

**FOR FURTHER INFORMATION CONTACT:**

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**SUPPLEMENTARY INFORMATION:** FDA is issuing this **Federal Register** notice to announce that eCTD validations 1306 and 1323, described in “Specifications for eCTD Validation Criteria,” have been raised to high validation errors.

Beginning March 1, 2022, FDA will reject submissions that fail either of these validations.

According to the guidance for industry entitled “Providing Regulatory Submissions in Electronic Format—Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications,” submissions subject to section 745A(a) of the Federal Food, Drug, and Cosmetic Act must be submitted in eCTD format using the version of eCTD currently supported by FDA (unless such submission is exempt from the electronic submission requirements or if FDA has granted a waiver). The version of eCTD currently supported by FDA is specified in the Data Standards Catalog. eCTD submissions must follow FDA eCTD technical specification entitled “The Comprehensive Table of Contents Headings and Hierarchy.” Documents which are not properly referenced in the eCTD backbone as described in the “M2 eCTD: Electronic Common Technical Document Specification” and “The eCTD Backbone Files Specification for Module 1,” result in content that is not accessible within FDA eCTD technical specification “The Comprehensive Table of Contents Headings and Hierarchy.” eCTD validations 1306 (“No leaf element for file”) and 1323 (“No file for leaf element”), within the “Specifications for eCTD Validation Criteria,” describe parts of the eCTD specifications which were not followed correctly. Rejection for failing to pass either eCTD validations 1306 or 1323 will begin on March 1, 2022.

Dated: August 18, 2021.

**Lauren K. Roth,**

*Acting Principal Associate Commissioner for Policy.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES****Food and Drug Administration**

[Docket No. FDA–2021–N–0356]

**Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Establishment and Operation of Clinical Trial Data Monitoring Committees**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA, Agency, or we) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

**DATES:** Submit written comments (including recommendations) on the collection of information by September 24, 2021.

**ADDRESSES:** To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to <https://www.reginfo.gov/public/do/PRAMain>. Find this particular information collection by selecting “Currently under Review—Open for Public Comments” or by using the search function. The OMB control number for this information collection is 0910–0581. Also include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:**

Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–5733, *PRAStaff@fda.hhs.gov*.

**SUPPLEMENTARY INFORMATION:** In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

**Establishment and Operation of Clinical Trial Data Monitoring Committees**

*OMB Control Number 0910–0581—Extension*

This collection of information supports Agency regulations and associated Agency guidance. Sponsors are required to monitor studies evaluating new drugs, biologics, and devices (21 CFR 312.50 and 312.56 for drugs and biologics, and 21 CFR 812.40

and 812.46 for devices). Various individuals and groups play different roles in clinical trial monitoring. One such group is a data monitoring committee (DMC), appointed by a sponsor to evaluate the accumulating outcome data in some trials. A clinical trial DMC is a group of individuals with pertinent expertise that reviews on a regular basis accumulating data from one or more ongoing clinical trials. The DMC advises the sponsor regarding the continuing safety of current trial subjects and those yet to be recruited to the trial, as well as the continuing validity and scientific merit of the trial.

The guidance document entitled “Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees” (March 2006) is intended to assist sponsors of clinical trials in determining when a DMC is needed for monitoring a study and how such committees should operate and is available from our website at: <https://www.fda.gov/media/75398/download>. The guidance addresses the roles, responsibilities, and operating procedures of DMCs and describes certain reporting and recordkeeping responsibilities, including the following: (1) Sponsor reporting to FDA on DMC recommendations related to safety; (2) standard operating procedures (SOPs) for DMCs; (3) DMC meeting records; (4) sponsor notification to the DMC regarding waivers; and (5) DMC reports based on meeting minutes to the sponsor.

1. Sponsor Reporting to FDA on DMC Recommendations Related to Safety

The requirement of the sponsor to report DMC recommendations related to serious adverse events in an expedited manner in clinical trials of new drugs (§ 312.32(c)) (21 CFR 312.32(c)) would not apply when the DMC recommendation is related to an excess of events not classifiable as serious. Nevertheless, the Agency recommends in the guidance that sponsors inform FDA about all recommendations related to the safety of the investigational product whether or not the adverse event in question meets the definition of “serious.”

2. SOPs for DMCs

In the guidance, FDA recommends that sponsors establish procedures to do the following things:

- Assess potential conflicts of interest of proposed DMC members;
- ensure that those with serious conflicts of interest are not included in the DMC;

- provide disclosure to all DMC members of any potential conflicts that are not thought to impede objectivity and, thus, would not preclude service on the DMC;
- identify and disclose any concurrent service of any DMC member on other DMCs of the same, related, or competing products;
- ensure separation, and designate a different statistician to advise on the management of the trial, if the primary trial statistician takes on the responsibility for interim analysis and reporting to the DMC; and
- minimize the risks of bias that are associated with an arrangement under which the primary trial statistician takes on the responsibility for interim analysis and reporting to the DMC, if it appears infeasible or highly impractical for any other statistician to take over responsibilities related to trial management.

### 3. DMC Meeting Records

The Agency recommends in the guidance that the DMC or the group preparing the interim reports to the DMC maintain all meeting records. This information should be submitted to FDA with the clinical study report (21 CFR 314.50(d)(5)(ii)).

### 4. Sponsor Notification to the DMC Regarding Waivers

The sponsor must report to FDA certain serious and unexpected adverse events in drugs and biologics trials (§ 312.32) and unanticipated adverse device effects in the case of device trials (21 CFR 812.150(b)(1)). The Agency recommends in the guidance that sponsors notify DMCs about any waivers granted by FDA for expedited reporting of certain serious events.

### 5. DMC Reports of Meeting Minutes to the Sponsor

The Agency recommends in the guidance that DMCs should issue a written report to the sponsor based on the DMC meeting minutes. Reports to the sponsor should include only those data generally available to the sponsor.

The sponsor may convey the relevant information in this report to other interested parties, such as study investigators. Meeting minutes or other information that include discussion of confidential data would not be provided to the sponsor.

*Description of the Respondents:* The submission and data collection recommendations described in this document affect sponsors of clinical trials and DMCs.

*Burden Estimate:* Table 1 of this document provides the burden estimate of the annual reporting burden for the information to be submitted in accordance with the guidance. Table 2 of this document provides the burden estimate of the annual recordkeeping burden for the information to be maintained in accordance with the guidance. Table 3 of this document provides the burden estimate of the annual third-party disclosure burden for the information to be submitted in accordance with the guidance.

*Reporting, Recordkeeping, and Third-Party Disclosure Burdens:* Based on information from FDA review divisions, FDA estimates that there are approximately 740 clinical trials with DMCs regulated by the Center for Biologics Evaluation and Research, the Center for Drugs Evaluation and Research, and the Center for Devices and Radiological Health. FDA estimates that the average length of a clinical trial is 2 years, resulting in an annual estimate of 370 clinical trials. Because FDA has no information on which to project a change in the use of DMCs, FDA estimates that the number of clinical trials with DMCs will not change significantly. For purposes of this information collection, FDA estimates that each sponsor is responsible for approximately 10 trials, resulting in an estimated 37 sponsors that are affected by the guidance annually.

Based on information provided to FDA by sponsors that have typically used DMCs for the kinds of studies for which this guidance recommends them, FDA estimates that the majority of

sponsors have already prepared SOPs for DMCs, and only a minimum amount of time is necessary to revise or update them for use for other clinical studies. FDA receives very few requests for waivers regarding expedited reporting of certain serious events; therefore, FDA has estimated one respondent per year to account for the rare instance a request may be made. Based on FDA's experience with clinical trials using DMCs, FDA estimates that the sponsor on average would issue two interim reports per clinical trial to the DMC. FDA estimates that the DMCs would hold two meetings per year per clinical trial resulting in the issuance of two DMC reports of meeting minutes to the sponsor. One set of both of the meeting records should be maintained per clinical trial.

The "Average Burden per Response" and "Average Burden per Recordkeeping" are based on FDA's experience with comparable recordkeeping and reporting provisions applicable to FDA regulated industry. The "Average Burden per Response" includes the time the respondent would spend reviewing, gathering, and preparing the information to be submitted to the DMC, FDA, or the sponsor. The "Average Burden per Recordkeeping" includes the time to record, gather, and maintain the information.

The information collection provisions in the guidance for 21 CFR 312.30, 312.32, 312.38, 312.55, and 312.56 have been approved under OMB control number 0910-0014; 21 CFR 314.50 has been approved under OMB control number 0910-0001; and 21 CFR 812.35 and 812.150 have been approved under OMB control number 0910-0078.

In the **Federal Register** of April 29, 2021 (86 FR 22690), we published a 60-day notice requesting public comment on the proposed collection of information. No comments were received.

We estimate the burden of the information collection as follows:

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN<sup>1</sup>

Section of guidance/reporting activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
5.—Sponsor reporting to FDA on DMC recommendations related to safety.	37	1	37	0.50 (30 minutes) ...	18.5
Total .....	.....	.....	.....	.....	18.5

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN<sup>1</sup>

Section of guidance/recordkeeping activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
4.1. and 6.4—SOPs for DMCs .....	37	1	37	8	296
4.4.3.2.—DMC meeting records .....	370	1	370	2	740
<b>Total .....</b>	.....	.....	.....	.....	<b>1,036</b>

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 3—ESTIMATED ANNUAL THIRD-PARTY DISCLOSURE BURDEN<sup>1</sup>

Section of guidance/disclosure activity	Number of respondents	Number of disclosures per respondent	Total annual disclosures	Average burden per disclosure	Total hours
4.4.1.2.—Sponsor notification to the DMC regarding waivers.	1	1	1	0.25 (15 minutes) ...	0.25
4.4.3.2.—DMC reports of meeting minutes to the sponsor.	370	2	740	1 .....	740
<b>Total .....</b>	.....	.....	.....	.....	<b>740.25</b>

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

Based on a review of the information collection since our last request for OMB approval, we have made no adjustments to our burden estimate.

Dated: August 5, 2021.

**Lauren K. Roth,**  
Acting Principal Associate Commissioner for Policy.  
[FR Doc. 2021-18235 Filed 8-24-21; 8:45 am]  
**BILLING CODE 4164-01-P**

## DEPARTMENT OF HOMELAND SECURITY

### Transportation Security Administration

[Docket No. TSA-2004-19147]

### Intent To Request Revision From OMB of One Current Public Collection of Information: Flight Training Security

**AGENCY:** Transportation Security Administration, DHS.

**ACTION:** 60-Day notice.

**SUMMARY:** The Transportation Security Administration (TSA) invites public comment on one currently approved Information Collection Request (ICR), Office of Management and Budget (OMB) control number 1652-0021, that we will submit to OMB for a revision, in compliance with the Paperwork Reduction Act (PRA). The ICR describes the nature of the information collection and its expected burden. The collection involves information necessary to conduct security threat assessments for all non-U.S. citizens, non-U.S. nationals, and other designated individuals seeking flight instruction (“candidates”) from Federal Aviation

Administration (FAA)-certified flight training providers. Pursuant to statute, TSA will use the information collected to determine whether a candidate poses or is suspected of posing a threat to aviation or national security, and is thus prohibited from receiving flight training. Additionally, flight training providers are required to conduct a security awareness training program for their employees and to maintain records associated with this training.

**DATES:** Send your comments by October 25, 2021.

**ADDRESSES:** Comments may be emailed to [TSAPRA@dhs.gov](mailto:TSAPRA@dhs.gov) or delivered to the TSA PRA Officer, Information Technology (IT), TSA-11, Transportation Security Administration, 6595 Springfield Center Drive, Springfield, VA 20598-6011.

**FOR FURTHER INFORMATION CONTACT:** Christina A. Walsh at the above address, or by telephone (571) 227-2062.

### SUPPLEMENTARY INFORMATION:

#### Comments Invited

In accordance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*), an agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a valid OMB control number. The ICR documentation will be available at <http://www.reginfo.gov> upon its submission to OMB. Therefore, in preparation for OMB review and approval of the following information collection, TSA is soliciting comments to—

(1) Evaluate whether the proposed information requirement is necessary for

the proper performance of the functions of the agency, including whether the information will have practical utility;

(2) Evaluate the accuracy of the agency's estimate of the burden;

(3) Enhance the quality, utility, and clarity of the information to be collected; and

(4) Minimize the burden of the collection of information on those who are to respond, including using appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology.

### Information Collection Requirement

*OMB Control Number 1652-0021, Flight Training Security.* Under 49 CFR part 1552, TSA conducts security threat assessments for all non-U.S. citizens, non-U.S. nationals, and other designated individuals seeking flight instruction with Federal Aviation Administration (FAA)-certified flight training providers.<sup>1</sup> The purpose of this requirement is to ensure flight training candidates do not pose a threat to aviation or national security and thus can be permitted to receive flight training. The collection of information required under 49 CFR part 1552 includes candidates' biographic information and fingerprints, which TSA uses to perform the security threat assessment.

Additionally, flight training providers are required to maintain records of security awareness training provided to their employees. See subpart B of 49 CFR part 1552. This training, which is

<sup>1</sup> See also 49 U.S.C. 44939.