials of a drug

[17] 21 U.S.C. 331(jj).
[18] 42 U.S.C. 282(j)(5)(B).
[19] Because investigators may not be able to assess whether required clinical trial information has been submitted to the ClinicalTrials.gov databank at the time of an inspection, FDA does not intend to include on Forms FDA 483 any observations regarding potential violations of requirements relating to the ClinicalTrials.gov data bank; however, information that is collected by an investigator regarding potential violations of such requirements will be included in the Establishment Inspection Report and provided to the relevant Center for further evaluation.

product, biological product, or device product that has not previously been approved, licensed, or cleared by FDA and is intended to treat a serious and/or life-threatening disease or condition and applicable clinical trials involving vulnerable populations (such as pediatrics), rare diseases, or emergency research conducted without informed consent under 21 CFR 50.24.

- Responsible parties or submitters who have had a pattern of previous noncompliance with the requirements to submit clinical trial information and/or certifications under section 402(j) of the PHS Act, including its implementing regulations in 42 CFR part 11.

- Applicable clinical trials for which noncompliance with the requirements under section 402(j) of the PHS Act, including its implementing regulations in 42 CFR part 11, exists in conjunction with noncompliance with other statutory and/or regulatory requirements pertaining to the conduct of the trial, for example the failure to retain clinical trial records or the failure to obtain informed consent.

Pre-Notice Letters will be sent by certified mail, registered mail, mail delivery service, or personal delivery to the responsible party for the applicable clinical trial at the address specified in the ClinicalTrials.gov Protocol Registration and Results System (PRS), or to the submitter at the address specified in the FDA application/submission. If a Center cannot reach the entity or its agent at the address to which the Pre-Notice Letter is sent, the Center intends to attempt to reach the entity or its agent through other means, for example, through other addresses otherwise identified by the Center in applications or submissions provided to the Agency. Pre-Notice Letters will include an FDA contact to whom a response may be submitted and who can address any questions or concerns of the responsible party/submitter.

After a Pre-Notice Letter has been received and the 30 calendar day period for any necessary action has passed, the Center intends to review the information submitted to the ClinicalTrials.gov data bank for that applicable clinical trial, the application/submission in FDA files, and/or any other information available to the Agency, to determine whether a violation exists. If the Center determines that a responsible party failed to submit any required clinical trial information to the ClinicalTrials.gov data bank and/or submitted information that is false or misleading in any particular, the Agency will issue the responsible party a Notice of Noncompliance under section 402(j)(5)(C)(ii) of the PHS Act.[20] If the Center determines that a submitter failed to submit the required certification to FDA or knowingly submitted a false certification, the Agency intends to issue a Notice of Noncompliance to the submitter. A Notice of Noncompliance will notify the recipient of the Center's determination and give the recipient an opportunity to remedy noncompliance not later than 30 calendar days after the notification. FDA intends to post the Notice of Noncompliance on the Agency's

[20] 42 U.S.C. 282(j)(5)(C)(ii). The Secretary delegated to the Commissioner of Food and Drugs the authority to issue Notices of Noncompliance under this section. *See* https:/www.gpo.gov/fdsys/pkg/FR-2012-09-26/pdf/2012-23598.pdf.

website and to transmit the Notice of Noncompliance to NIH so it can include the notice regarding noncompliance required under section 402(j)(5)(E) of the PHS Act[21] in the ClinicalTrials.gov data bank.

In determining whether to seek civil money penalties, FDA intends to take into consideration any corrective action taken by a responsible party or submitter after receiving a Notice of Noncompliance. If a responsible party or submitter does not remedy noncompliance within 30 calendar days after receiving a Notice of Noncompliance, the Center generally intends to seek civil money penalties, taking into account the type of noncompliance and the circumstances associated with the lack of remediation.

D. What procedures apply when a Center seeks civil money penalties?

FDA regulations governing civil monetary penalty proceedings are found at 21 CFR part 17. Civil money penalty actions are initiated when the Center with principal jurisdiction over the matter involved files a Complaint with FDA's Division of Dockets Management and serves the Complaint on the respondent (in this case, the responsible party or submitter). The Complaint will be signed by the FDA Office of Chief Counsel attorney for the Center and include allegations of liability against the respondent, the violations that are the basis for the alleged liability, the reasons that the respondent is responsible for the violations, and the amount of penalties and assessments that the Center is seeking. Additionally, the Complaint will include instructions for filing an Answer to request a hearing and will warn that failure to file an Answer within 30 days of service of the Complaint will result in the imposition of the proposed amount of penalties and assessments, as provided in 21 CFR 17.11.[22]

Upon being served, the respondent generally responds by: (1) either paying the penalty sought in the Complaint; or (2) filing an Answer with the Division of Dockets Management and contesting some or all of the Center's allegations.[23]

If a respondent chooses to contest the matter, it must file an Answer to the Complaint within 30 days after the date of service of the Complaint.[24] The Answer must admit or deny each of the allegations made in the Complaint, and include any and all defenses to the action and all reasons or explanations why the penalty and assessment should be less than the amount requested in the Complaint.[25] If the respondent files an Answer within the time prescribed, the respondent is entitled to a hearing according to the procedures established in FDA's regulations governing civil money penalty proceedings, codified in 21 CFR part 17.

[21] 42 U.S.C. 282(j)(5)(E).
[22] 21 CFR 17.5.
[23] 21 CFR 17.9.
[24] 21 CFR 17.9.
[25] 21 CFR 17.9.

After submitting an Answer, a respondent and its representatives may engage in settlement discussions with the Center regarding the civil money penalty.[26] Respondents may present relevant mitigating factors or arguments for the Center to consider reducing the penalty amount. The parties may at any time before a decision on appeal agree to settle all or part of the matter. After the respondent pays any agreed-upon penalty amount and the parties sign a settlement agreement that is filed in the docket for the matter, the case will be completely or partially resolved as designated by the settlement agreement.[27]

Cases that are not settled will be decided by a presiding officer,[28] either after an administrative hearing or after a party files a motion for summary decision pursuant to 21 CFR 17.17 and briefing is completed. Upon request, for appropriate cause, the presiding officer may expedite the schedule for various aspects of the hearing.

In advance of a hearing, parties are required to exchange exhibits and written testimony.[29] Parties can choose to "rest" after the exchange of exhibits and written testimony, or request an opportunity to cross-examine the opposing party at an oral hearing and/or submit legal briefs. After resting, or after an oral hearing and/or further briefing, the presiding officer will render an initial decision based on the administrative record. The initial decision shall contain findings of fact, conclusions of law, and the amount of any penalties and assessments imposed.[30]

Under section 303(f)(6) of the FD&C Act,[31] after the presiding officer renders an initial decision, either party can appeal to the Department of Health and Human Services (HHS) Departmental Appeals Board (DAB).[32] The respondent may appeal an adverse DAB decision to the U.S. Court of Appeals for the District of Columbia or any other circuit in which the respondent resides or transacts business.

E. What civil money penalty amounts may be assessed?

Civil money penalties may be assessed under section 301(jj) of the FD&C Act[33] for (1) failing to submit required clinical trial registration and/or results information to the ClinicalTrials.gov data bank, (2) submitting false or misleading information to the ClinicalTrials.gov data bank, (3) failing to submit the required certification to FDA, or (4) knowingly submitting a false certification to FDA.

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[26] 21 CFR 17.15(b).
[27] 21 CFR 17.15(b).
[28] The regulations define "presiding officer" to mean "an administrative law judge qualified under 5 U.S.C. 3105." 21 CFR 17.3(c).
[29] 21 CFR 17.25 and 17.37.
[30] 21 CFR 17.45.
[31] 21 U.S.C. 333(f)(6).
[32] 21 CFR 17.47.
[33] 21 U.S.C. 331(jj).

The statutory maximum penalties under section 303(f)(3)(A) of the FD&C Act[34] for committing these prohibited acts are not more than $10,000 for all violations adjudicated in a single proceeding and, if a violation is not corrected within 30 days following notification of such violation, section 303(f)(3)(B) of the FD&C Act[35] provides for an additional civil money penalty of not more than $10,000 for each day that the violation continues after such period until the violation is corrected.[36]

Pursuant to section 303(f)(5)(B) of the FD&C Act,[37] in determining the amount of civil money penalty under the relevant statutory limits, the following factors are considered: the nature, circumstances, extent, and gravity of the violation(s) and, with respect to the violator, ability to pay, effect on ability to continue to do business, any history of prior such violations, the degree of culpability and such other matters as justice may require.

[34] 21 U.S.C. 333(f)(3)(A).
[35] 21 U.S.C. 333(f)(3)(B).
[36] The civil money penalty amounts listed in this guidance reflect the amounts listed in the statute. These amounts are updated annually to reflect inflation, as required by the Federal Civil Penalties Inflation Adjustment Act of 1990 (Pub. L. No. 101-410, 104 Stat. 890 (1990) (codified as amended at 28 U.S.C. 2461 note 2(a)), as amended by the Federal Civil Penalties Inflation Adjustment Act Improvements Act of 2015 (Sec. 701 of the Bipartisan Budget Act of 2015, Pub. L. No. 114-74, November 2, 2015). For the most up-to-date amounts, please *see* 45 CFR 102.3.
[37] 21 U.S.C. 333(f)(5)(B).