§ 39.13 [Amended]

■ 2. The FAA amends § 39.13 by adding the following new airworthiness directive:

Airbus SAS: Docket No. FAA–2026–2729; Project Identifier MCAI–2025–00726–T.

(a) Comments Due Date

The FAA must receive comments on this airworthiness directive (AD) by May 14, 2026.

(b) Affected ADs

None.

(c) Applicability

This AD applies to Airbus SAS Model A350–941 airplanes, certificated in any category, as identified in European Union Aviation Safety Agency (EASA) AD 2025–0150, dated July 14, 2025 (EASA AD 2025–0150).

(d) Subject

Air Transport Association (ATA) of America Code 32, Landing gear.

(e) Unsafe Condition

This AD was prompted by a report of a missing main landing gear (MLG) brake rod center pin nut sub-assembly detected during an inspection. The FAA is issuing this AD to address discrepancies of the MLG brake rod center pin and nut that could lead to detachment of the MLG brake rod center pin nut sub-assembly. This condition, if not addressed, could prevent the extension of the MLG, possibly resulting in damage to the airplane and injury to occupants.

(f) Compliance

Comply with this AD within the compliance times specified, unless already done.

(g) Requirements

Except as specified in paragraph (h) of this AD: Comply with all required actions and compliance times specified in, and in accordance with, EASA AD 2025–0150.

(h) Exceptions to EASA AD 2025–0150

(1) Where EASA AD 2025–0150 refers to its effective date, this AD requires using the effective date of this AD.

(2) Where EASA AD 2025–0150 refers to May 9, 2025 (the effective date of EASA AD 2025–0095), this AD requires using the effective date of this AD.

(3) This AD does not adopt the ''Remarks'' section of EASA AD 2025–0150.

(i) Additional AD Provisions

The following provisions also apply to this AD:

(1) *Alternative Methods of Compliance (AMOCs):* The Manager, AIR–520, Continued Operational Safety Branch, FAA, has the authority to approve AMOCs for this AD, if requested using the procedures found in 14 CFR 39.19. In accordance with 14 CFR 39.19, send your request to your principal inspector or responsible Flight Standards Office, as appropriate. If sending information directly to the manager of the Continued Operational Safety Branch, send it to the attention of the person identified in paragraph (j) of this AD and email to: *AMOC@faa.gov*. Before using any approved AMOC, notify your appropriate principal inspector, or lacking a principal inspector, the manager of the responsible Flight Standards Office.

(2) *Contacting the Manufacturer:* For any requirement in this AD to obtain instructions from a manufacturer, the instructions must be accomplished using a method approved by the Manager, AIR–520, Continued Operational Safety Branch, FAA; or EASA; or Airbus SAS's EASA Design Organization Approval (DOA). If approved by the DOA, the approval must include the DOA-authorized signature.

(3) *Required for Compliance (RC):* Except as required by paragraph (i)(2) of this AD, if any material referenced in EASA AD 2025–0150 contains paragraphs that are labeled as RC, the instructions in RC paragraphs, including subparagraphs under an RC paragraph, must be done to comply with this AD; any paragraphs, including subparagraphs under those paragraphs, that are not identified as RC are recommended. The instructions in paragraphs, including subparagraphs under those paragraphs, not identified as RC may be deviated from using accepted methods in accordance with the operator's maintenance or inspection program without obtaining approval of an AMOC, provided the instructions identified as RC can be done and the airplane can be put back in an airworthy condition. Any substitutions or changes to instructions identified as RC require approval of an AMOC.

(j) Additional Information

For more information about this AD, contact Andrew Younglove, Aviation Safety Engineer, FAA, 2200 South 216th St., Des Moines, WA 98198; phone: 206–231–3644; email: *andrew.e.younglove@faa.gov.*

(k) Material Incorporated by Reference

(1) The Director of the Federal Register approved the incorporation by reference of the material listed in this paragraph under 5 U.S.C. 552(a) and 1 CFR part 51.

(2) You must use this material as applicable to do the actions required by this AD, unless this AD specifies otherwise.

(i) European Union Aviation Safety Agency (EASA) AD 2025–0150, dated July 14, 2025.

(ii) Reserved.

(3) For EASA material identified in this AD, contact EASA, Konrad-Adenauer-Ufer 3, 50668 Cologne, Germany; telephone +49 221 8999 000; email *ADs@easa.europa.eu.* You may find this material on the EASA website at *ad.easa.europa.eu.*

(4) You may view this material at the FAA, Airworthiness Products Section, Operational Safety Branch, 2200 South 216th St., Des Moines, WA. For information on the availability of this material at the FAA, call 206–231–3195.

(5) You may view this material at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, visit *www.archives.gov/federal-register/cfr/ibr-locations* or email *fr.inspection@nara.gov.*

Issued on March 25, 2026.

Lona C. Saccomando,

Acting Deputy Director, Integrated Certificate Management Division, Aircraft Certification Service.

[FR Doc. 2026–06085 Filed 3–27–26; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2026–N–2590]

Microbiology Devices; Reclassification of Mycobacterium Tuberculosis Cell-Mediated Immunity Tests and Immune Response Enzyme-Linked Immunospot Tests

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed amendment; proposed order; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is proposing to reclassify *Mycobacterium tuberculosis* cell-mediated immunity tests and *Mycobacterium tuberculosis* cell-mediated immune response enzyme-linked immunospot tests intended for use as an aid in the diagnosis of *Mycobacterium tuberculosis* infection (product codes NCD and OJN, respectively), both of which are postamendments class III devices (premarket approval), into class II (special controls), subject to premarket notification. FDA is also proposing a new device classification regulation along with the special controls that FDA believes are necessary to provide a reasonable assurance of safety and effectiveness for these devices.

DATES: Submit electronic or written comments on the proposed order by May 29, 2026. Please see section X of this document for the proposed effective date when the new requirements would apply and for the proposed effective date of a final order based on this proposed order.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of May 29, 2026. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal Rulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2026–N–2590 for ''Microbiology Devices; Reclassification of *Mycobacterium tuberculosis* Cell-Mediated Immunity Tests and Immune Response Enzyme-Linked Immunospot Tests.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday Eastern Time, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' FDA will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents, the plain language summary of the proposed order of not more than 100 words consistent with the ''Providing Accountability Through Transparency Act,'' or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Noel Gerald, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3114, Silver Spring, MD 20993, 301–796–4695, *Noel.Gerald@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background—Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended, establishes a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) establishes three classes of devices reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three classes of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Section 513(a)(1) of the FD&C Act defines the three classes of devices. Class I devices are those devices for which the general controls of the FD&C Act (controls authorized by or under sections 501, 502, 510, 516, 518, 519, or 520 (21 U.S.C. 351, 352, 360, 360f, 360h, 360i, or 360j) or any combination of such sections) are sufficient to provide reasonable assurance of safety and effectiveness of the device; or those devices for which insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of safety and effectiveness or to establish special controls to provide such assurance, but because the devices are not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and do not present a potential unreasonable risk of illness or injury, are to be regulated by general controls (section 513(a)(1)(A) of the FD&C Act).

Class II devices are those devices for which general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, and for which there is sufficient information to establish special controls to provide such assurance, including the issuance of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions FDA (the Agency or we) deems necessary to provide such assurance (section 513(a)(1)(B) of the FD&C Act).

Class III devices are those devices for which insufficient information exists to determine that general controls and special controls would provide a reasonable assurance of safety and effectiveness, and are purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury (section 513(a)(1)(C) of the FD&C Act).

Devices that were not introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976 (generally referred to as ''postamendments devices'') are automatically classified by section 513(f)(1) of the FD&C Act into class III without any FDA action. Those devices remain in class III and require approval of a premarket approval application (PMA), unless, and until: (1) FDA reclassifies the device into class I or II,

or (2) FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to predicate devices by means of the premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807, subpart E, of FDA's regulations (21 CFR part 807, subpart E).

A postamendments device that has been initially classified in class III under section 513(f)(1) of the FD&C Act may be reclassified into class I or class II under section 513(f)(3) of the FD&C Act. Section 513(f)(3) of the FD&C Act provides that FDA, acting by administrative order, can reclassify the device into class I or class II on its own initiative, or in response to a petition from the manufacturer or importer of the device. To change the classification of the device, the proposed new class must have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.[1]

FDA relies upon ''valid scientific evidence'', as stated in section 513(a)(3) of the FD&C Act and defined in 21 CFR 860.7(c)(2), in the classification process to determine the level of regulation for devices.[2] In general, to be considered in the reclassification process, the ''valid scientific evidence'' upon which the Agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, *e.g.,* the contents of a pending PMA (see section 520(c) of the FD&C Act). Section 520(h)(4) of the FD&C Act provides that FDA may use, for reclassification of a device, certain information in a PMA 6 years after the application has been approved. This includes information from clinical and preclinical tests or studies that demonstrate the safety and effectiveness of the device, but it does not include the descriptions of methods of manufacture and product composition and other trade secrets.

In accordance with section 513(f)(3) of the FD&C Act, FDA is issuing this proposed order to reclassify *Mycobacterium tuberculosis* cell-mediated immunity tests (product code NCD)[3] and *Mycobacterium tuberculosis* cell-mediated immune response enzyme-linked immunospot tests (product code OJN), both qualitative assays intended for use as an aid in the diagnosis of *Mycobacterium tuberculosis* (TB) infection, hereafter collectively referred to as ''qualitative TB immune response assays,'' which are postamendments class III devices, into class II (special controls), subject to premarket notification, under a new device classification regulation with the name ''Qualitative *Mycobacterium tuberculosis* cell-mediated immune response assay.''

Based upon the PMA data available to FDA in accordance with section 520(h)(4) of the FD&C Act,[4] [5] clinical practice guidelines, deliberations and recommendations from the Microbiology Devices Panel of the Medical Devices Advisory Committee discussions held in 2001, 2011, and 2023, and data available to the Agency demonstrating a lack of significant postmarket safety signals with these assays, FDA believes there is sufficient information to reclassify these devices from class III (premarket approval) into class II (special controls). FDA believes the standard in section 513(a)(1)(B) of the FD&C Act is met as there is sufficient information to establish special controls, which, in addition to general controls, would provide reasonable assurance of the safety and effectiveness of these devices.[6] Therefore, FDA is proposing to establish a new device classification regulation, ''Qualitative *Mycobacterium tuberculosis* cell-mediated immune response assay,'' and classify these devices into class II with the special controls that the Agency believes are necessary to provide a reasonable assurance of the safety and effectiveness for these devices.

Under the FD&C Act, premarket notification (510(k)) submissions are required to reasonably assure the safety and effectiveness of class II devices unless FDA determines that the device type should be exempt from 510(k) requirements under section 510(m) of the FD&C Act.[7] FDA has not made this determination for qualitative *Mycobacterium tuberculosis* cell-mediated immune response assays and therefore, FDA is not proposing that this class II device type be exempt from the 510(k) requirements. If this proposed order is finalized, persons who intend to market this type of device will have to submit to FDA a premarket notification under section 510(k) of the FD&C Act prior to marketing the device.

II. Regulatory History of the Devices

In accordance with section 513(f)(1) of the FD&C Act, qualitative TB immune response assays are automatically classified into class III because they were not introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, have not been reclassified into

[1] See generally section 513 of the FD&C Act.

[2] See generally id.

[3] FDA's Center for Devices and Radiological Health (CDRH) uses product codes to assist in accurate identification and tracking of current medical devices and to allow for tracking of and easy reference to predicate device types. CDRH and a subset of Center for Biologics Evaluation and Research regulated medical device product codes consist of a three-letter combination which associates a device's type with a product classification designated for the application. There is no definitive meaning for the three-digit classification product codes in CDRH's Product Classification Database. See FDA guidance titled, ''Medical Device Classification Product Codes'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/medical-device-classification-product-codes-guidance-industry-and-food-and-drug-administration-staff.*

[4] In proposing to reclassify, on its own initiative, qualitative TB immune response assays from class III to class II, FDA is relying on data from PMAs with product codes of NCD or OJN that are available to FDA in accordance with the six-year rule (see section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4))) (see also, FDA guidance titled ''Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997—Guidance for Industry and for FDA Reviewers,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-section-216-food-and-drug-administration-modernization-act-1997-guidance-industry-and-fda*). This data was from PMAs approved after November 28, 1990 and before December 1, 2019, for this specific proposed reclassification as noted in section II of this proposed order. See also FDA's premarket approval database, available at *https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm.*

[5] For the purpose of this proposed order, PMA data considered in accordance with section 520(h)(4) includes only that data which was submitted to and therefore considered by FDA at the time the PMA was reviewed and approval was issued.

[6] FDA notes that the ''ACTION'' caption for this proposed order is styled as ''Proposed amendment; proposed order; request for comments,'' rather than ''Proposed order.'' Beginning in December 2019, this editorial change was made to indicate that the document, if finalized, will amend the Code of Federal Regulations. The change was made in accordance with the Office of the Federal Register's (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

[7] In considering whether to exempt class II devices from premarket notification, FDA considers whether premarket notification for the type of device is necessary to provide reasonable assurance of safety and effectiveness of the device. FDA generally considers the factors initially identified in the January 21, 1998, **Federal Register** notice (63 FR 3142) and further explained in FDA's guidance issued on February 19, 1998, titled ''Procedures for Class II Device Exemptions from Premarket Notification, Guidance for Industry and CDRH Staff'', available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/procedures-class-ii-device-exemptions-premarket-notification-guidance-industry-and-cdrh-staff,* in determining whether premarket notification is necessary for class II devices. FDA also considers that, even when exempting devices from the 510(k) requirements, these devices would still be subject to certain limitations on exemptions, for example, the general limitations set forth in 21 CFR 866.9.

class I or II, and have not been found substantially equivalent to a device placed in commercial distribution after May 28, 1976, which was subsequently classified or reclassified into class II or class I. Therefore, these devices are subject to the PMA requirements under section 515 of the FD&C Act (21 U.S.C. 360e).

On June 1, 2001, FDA filed an original PMA (P010033) for the QuantiFERON®–TB (Ref. 1). At a meeting on October 12, 2001, the Microbiology Devices Panel (2001 Panel) of the Medical Devices Advisory Committee deliberated and made recommendations on the QuantiFERON–TB PMA (Ref. 2). The 2001 Panel unanimously recommended the PMA be considered Approvable with Conditions, which conditions included, among other items, stratification of the data by risk groups, labeling warnings or limitations, and interpretation of results and recommendations for use of the test provided in the labeling. On November 28, 2001, FDA approved the original PMA for the Cellestis Limited's (now QIAGEN) QuantiFERON–TB, (P010033, product code NCD) for the qualitative measurement of interferon-gamma (IFN-γ) generated by human lymphocytes in whole blood in response to stimulation antigens for use as an aid in the detection of infection with *Mycobacterium tuberculosis,* through its PMA process under section 515 of the FD&C Act (21 U.S.C. 360e) (Ref. 3).

Since the first approval order for a qualitative TB immune response assay issued on November 28, 2001, FDA has approved an additional original PMA, on November 26, 2019, for a qualitative TB immune response assay (product code NCD, DiaSorin, Inc.'s LIAISON QuantiFERON—TB Gold Plus, LIAISON Control QuantiFERON—TB Gold Plus and LIAISON QuantiFERON Software, P180047, collectively ''LIAISON QuantiFERON—TB Gold Plus'') for the detection of IFN-γ generated by human lymphocytes in whole blood in response to stimulation antigens for use as a qualitative indirect test for *Mycobacterium tuberculosis* infection (including disease) (Ref. 4). The QuantiFERON–TB and LIAISON QuantiFERON—TB Gold Plus are prescription devices intended for use as an aid in the detection of infection with *Mycobacterium tuberculosis* and are intended for use in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations to assist the clinician in making individual patient management decisions.

On July 30, 2008, FDA approved a qualitative TB immune response enzyme-linked immunospot assay (product code OJN, Oxford Immunotec, Inc.'s T–SPOT®-*TB,* P070006) for the detection of effector T cells that respond to stimulation by *Mycobacterium tuberculosis* antigens by capturing IFN-γ in the vicinity of T cells in human whole blood for use as an aid in the diagnosis of *Mycobacterium tuberculosis* infection, through its PMA process under section 515 of the FD&C Act (21 U.S.C. 360e) (Ref. 5).

As of the date of issuance of this proposed order, fewer than 6 years have passed since FDA's approval of certain PMA supplements for these three PMAs. Therefore, in accordance with the ''six-year rule'' described in section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4)), no information from those PMA supplements has been used in support of this proposed order to reclassify qualitative TB immune response assays into class II (see section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4))).

Since the 2001 Panel discussed the first PMA for this device type, there have been two other panel meetings that have considered reclassification of qualitative TB immune response assays. At a meeting on June 29, 2011, the Microbiology Devices Panel of the Medical Devices Advisory Committee (2011 Panel) discussed the possible reclassification of immunologically-based tests such as interferon gamma release assays (IGRAs) that are intended for the detection of tuberculosis infection by indirect means, and specifically considered appropriate validation, the risks of inaccurate results, and labeling limitations to mitigate risks (Ref. 6). While the overall 2011 Panel agreed that reclassification could be considered, multiple concerns were expressed with down classification, and several members were not in favor. It was noted that then-ongoing studies of existing IGRAs may provide additional information important for identifying appropriate special controls. At the time of the 2011 Panel, FDA had approved the QuantiFERON–TB (P010033) (product code NCD) and the T–SPOT–*TB* (P070006) (product code OJN). However, it was several years after the 2011 Panel that FDA approved the LIAISON QuantiFERON—TB Gold Plus (P180047), the second PMA assigned product code NCD.

On September 7, 2023, the Microbiology Devices Panel of the Medical Devices Advisory Committee (2023 Panel) convened to discuss and make recommendations regarding the reclassification of qualitative *Mycobacterium tuberculosis* (TB) cell mediated immune reactivity/Interferon Gamma Release Assays from class III (premarket approval) to class II (special controls) (Ref. 7). The 2023 Panel members unanimously agreed with down classification from class III to class II for these assays, and that there was sufficient data to proceed with the reclassification (see ''MDP Sept. 7, 2023 Transcript'' and ''MDP Sept. 7, 2023 Summary Minutes'' of the 2023 Panel materials, Ref. 7). The 2023 Panel agreed with the FDA-identified risks (false negative or false positive results, including from incorrectly operating the device and incorrectly interpreting the results) and identified additional risk(s) to include in the overall risk assessment. These additional risks included the higher risks posed by false results for specific populations, such as immunocompromised individuals; risk of an indeterminate result where the clinical interpretation is not clear; risk of inappropriate use of the test for a particular patient; and risk of an incorrect result that leads to treatment delays for other diseases (see ''MDP Sept. 7, 2023 Summary Minutes'' of the 2023 Panel materials, Ref. 7). The 2023 Panel also discussed potential mitigation measure(s)/control(s) FDA should consider for each of the identified risks and recommended that, as part of any reclassification, new devices should be held to the same level of clinical and analytical validation with the same performance criteria as currently approved tests, including adequate validation of the pre-analytical stages of specimen preparation that have the potential to impact the performance of these tests and that labeling should clarify how risks differ depending on the population being tested and the pre-test probability of disease.

A review of data from FDA's Manufacturer and User Facility Device Experience (MAUDE) database, which contains the medical device reports (MDRs) of adverse events using product codes NCD and OJN, indicates that as of October 23, 2025, there were 27 MDRs for qualitative TB immune response assays (all 27 are for product code NCD and there are none identified for OJN). Of these MDRs, approximately half were determined by FDA to be of no known impact or consequence to the patient. Of the events that were reported to have resulted in patient misdiagnosis or inappropriate treatment, a majority were reported due to adverse effects of antibiotic treatment, with a small number of cases reporting worsening of other medical conditions. As of October 23, 2025, there have been two class III recalls, six class II recalls, and no class

I recalls [8] involving qualitative TB immune response assays. The class II recalls occurred in 2013, 2016, and 2022, due to the potential presence of endotoxin or other contamination in assay components, and products being stored at temperatures outside the validated storage conditions. The class III recalls occurred in 2020, due to incorrect expiration dating included in the kit labeling. No patient harm was identified related to the recalls. The issues leading to these recall events were considered and incorporated into the risks to health identified in section V. These facts, coupled with the low number of MDRs that could have caused patient harm, indicate a lack of significant postmarket safety signals for this device class. FDA believes the special controls proposed herein, in addition to general controls, can effectively mitigate the risks to health identified to provide a reasonable assurance of the safety and effectiveness of qualitative TB immune response assays.

Following the meeting of the 2011 Panel, but prior to the meeting of the 2023 Panel, FDA received a petition requesting that the FDA reclassify *Mycobacterium tuberculosis* cell-mediated immunity tests (product code NCD) from class III to class II (FDA–2019–P–1800). As discussed in this proposed order, FDA has considered the information available to the Agency and believes that there is sufficient information available to establish special controls, and that the special controls proposed in section VII, together with general controls, would provide a reasonable assurance of the safety and effectiveness of qualitative TB immune response assays, including qualitative *Mycobacterium tuberculosis* cell-mediated immunity tests (product code NCD). Accordingly, FDA is proposing, on its own initiative, that qualitative *Mycobacterium tuberculosis* cell-mediated immunity tests (product code NCD) and *Mycobacterium tuberculosis* cell-mediated immune response enzyme-linked immunospot tests (product code OJN) be reclassified from class III to class II.

III. Device Description

The qualitative TB immune response assays intended for use as an aid in the diagnosis of *Mycobacterium tuberculosis* infection that are the subject of this proposed order are postamendments prescription in vitro diagnostic devices classified into class III under section 513(f)(1) of the FD&C Act.

The immune response to infection with *Mycobacterium tuberculosis* is predominantly a cell-mediated immune response that results in sensitization of T-cell lymphocytes specific to *Mycobacterium tuberculosis* antigens. A TB immune response assay for the qualitative measurement of IFN-γ generated by human lymphocytes in response to stimulation antigens is a prescription in vitro diagnostic device intended for use as an aid in the diagnosis of *Mycobacterium tuberculosis* infection. A TB immune response enzyme-linked immunospot assay is a prescription in vitro diagnostic device intended for use for the qualitative detection of effector T cells that respond to stimulation by *Mycobacterium tuberculosis* antigens by capturing IFN-γ in the vicinity of the T cell in human whole blood and as an aid in the diagnosis of *Mycobacterium tuberculosis* infection. Qualitative TB immune response assays are intended for use in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations. Diagnosis of TB infection should not be established based on a single test result from a qualitative TB immune response assay.

Currently, qualitative TB immune response assays are used as an aid in the diagnosis of tuberculosis infection, including disease. Qualitative TB immune response assays can be used to assess for latent and active tuberculosis infection, however, such assays cannot differentiate between latent and active tuberculosis. Additional diagnostic testing is necessary to determine if there is active tuberculosis before selecting a treatment regimen. Qualitative TB immune response assays are preferred over the Mantoux tuberculin skin test method when evaluating patients with a history of bacille Calmette-Guérin (BCG) vaccine and in clinical scenarios where a single patient visit is advantageous (Ref. 8). Epidemiological, demographic, and clinical factors should be considered when determining the appropriate patients for testing with a qualitative TB immune response assay and should inform any additional diagnostic workup that may be necessary to guide therapeutic decisions (Ref. 8).

Healthcare professionals may refer to clinical practice guidelines from the American Thoracic Society (Ref. 8), Infectious Disease Society of America (Ref. 8), or Centers for Disease Control and Prevention (Ref. 8) when determining how to use qualitative TB immune response assays to manage patients suspected of latent or active tuberculosis, or patients with risk factors for tuberculosis infection. Since the original FDA approval of the QuantiFERON–TB *Mycobacterium tuberculosis* cell-mediated immune response assay in 2001, qualitative TB immune response assays have become an important part of the management of tuberculosis infection and are one component of a larger diagnostic approach for the evaluation of patients with potential tuberculosis infections (Ref. 8). However, management of tuberculosis should be determined in conjunction with patient-specific clinical and epidemiological risk factors and other diagnostic information, such as supportive radiographic imaging and other laboratory testing (Ref. 9).

FDA is proposing to reclassify qualitative TB immune response assays from class III (premarket approval) to class II (special controls) and to establish a new name for the device type within the classification regulations. FDA proposes to revise 21 CFR part 866 to create a new device classification regulation with the name ''Qualitative *Mycobacterium tuberculosis* cell-mediated immune response assay.'' FDA believes that this name and the proposed identification language most accurately describes this device type.

A qualitative *Mycobacterium tuberculosis* cell-mediated immune response assay is tentatively identified as a prescription in vitro diagnostic device intended to aid in the diagnosis of *Mycobacterium tuberculosis* infection. Qualitative *Mycobacterium tuberculosis* cell-mediated immune response assays measure the production of IFN-γ or other cytokines by human lymphocytes in response to stimulation antigens. The assay is intended for use by a licensed healthcare professional as an aid in the diagnosis of *Mycobacterium tuberculosis* infection in conjunction with risk assessment, radiographic imaging, and other medical and diagnostic evaluations.

IV. Proposed Reclassification and Summary of Reasons for Reclassification

In accordance with section 513(f)(3) of the FD&C Act and 21 CFR part 860, subpart C, FDA is proposing to reclassify the qualitative TB immune response assays that are the subject of this proposed order from class III to class II, subject to premarket notification (510(k)) requirements.

FDA believes that at this time, sufficient data and information exist such that the risks to health identified in section V can be mitigated by establishing special controls, and that

[8] Class I, II, and III recalls are defined in 21 CFR 7.3(m).

these special controls, together with general controls, are necessary to provide a reasonable assurance of the safety and effectiveness of these qualitative TB immune response assays and therefore proposes these devices be reclassified from class III (premarket approval) to class II (special controls). FDA believes that the information available to FDA through the QuantiFERON–TB (P010033), LIAISON QuantiFERON—TB Gold Plus (P180047), and T–SPOT-*TB* (P070006) PMAs [9] (Refs. 3–5) that may be considered under section 520(h)(4) of the FD&C Act, deliberations and recommendations from associated panel discussions held during the 2001 Panel, 2011 Panel, and 2023 Panel, published clinical practice guidelines (Refs. 8–9), and FDA's publicly available MAUDE and the Medical Device Recall databases is sufficient to establish special controls that, together with general controls, effectively mitigate the risks to health identified in section 0. FDA does not believe that the general controls applicable to the devices are sufficient to effectively mitigate the risks to health identified for these devices, and therefore does not believe that the general controls applicable to the devices are sufficient to provide reasonable assurance of the safety and effectiveness of these devices.

FDA is proposing to revise 21 CFR part 866 to create a new device classification regulation with the name ''Qualitative *Mycobacterium tuberculosis* cell-mediated immune response assay.'' If the proposed order is finalized, qualitative *Mycobacterium tuberculosis* cell-mediated immune response assays will be identified as prescription in vitro diagnostic devices. Such devices are subject to the prescription labeling requirements for in vitro diagnostic products (see 21 CFR 809.10(a)(4) and (b)(5)(ii)). In this proposed order, FDA has identified the special controls under section 513(a)(1)(B) of the FD&C Act that it believes, together with general controls, will provide a reasonable assurance of the safety and effectiveness of these assays.

Under the FD&C Act, 510(k) submissions are required to reasonably assure the safety and effectiveness of class II devices unless FDA determines that the device type should be exempt from 510(k) requirements under section 510(m) of the FD&C Act.[10] FDA has not made this determination for these qualitative TB immune response assays, and therefore, FDA is not proposing that this class II device type be exempt from 510(k) requirements. If this proposed order is finalized, persons who intend to market qualitative TB immune response assays will need to submit to FDA a 510(k) and receive clearance prior to marketing the device.

This proposed order, if finalized, will decrease regulatory burden on industry, as manufacturers will no longer have to submit a PMA for this type of device but can instead submit a 510(k) to the Agency for review prior to marketing their device. The 510(k) pathway is less burdensome and generally more cost-effective for industry and FDA than the PMA pathway, the most stringent type of device marketing pathway. A 510(k) typically results in a shorter premarket review timeline compared to a PMA, which ultimately may provide more timely patient access to this type of device. FDA expects that the reclassification of these devices would enable more manufacturers to develop this type of device such that patients would benefit from increased access to appropriately safe and effective tests.

Additionally, manufacturers may wish to use predetermined change control plans (PCCPs) as a way to implement future modifications to their devices without needing to submit a new 510(k) for each significant change or modification [11] while continuing to provide a reasonable assurance of device safety and effectiveness.[12] FDA reviews a PCCP as part of a marketing submission for a device to ensure the continued safety and effectiveness of the device without necessitating additional marketing submissions for implementing each modification described in the PCCP. When used appropriately, PCCPs authorized by FDA are expected to be least burdensome for manufacturers and FDA.[13]

V. Risks to Health

FDA is providing a substantive summary of the valid scientific evidence concerning the public health benefits of the use of qualitative TB immune response assays (see also ''MDP Sept. 7, 2023 FDA Executive Summary'' of the 2023 Panel materials, Ref. 7), and the nature (and if known, the incidence) of the risks to health of the devices (see further discussion of the special controls being proposed to mitigate these risks in section VII of this proposed order). FDA considered data from three PMAs available to FDA under section 520(h)(4) of the FD&C Act, deliberations and recommendations from associated panel discussions held during the 2001 Panel, 2011 Panel, and 2023 Panel (Refs. 2, 6–7), published clinical practice guidelines (Refs. 8–9), and postmarket information regarding qualitative TB immune response assays.

Qualitative TB immune response assays provide a benefit to the public health by aiding in the diagnosis of *Mycobacterium tuberculosis* infection. The incidence of tuberculosis infection varies considerably with epidemiological risk factors such as immigration from a country with high tuberculosis prevalence or close contacts with known active tuberculosis cases (Ref. 8). Certain patients who may be at increased risk of progression from latent to active tuberculosis include young children, individuals with human immunodeficiency virus (HIV) or those receiving immunosuppressive medications (Ref. 8). Individuals considered to be at higher risk for progression to active tuberculosis infection may benefit from testing with a qualitative TB immune response assay. Treatment of latent tuberculosis in high-risk individuals can decrease the risk of developing active tuberculosis and clinicians may assess tuberculosis status using a qualitative TB immune response assay in patients prior to starting immunosuppressive medications, or in patients with other known risk factors for tuberculosis. Distinguishing between latent and active tuberculosis requires additional diagnostic evaluation; however, qualitative TB immune response assays are considered an important part of the diagnostic workup for tuberculosis. Additionally, qualitative TB immune

[9] In accordance with section 520(h)(4) of the FD&C Act, FDA has not relied on information in PMAs and PMA supplements approved within the last 6 years to develop the proposed special controls or to otherwise inform this proposed reclassification action.

[10] See *supra* note 7.

[11] For the purpose of this proposed order reference to ''modification'' means a significant change or modification that would generally require a new premarket notification under 21 CFR 807.81(a)(3).

[12] Section 3308 of the Food and Drug Omnibus Reform Act of 2022, Title III of Division FF of the Consolidated Appropriations Act, 2023, Public Law 117–328 (''FDORA''), enacted on December 29, 2022, added section 515C ''Predetermined Change Control Plans for Devices'' to the FD&C Act. Section 515C has provisions regarding predetermined change control plans (PCCPs) for devices requiring premarket approval or premarket notification. Under section 515C, supplemental applications (section 515C(a)) and new premarket notifications (section 515C(b)) are not required for a change to a device that would otherwise require a premarket approval supplement or new premarket notification if the change is consistent with a PCCP approved or cleared by FDA.

[13] Sections 513 and 515 of the FD&C Act. See also, FDA's guidance ''The Least Burdensome Provisions: Concept and Principles'', available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.*

response assays are preferred in patients with prior BCG vaccination and in patients where a single clinical visit is advantageous (Ref. 8). Qualitative TB immune response assays provide a further benefit to the public health by linking TB infected individuals to appropriate care and potentially reducing the risk of TB transmission. Antibiotic regimens to treat latent TB infection and active TB disease are available.

The probable risks associated with qualitative TB immune response assays, when used as intended, are those related to risks of inaccurate results, including failure to correctly interpret the test results, the risk of false test results, and failure to correctly operate the device causing false results. Factors that may cause an increased rate of inaccurate results include, but are not limited to, incorrect blood sample collection or improper handling of the specimen affecting lymphocyte function, inaccurate lymphocyte quantification, and co-morbid conditions that affect immune functions. Based on FDA's review of data in the PMAs for QuantiFERON–TB (P010033), LIAISON QuantiFERON—TB Gold Plus (P180047), and T–SPOT–*TB* (P070006) available to FDA under section 520(h)(4) of the FD&C Act, deliberations and recommendations from associated panel discussions held during the 2001 Panel, 2011 Panel, and 2023 Panel for the reclassification of these devices (see ''MDP Sept. 7, 2023 Summary Minutes'' and ''MDP Sept. 7, 2023 Transcript'' of the 2023 Panel materials, Ref. 7), postmarket information, and the clinical practice guidelines (Refs. 8–9), FDA has identified the following probable risks to health associated with qualitative TB immune response assays. These risks to health (and the proposed special controls in section VII) incorporate feedback from the 2023 Panel, including the higher risks posed by false results for specific populations, such as immunocompromised individuals; risk of an indeterminate result where the clinical interpretation is not clear; risk of inappropriate use of the test for a particular patient; and risk of an incorrect result that leads to treatment delays for other diseases.

- *Failure to correctly interpret the test results.* Failure to correctly interpret the test results, such as incorrectly interpreting the qualitative TB immune response assay result by a clinician as either a negative or positive result may negatively influence patient management decisions. A positive test result misinterpreted as negative may lead to a non-diagnosis or delay in diagnosis of active or latent TB infection with an associated delay in therapy and potential for progression of active infection or reactivation of latent TB disease, which can contribute to an increased risk of TB-related morbidity or mortality. Additionally, incorrectly interpreting a positive test result as a negative result may facilitate the spread of *Mycobacterium tuberculosis* to other individuals in the community. Incorrectly interpreting the test result as a negative result may represent a missed opportunity for evaluation and subsequent treatment of underlying immunocompromising conditions such as HIV, as well as a missed opportunity to provide antimicrobial therapy for latent tuberculosis infection. Incorrectly interpreting the test result as positive may contribute to improper patient management including unnecessary additional testing and radiologic imaging, patient isolation, public health contact tracing leading to wasted healthcare resources, as well as unnecessary antimicrobial treatment for TB infection with associated drug toxicities, and the risk of delayed treatment for the true cause of disease.
- *False negative/positive result.* A false negative qualitative TB immune response assay result may lead to a non-diagnosis or delay in diagnosis of active or latent TB infection with an associated delay in therapy and potential for progression of active infection or reactivation of latent TB disease, which can contribute to an increased risk of TB-related morbidity or mortality. Additionally, a false negative result may facilitate the spread of *Mycobacterium tuberculosis* to other individuals in the community. A false negative result may represent a missed opportunity for evaluation and subsequent treatment of underlying immunocompromising conditions such as HIV, as well as a missed opportunity to provide antimicrobial therapy for latent tuberculosis infection. A false positive qualitative TB immune response assay result may contribute to improper patient management including unnecessary additional testing and radiologic imaging, patient isolation, public health contact tracing leading to wasted healthcare resources, as well as unnecessary antimicrobial treatment for TB infection with associated drug toxicities, and the risk of delayed treatment for the true cause of disease.
- *Failure to correctly operate the assay.* Failure to correctly operate the qualitative TB immune response assay may cause a false negative or false positive result, which may lead to the risks to health discussed in the preceding bullet.

VI. Summary of Data Upon Which the Reclassification Is Based

The safety and effectiveness of these devices have become well established since the initial approval of the first qualitative TB immune response assay in 2001. FDA believes that qualitative TB immune response assays should be reclassified from class III (premarket approval) into class II (special controls) on the basis that special controls, in addition to general controls, can be established to mitigate the risks to health identified in section V and there is sufficient information to establish special controls, which, in addition to general controls, would provide a reasonable assurance of the safety and effectiveness of these devices. The proposed special controls are identified by FDA in section VII of this proposed order.

Taking into account the available evidence, including the health benefits of the use of these devices and the nature and known incidence of the risks to health of the devices, FDA, on its own initiative, is proposing to reclassify these postamendments class III devices into class II. FDA has considered and analyzed the following information to support this proposed reclassification: (1) clinical practice guidelines from professional organizations and government organizations, such as the Centers for Disease Control and Prevention, the American Thoracic Society, and the Infectious Diseases Society of America (see Refs. 8 and 9), that discuss the appropriate use and interpretation of qualitative TB immune response assays, (2) data from three PMAs for qualitative TB immune response assays available to FDA in accordance with section 520(h)(4) of the FD&C Act, (3) input from the 2001, 2011 and 2023 Panel meetings, and (4) postmarket information regarding qualitative TB immune response assays, including information from FDA's publicly available MAUDE and Medical Device Recall databases. The available evidence demonstrates that there are public health benefits derived from the use of qualitative TB immune response assays indicated for use as an aid in the diagnosis of TB infection. In addition, the nature of the associated risks to health are known, and special controls can be established to sufficiently mitigate these risks.

FDA considered the safety and effectiveness of qualitative TB immune response assays through review of PMA data from the following three original PMAs, in accordance with section 520(h)(4) of the FD&C Act: QIAGEN's QuantiFERON–TB (P010033), DiaSorin,

Inc.'s LIAISON QuantiFERON—TB Gold Plus (P180047), and Oxford Immunotec, Inc.'s T–SPOT–*TB* (P070006) (Refs. 3–5).

As part of the Agency's analysis in proposing to reclassify qualitative TB immune response assays, FDA reviewed and considered information provided within each of these applications, including information available in the Summary of Safety and Effectiveness Data and device labeling for each application, which helped to demonstrate reasonable assurance of safety and effectiveness for the devices. The Agency considered the analytical and clinical studies performed and device performance data demonstrating appropriate performance of the device, which supported each approval, when developing the proposed special controls which FDA believes can effectively mitigate the risks to health identified in section V and, along with general controls, can provide a reasonable assurance of the safety and effectiveness for qualitative TB immune response assays. Additionally, FDA identified the probable adverse effects or risks to health of the devices, consistent with information provided within the applications, to be failure to correctly interpret the test results, false positive/negative results, and failure to correctly operate the device. Consistent with data collected in the corresponding clinical studies submitted in support of the approvals, the adverse event profile for these devices was generally deemed acceptable.

On November 28, 2001, FDA approved the original PMA for the QuantiFERON–TB, the first TB immune response assay approved for the qualitative measurement of IFN-γ generated by human lymphocytes in whole blood in response to stimulation antigens for use as an aid in the detection of infection with *Mycobacterium tuberculosis* (product code NCD) (P010033) (Ref. 3). The Agency considered the submitted studies and data in the original PMA, which demonstrated that the QuantiFERON–TB has acceptable performance in detecting immune responses associated with *Mycobacterium tuberculosis* infection. Such studies included analytical performance studies in addition to clinical studies demonstrating that the QuantiFERON–TB has acceptable performance, including clinical sensitivity and clinical specificity from a number of study subjects including individuals with confirmed active tuberculosis, individuals with no known risk factors for tuberculosis, and individuals with at least one known risk factor for tuberculosis and/or latent tuberculosis. Potential adverse effects of the device included the identified risks of false positive or false negative test results, failure to correctly interpret the test results, and failure to correctly operate the device. FDA's review of the PMA determined that the data generated from these studies was sufficient to demonstrate a reasonable assurance of the safety and effectiveness of this device when used as intended and these studies demonstrated appropriate performance of the device.

Additionally, on July 30, 2008, FDA approved the original PMA for the T–SPOT–*TB,* the second qualitative TB immune response assay and first enzyme-linked immunospot assay approved for the detection of effector T cells that respond to stimulation by *Mycobacterium tuberculosis* antigens by capturing IFN-γ in the vicinity of T cells in human whole blood for use as an aid in the diagnosis of *Mycobacterium tuberculosis* infection (product code OJN) (P070006) (Ref. 5). Analytical and clinical data provided in this PMA supported that there is reasonable assurance of safety and effectiveness of this device for its intended use, including appropriate clinical study data from individuals with nontuberculous mycobacterial infection, individuals who had received the BCG vaccine, and specific populations at high risk of disease, such as immunocompromised individuals. Potential adverse effects of the T–SPOT–*TB* include false positive test results or false negative test results. Conclusions drawn from non-clinical and clinical studies indicated overall acceptable performance including specificity and reproducibility demonstrating that the device is reasonably safe and effective for its intended use and supported PMA approval.

On November 26, 2019, FDA approved through an original PMA, a third TB immune response assay, LIAISON QuantiFERON—TB Gold Plus, which is a qualitative indirect test for *Mycobacterium tuberculosis* infection (including disease) and is intended for use in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations to assist the clinician in making individual patient management decisions (product code NCD) (P180047) (Ref. 4). The Agency considered the submitted studies and data in the original PMA, which demonstrated that the LIAISON QuantiFERON—TB Gold Plus has acceptable performance in detecting immune responses associated with *Mycobacterium tuberculosis* infection. Such studies included analytical performance studies in addition to clinical studies demonstrating that the LIAISON QuantiFERON—TB Gold Plus has acceptable performance, including clinical sensitivity and clinical specificity from a number of study subjects including individuals with confirmed active tuberculosis, individuals with no known risk factors for tuberculosis, and individuals with at least one known risk factor for tuberculosis and/or latent tuberculosis. Potential adverse effects of the device included the identified risks of false positive or false negative test results, failure to correctly interpret the test results, and failure to correctly operate the device. FDA's review of the PMA determined that the data generated from these studies was sufficient to demonstrate a reasonable assurance of the safety and effectiveness of this device when used as intended and these studies demonstrated appropriate performance of the device.

Finally, a search of FDA's publicly available MAUDE database revealed that as of October 23, 2025, there were 27 reported events for qualitative TB immune response assays under the product codes NCD and OJN, and approximately half were determined by FDA to be of no known impact or consequence to the patient. A search of FDA's publicly available Medical Device Recall database revealed that as of October 23, 2025, there have been two class III recalls, six class II recalls, and no class I recalls involving qualitative TB immune response assays; however, none of the recalls were determined to have caused or led to patient harm. This postmarket data demonstrating a low number of reported events indicate a lack of significant postmarket safety signals for these devices (see further discussion of the MDR and recall data in section II of this proposed order).

Based on our review of the information described in this proposed order, FDA has determined that special controls, in addition to general controls, are necessary to provide a reasonable assurance of safety and effectiveness for qualitative TB immune response assays, and that sufficient information exists to establish such special controls. Therefore, FDA, on its own initiative, is proposing to reclassify these postamendment devices from class III (premarket approval) into class II (special controls), subject to premarket notification (510(k)) requirements.

VII. Proposed Special Controls

FDA believes that qualitative TB immune response assays can be

reclassified into class II with the establishment of special controls. FDA believes that the following proposed special controls would mitigate each of the risks to health described in section V and that these special controls, in addition to general controls, would provide a reasonable assurance of safety and effectiveness for qualitative TB immune response assays. Table 1 demonstrates how FDA believes each risk to health described in section V would be mitigated by the proposed special controls.

The risk of inaccurate interpretation of test results can be mitigated by special controls requiring certain labeling, including providing clearly stated warnings and limitations such as directing licensed healthcare professionals to consult appropriate public health authority resources that assist in diagnosing tuberculosis infection, information on principles of operation and procedures in performing the test, a detailed explanation of the interpretation of results including indeterminate results, and a statement that diagnosis of tuberculosis disease and assessment of the probability of latent tuberculosis infection is based on a combination of epidemiological, clinical and diagnostic findings (including historical and medical); certain design verification and validation information including information related to performance studies. Design verification and validation documentation would be required to include a detailed description of the device, all critical reagents, risk analysis demonstrating how risk control measures are implemented to address device hazards, lot release criteria, and stability studies.

Risks associated with false results (*e.g.,* false negative and false positive test results) can be mitigated through a combination of special controls including certain labeling requirements, certain design verification and validation information, including information related to performance studies. Examples of information to be included in the design verification and validation documentation for the device include documentation of analytical studies and device performance data from clinical studies. In addition, design verification and validation documentation would be required to include a detailed description of the device, all critical reagents, a risk analysis demonstrating how risk control measures are implemented to address device hazards, lot release criteria, and stability studies. Required statements in the labeling can aid in mitigating false results, for example by providing a detailed explanation of the interpretation of results including indeterminate results and clearly stated warnings and limitations such as directing licensed healthcare professionals to consult appropriate public health authority resources that assist in diagnosing tuberculosis infection.

Risks associated with the failure to correctly operate the device can be mitigated through labeling information and design verification and validation information, including a detailed description of the device, all critical reagents, a risk analysis demonstrating how risk control measures are implemented to address device hazards, lot release criteria, and stability studies. Required statements in labeling can aid in mitigating the failure to operate the device or interpret the results correctly. For example, a statement that results must be interpreted by licensed healthcare professionals in conjunction with risk assessment, radiographic imaging, and other medical and diagnostic evaluations, clearly stated warnings and limitations such as directing licensed healthcare professionals to consult appropriate public health authority resources that assist in diagnosing tuberculosis infection, and providing a detailed explanation of the interpretation of results including indeterminate results.

TABLE 1—RISKS TO HEALTH AND MITIGATION MEASURES FOR QUALITATIVE MYCOBACTERIUM TUBERCULOSIS CELL-MEDIATED IMMUNE RESPONSE ASSAYS

Identified risks to health	Mitigation measures
Failure to correctly interpret the test results.	Certain labeling information, including warnings, limitations, results interpretation information, and explanation of procedures. Certain design verification and validation information, including certain device description information, critical reagent information, risk analysis strategies, lot release criteria, and stability studies.
False negative/positive result	Certain labeling information, including warnings, limitations, results interpretation information, and explanation of procedures. Certain design verification and validation information, including certain device description information, risk analysis strategies, lot release criteria, stability studies, and performance studies, including analytical studies and clinical studies.
Failure to correctly operate the assay.	Certain labeling information, including warnings, limitations, results interpretation information, and explanation of procedures. Certain design verification and validation information, including certain device description information, critical reagent information, risk analysis strategies, lot release criteria, and stability studies.

If this proposed order is finalized, qualitative TB immune response assays will be identified as prescription in vitro diagnostic (IVD) devices. Therefore, these devices would be subject to the prescription labeling requirements for IVD products (see 21 CFR 809.10(a)(4) and (b)(5)(ii)).

If this proposed order is finalized, qualitative TB immune response assays will be reclassified into class II (special controls) and will be subject to premarket notification requirements under section 510(k) of the FD&C Act. As discussed in this proposed order, the intent is for the reclassification to be codified in 21 CFR 866.3371. If finalized, firms will be required to comply with the particular mitigation measures set forth in the special controls. FDA believes that adherence to the special controls, in addition to the general controls, is necessary to provide a reasonable assurance of safety and effectiveness of qualitative TB immune response assays.

VIII. Analysis of Environmental Impact

We have determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

While this proposed order contains no new collections of information, it does

refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The collections of information in 21 CFR part 820 (Quality Management System Regulation) have been approved under OMB control number 0910–0073; the collections of information in 21 CFR part 807, subpart E (Premarket Notification Procedures), have been approved under OMB control number 0910–0120; and the collections of information in 21 CFR parts 801 and 809 (Device Labeling) have been approved under OMB control number 0910–0485.

X. Proposed Effective Date

FDA proposes that any final order based on this proposed order become effective 30 days after the date of its publication in the **Federal Register**.

XI. Codification of Orders

Under section 513(f)(3) of the FD&C Act, FDA may issue final orders to reclassify devices. FDA will continue to codify classifications and reclassifications in the Code of Federal Regulations (CFR). Changes resulting from final orders will appear in the CFR as newly codified orders. Therefore, under section 513(f)(3) of the FD&C Act, in the proposed order, we are proposing to codify Qualitative *Mycobacterium tuberculosis* Cell-Mediated Immune Response Assay in the new 21 CFR 866.3371, under which these qualitative TB immune response assays would be reclassified from class III into class II.

XII. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at *https://www.regulations.gov.* References without asterisks are not on public display at *https://www.regulations.gov* because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. Although FDA verified the website addresses in this document, please note that websites are subject to change over time.

* 1. P010033 Approval Order, available at: *https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P010033.*
* 2. October 11–12, 2001: Microbiology Devices Panel Meeting Summary (available at *https://wayback.archive-it.org/7993/20170405192838/https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/MicrobiologyDevicesPanel/ucm124771.htm*).
* 3. P010033 Summary of Safety and Effectiveness, available at: *https://www.accessdata.fda.gov/cdrh_docs/pdf/P010033B.pdf.*
* 4. P180047 Summary of Safety and Effectiveness, available at: *https://www.accessdata.fda.gov/cdrh_docs/pdf18/P180047B.pdf.*
* 5. P070006 Summary of Safety and Effectiveness, available at: *https://www.accessdata.fda.gov/cdrh_docs/pdf7/P070006B.pdf.*
* 6. June 29, 2011: Meeting Materials of the Microbiology Devices Panel (available at *https://wayback.archive-it.org/7993/20170403223442/https:/www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/MicrobiologyDevicesPanel/ucm260517.htm*).
* 7. September 7–8, 2023: Microbiology Devices Panel of the Medical Devices Advisory Committee Meeting Announcement (available at *https://www.fda.gov/advisory-committees/advisory-committee-calendar/september-7-8-2023-microbiology-devices-panel-medical-devices-advisory-committee-meeting#event-materials*).
8. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children | Clinical Infectious Diseases | Oxford Academic *https://academic.oup.com/cid/article/64/2/e1/2629583?login=true. doi.org/10.1093/cid/ciw694.* Accessed March 18, 2026.
9. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis | Clinical Infectious Diseases | Oxford Academic *https://academic.oup.com/cid/article/63/7/e147/2196792. doi.org/10.1093/cid/ciw376.* Accessed March 18, 2026.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 866 be amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

■ 1. The authority citation for part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360*l,* 371.

■ 2. Add § 866.3371 to subpart D to read as follows:

§ 866.3371 Qualitative *Mycobacterium tuberculosis* Cell-Mediated Immune Response Assay.

(a) *Identification.* A qualitative *Mycobacterium tuberculosis* cell-mediated immune response assay is identified as a prescription in vitro diagnostic device intended to aid in the diagnosis of *Mycobacterium tuberculosis* infection. Qualitative *Mycobacterium tuberculosis* cell-mediated immune response assays measure the production of interferon-gamma or other cytokines by human lymphocytes in response to stimulation antigens. The assay is intended for use by a licensed healthcare professional as an aid in the diagnosis of *Mycobacterium tuberculosis* infection in conjunction with risk assessment, radiographic imaging, and other medical and diagnostic evaluations.

(b) *Classification.* Class II (special controls). The special controls for this device are:

(1) The labeling must include:

(i) A prominent statement that the assay is an indirect test for tuberculosis and that results must be interpreted by a licensed healthcare professional in conjunction with risk assessment, radiographic imaging, and other medical and diagnostic evaluations to assist the licensed healthcare professional in making individual patient management decisions.

(ii) A detailed explanation of the interpretation of results, including, as applicable, descriptions of borderline, equivocal, indeterminate, and invalid results.

(iii) Warnings and limitations that include statements that indicate, as applicable:

(A) Diagnosis or exclusion of tuberculosis disease and assessment of the probability of latent tuberculosis infection is based on a combination of epidemiological, clinical, and diagnostic findings.

(B) Licensed healthcare professionals are directed to consult resources from appropriate public health authorities that assist in diagnosing tuberculosis infection.

(C) The species of nontuberculous mycobacterium that may generate false positive results, as applicable.

(D) Negative test results do not exclude the possibility of exposure to, or infection with, *Mycobacterium tuberculosis.* A negative result must be considered with the individual's medical and historical data relevant to probability of *Mycobacterium tuberculosis* infection and potential risk of progression to tuberculosis disease, particularly for individuals with impaired immune function. Negative predictive values may be low for individuals suspected to have *Mycobacterium tuberculosis* disease.

(E) Positive results do not confirm the diagnosis of active tuberculosis disease.

(F) Assay results are qualitative and the magnitude of the measured assay numeric values cannot be correlated to stage or degree of infection, level of immune responsiveness, or likelihood for progression to active disease.

(G) Heterophilic antibodies, circulating interferon gamma, and other circulating factors may cause inaccurate results.

(H) Patient populations in which test performance characteristics have not been established, or patient populations where test performance may be affected.

(2) Design verification and validation must include the following:

(i) A detailed device description, including the computational path from collected raw data to reported result (*e.g.,* how collected raw signals are converted into a reported result), and rationale used to select stimulation antigens.

(ii) Documentation and characterization of all critical reagents (*e.g.,* determination of the identity, supplier, purity, and stability) and protocols for maintaining product integrity.

(iii) Final lot release criteria to be used for manufactured assay lots with appropriate evidence that lots released at the extremes of the specifications will meet the identified analytical and clinical performance characteristics as well as stability.

(iv) Risk analysis and documentation demonstrating how risk control measures are implemented to address device hazards, such as Failure Modes Effects Analysis and/or Hazard Analysis.

(v) Detailed documentation of analytical studies, including reproducibility, precision (including lot-to-lot precision studies, as appropriate), interference, cross reactivity, carryover, hook effect, sample and reagent stability, and other studies relevant to the technology and intended use (*e.g.,* linearity), as applicable.

(vi) Detailed documentation of device performance data from a multisite clinical study in geographically diverse areas with a design and performance that is appropriate for the intended use of the device. The study must be performed on populations consistent with the intended use population and compare the device performance to results obtained from a reference or comparator method that FDA has determined is appropriate. The clinical study must include testing of unique prospective (sequentially collected) samples and may, when determined to be acceptable by FDA, include additional characterized clinical samples. The clinical study must include a cohort of subjects with culture-confirmed or FDA-cleared or approved nucleic acid amplification test confirmed active tuberculosis infection, a cohort of subjects with no known risk factors for tuberculosis infection, and a mixed risk cohort of subjects with at least one known risk factor for tuberculosis and/or risk for latent tuberculosis infection. Enrolled subjects must include individuals who are immunosuppressed, individuals who have received the bacille Calmette-Guérin vaccine, or individuals with nontuberculous mycobacterial infections, as applicable. Documentation from the study must include a detailed study report that contains a study description, a summary of testing results, and results of all statistical analyses.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 716

[EPA–HQ–OPPT–2023–0360; FRL–13162–01–OCSPP]

RIN 2070–AL43

Reporting Deadline Extension for the Health and Safety Data Reporting Rule Under Toxic Substance Control Act (TSCA) Section 8(d)

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: The Environmental Protection Agency is proposing to extend the reporting deadline for the Health and Safety Data Reporting Rule under the Toxic Substance Control Act (TSCA) by one year to May 21, 2027. EPA is seeking public comment on this proposed action, including any considerations or concerns that stakeholders may have regarding the proposed extension of the reporting deadline. The proposed extension is intended to delay compliance with this one-time reporting rule during EPA's ongoing reconsideration of the rule.

DATES: Comments must be received on or before April 29, 2026.

ADDRESSES: Submit your comments for this action, identified by docket identification (ID) number EPA–HQ–OPPT–2023–0360, online at *https://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Additional information on how to comment, along with instructions for visiting the docket in-person, is available at *https://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: Lameka Smith, Chemical Information, Prioritization, and Toxics Release Inventory Division (7406M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001; telephone number: (202) 564–1629; email address: *smith.lameka@epa.gov.*

For general information contact: The TSCA-Hotline, ABVI-Goodwill of the Finger Lakes, 422 South Clinton Ave., Rochester, NY 14620; telephone number: (202) 554–1404; email address: *TSCA-Hotline@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. Executive Summary

A. Does this action apply to me?

You may be potentially affected by this action if you manufacture (including import) any of the chemical substances listed in 40 CFR 716.120(d) of the regulatory text of this document. The following list of North American Industrial Classification System (NAICS) codes affected by this rule are those that align with these activities:

- Chemical manufacturers (including importers), (NAICS code 325); and
- Petroleum refineries (NAICS code 324110).

This action applies to manufacturers in these NAICS codes who are currently manufacturing (including importing) a listed chemical substance (or will do so during the chemical's reporting period) or who have manufactured (including imported) or proposed to manufacture (including import) a listed chemical substance within the last 10 years.