and that the form has been submitted to OMB. This final rule is compliant with information collection requirements under the Paperwork Reduction Act. Accordingly, AMS made no changes to the rule as proposed after review and consideration of all comments received.

Lastly, to address comments concerning Executive Order 12866, AMS reiterates that this final rule falls within a category of regulatory actions that the Office of Management and Budget (OMB) exempted from the review process required by Executive Order 12866.

After consideration of all relevant material presented, including the information and recommendations submitted by the Board and other available information, AMS has determined that this final rule is consistent with and will effectuate the declared policy of the Act.

List of Subjects in 7 CFR Part 984

Marketing agreements, Nuts, Reporting and recordkeeping requirements.

For the reasons set forth in the preamble, the Agricultural Marketing Service amends 7 CFR part 984 as follows:

PART 984—WALNUTS GROWN IN CALIFORNIA

■ 1. The authority citation for 7 CFR Part 984 continues to read as follows:

Authority: 7 U.S.C. 601–674.

■ 2. Add § 984.348 to subpart B to read as follows:

§ 984.348 Payment of assessments.

(a) Each handler shall pay assessments on walnut receipts reported by the handler pursuant to § 984.473(a) in three installments, invoiced by the Board, on January 31, April 30, and July 31 of each marketing year.

(b) Each handler shall pay assessments on walnut receipts reported by the handler pursuant to § 984.473(b), as requested by the Board, on demand.

■ 3. Add § 984.349 to subpart B to read as follows:

§ 984.349 Late payment and interest charges.

(a) The Board shall impose a late payment charge of ten percent (10%) on any handler whose assessment payment has not been received within sixty (60) days of the invoice date shown on the handler's assessment statement.

(b) Payments not received more than sixty (60) days after the invoice date shown on the handler's assessment statement shall be subject to a one and one-half percent (1.5%) interest charge per month. Interest shall be applied to the total outstanding assessment balance, including any late payment charge, at the end of each subsequent thirty (30) day period until final payment is made.

■ 4. Revise § 984.473 to read as follows:

§ 984.473 Report of walnut receipts.

(a) Each handler shall file a report of his or her walnut receipts from growers on or before January 15 of each marketing year on forms supplied by the Board.

(b) Each handler acquiring walnuts from growers after submission of their initial report of walnut receipts pursuant to paragraph (a) of this section shall file a revised report of walnut receipts by the 15th of the month following such receipt on forms supplied by the Board.

Erin Morris,

Administrator, Agricultural Marketing Service.

[FR Doc. 2026–16723 Filed 8–14–26; 8:45 am]

BILLING CODE 3410–02–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 864

[Docket No. FDA–2025–N–1243]

Hematology and Pathology Devices; Reclassification of In Situ Hybridization Test Systems for Use With a Corresponding Approved Oncology Therapeutic Product

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is issuing a final order reclassifying in situ hybridization (ISH) test systems indicated for use with a corresponding approved oncology therapeutic product (product codes NYQ, MVD, OWE, and PNK), all postamendments class III (premarket approval) devices, into class II (special controls), subject to premarket notification. FDA is also establishing a new device classification regulation, along with the special controls that are necessary to provide a reasonable assurance of safety and effectiveness of this device type.

DATES: This order is effective September 16, 2026. See further discussion in section IV, ''Implementation Strategy.''

FOR FURTHER INFORMATION CONTACT: Soma Ghosh, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3316, Silver Spring, MD 20993, 240–402–5333, *Soma.Ghosh@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) established 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).

Devices that were not introduced or delivered for introduction into interstate commerce for commercial distribution prior to 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 rulemaking process. Those devices remain in class III and require approval of a premarket approval application (PMA), unless and until: (1) the Food and Drug Administration (FDA) reclassifies the device into class I or class 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. FDA determines whether new devices are substantially equivalent to predicate devices by means of the procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and our implementing regulations (part 807, subpart E (21 CFR part 807, subpart E)).

A postamendments device that has been initially classified into 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 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

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

860.7(c)(2), in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the ''valid scientific evidence'' upon which the Agency relies generally 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 (21 U.S.C. 360j(c))). Section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4)) 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.[2]

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the requirements under section 510(k) of the FD&C Act if FDA determines that a premarket notification (510(k)) is not necessary to provide reasonable assurance of the safety and effectiveness of the device type.

On June 11, 2025, FDA published a proposed order[3] in the **Federal Register** (90 FR 24540) (''proposed order'') to reclassify in situ hybridization (ISH) test systems indicated for use with a corresponding approved oncology therapeutic product (product codes NYQ, MVD, OWE, and PNK)[4] (hereinafter referred to as oncology therapeutic ISH-based test systems) from class III to class II. FDA has considered the information available to the Agency, as described in the June 11, 2025, proposed order, and considered comments received from the public docket on the proposed order (as discussed in section II of this document), to determine that there is sufficient information to establish special controls to effectively mitigate the risks to health (updated as discussed in section II of this document). FDA has also determined based on this information that the special controls, together with general controls, provide a reasonable assurance of safety and effectiveness when applied to these devices.

Therefore, in accordance with section 513(f)(3) of the FD&C Act, FDA, on its own initiative, is issuing this final order to reclassify oncology therapeutic ISH-based test systems from class III to class II (special controls).[5] Absent the special controls identified in this final order, general controls applicable to the device type are insufficient to provide a reasonable assurance of safety and effectiveness. Specifically, general controls are insufficient to effectively mitigate the risks identified for this device type, such as the risk of false test results (*i.e.,* false positive and false negative test results), which may negatively influence treatment decisions for cancer patients—for example, by delaying access to an available and appropriate alternative therapy. FDA expects that the reclassification of these devices will enable more manufacturers to develop this type of device such that patients will benefit from increased access to oncology therapeutic ISH-based test systems for which there is a reasonable assurance of safety and effectiveness.

After the effective date of this order, for these class II devices, manufacturers may submit a premarket notification and obtain FDA clearance of the devices before marketing them, as opposed to having to submit a PMA and receive approval. This action 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. A 510(k) typically results in a shorter premarket review timeline compared to a PMA, which ultimately provides patients with more timely access to this type of device.

II. Comments on the Proposed Order and FDA Responses

A. Introduction

FDA received comments from fewer than 5 commenters on the proposed order published in the **Federal Register** on June 11, 2025. The comment period on the proposed order closed on August 11, 2025. The majority of the comments received by the close of the comment period came from members of the medical device industry. Some commenters provided multiple comments on one or more issues. All commenters provided support for the proposed reclassification with some comments also providing recommendations or proposed modifications for clarity.

We describe and respond to the comments in section II.B of this document. The order of the comments and our response to them is purely for organizational purposes and does not signify the comment's value or importance nor the order in which comments were received. Certain comments are grouped together under a single number because the subject matter is similar. Please note that in some cases we separated different issues discussed by the same commenter and designate them as distinct comments for purposes of our responses.

B. Description of Comments and FDA Response

(Comment 1) FDA received numerous comments supporting the proposed reclassification of oncology therapeutic ISH-based test systems, from class III to class II, subject to special controls. Citing, among other things, ISH as a long-established technology, commenters stated they believe that special controls could be established to provide reasonable assurance of the safety and effectiveness of these devices. In addition, commenters noted that the decreased regulatory burden resulting from the reclassification could increase development and availability of these tests, thus offering better diagnostic options for clinicians and improving patient access to diagnostics and therapies.

[2] Since the publication of the proposed order, data from one additional PMA and several PMA supplements have become available for consideration by FDA in accordance with section 520(h)(4) of the FD&C Act. FDA has determined that the data from the additional PMA and PMA supplements are cumulative of, and consistent with, the information addressed in the proposed order and do not raise any new or different questions regarding the safety and effectiveness of oncology therapeutic ISH-based test systems.

[3] FDA notes that the ''ACTION'' caption for the proposed order was 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 ''amends'' the Code of Federal Regulations. The change was made in accordance with the Office of **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.

[4] 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. A medical device product code consists of a three-letter combination which associates a device's type with a product classification designated for the application. The three-digit classification product codes in CDRH's Product Classification Database carry no other significance. 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*.

[5] FDA notes that the ''ACTION'' caption for this final order is styled as ''Final amendment; final order,'' rather than ''Final order.'' Beginning in December 2019, this editorial change was made to indicate that the document ''amends'' the Code of Federal Regulations. The change was made in accordance with the Office of **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.

(Response 1) FDA agrees with the comments supporting this reclassification. Based on the information the Agency considered and analyzed in proposing to reclassify these devices, as well as comments received in response to the proposed order, FDA has determined that reclassifying oncology therapeutic ISH-based test systems from class III (premarket approval) into class II (special controls) is appropriate. Specifically, based on the totality of information available, FDA has determined that general controls are insufficient to provide a reasonable assurance of safety and effectiveness for these devices and there is sufficient information to establish special controls for these devices that together with general controls will provide a reasonable assurance of safety and effectiveness. In addition, FDA also expects that the reclassification of these devices will enable more manufacturers to develop this type of device such that health care providers and patients will benefit from increased access to appropriately safe and effective tests.

(Comment 2) One commenter requested the Agency's guidance and further deliberation on these matters, either preceding or during a reclassification panel meeting.

(Response 2) FDA has determined that a classification panel is unnecessary to reclassify oncology therapeutic ISH-based test systems from class III to class II. Section 513(f)(3) of the FD&C Act provides that FDA may ask an appropriate panel to review information and make a recommendation before issuing an order reclassifying a postamendments device (see also 21 CFR 860.134(c)(2)). FDA is reclassifying these postamendments class III devices on its own initiative and does not believe a panel recommendation is needed to help determine whether these devices should be reclassified from class III to class II nor to identify appropriate special controls. FDA has determined, based on the information discussed in the preamble to the proposed order and FDA's consideration of public comments, that the standard in section 513(a)(1)(B) of the FD&C Act is met. Specifically, FDA has determined that general controls are insufficient to provide a reasonable assurance of safety and effectiveness, and there is sufficient information to establish special controls, which with general controls will provide a reasonable assurance of the safety and effectiveness when applied to these devices.

(Comment 3) One commenter expressed appreciation for the Agency's use of the least burdensome approach through discussion of predetermined change control plans (PCCPs) in the preamble to the proposed order. The commenter requested the Agency allow applicants to seek FDA's alignment on device-specific PCCPs via pre-submission rather than a pre-market notification and further requested that the Agency consider permitting PCCPs for a planned modification to already PMA-approved devices to include artificial intelligence (AI)/machine learning (ML) driven digital pathology (DP) algorithms intended to aid the end user or seek aid from the end user for end result generation, via PCCPs.

(Response 3) The new classification regulation at § 864.1890 (21 CFR 864.1890) applies to previously approved oncology therapeutic ISH-based test systems and new devices that are determined to be substantially equivalent. We note that, at the time of publication of this final order, FDA has not classified, cleared, approved, or granted authorization for any oncology therapeutic ISH-based test systems that incorporate DP devices, including AI/ML algorithm-assisted DP devices.

As described in the preamble of the proposed order, manufacturers may wish to use 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 [6] while continuing to provide reasonable assurance of device safety and effectiveness. 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 (see section 515C of the FD&C Act (21 U.S.C. 360e-4)). Thus, FDA's consideration of a device-specific PCCP, and the determination of whether the inclusion of a device modification, to include a modification to an AI/ML-enabled device via a PCCP is appropriate, will be based on the Agency's review and consideration of the information submitted at the time of a premarket submission. FDA encourages manufacturers to leverage the Q-Submission program to obtain FDA feedback on their approach to using a PCCP for a device prior to submitting a marketing submission. Additional information regarding the Q-Submission program can be found in FDA's final guidance document titled ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program'' (Ref. 1). For additional information regarding marketing submissions that include a PCCP for AI/ML-enabled devices, see FDA's guidance, ''Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence-Enabled Device Software Functions'' (Ref. 2).

(Comment 4) One comment recommended the Agency reference and ''include the principles'' of FDA's guidance, ''Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices'' in this final order.

(Response 4) FDA appreciates this comment and acknowledges that the guidance ''Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices'' may be applicable under certain circumstances to oncology therapeutic ISH-based test systems (Ref. 3). When evaluating the applicability of this guidance to specific modifications to a particular test system, interested parties should follow the logic scheme and recommendations contained in the guidance.

(Comment 5) One commenter requested several changes to the proposed classification regulation. The commenter recommended revising the proposed codified text for § 864.1890 by adding a new paragraph titled ''Device Description and Principle of Operation,'' as § 864.1890(b). The suggested language would require, presumably in a submission to FDA and/or in the device labeling, detailed elements of a device's intended use/indication for use including specifications for the intended use population(s), biomarker lists, specimen type(s), system components, biomarker definitions as used in the therapeutic product trials and as detected by the test, along with the corresponding therapeutic product(s) or therapeutic product group, and a description of whether the device is qualitative, semi-quantitative, or quantitative. The commenter also proposed renumbering the identification provision as paragraph (a) and classification provision as paragraph (c).

The commenter also recommended adding a new labeling special control, to be incorporated as § 864.1890(c)(2)(i), which would require § 809.10 (21 CFR 809.10) compliant labeling and any product information and test output generated to include the intended use statement as outlined in the commenter's proposed § 864.1890(b).

(Response 5) While FDA agrees that labeling special controls, in addition to general controls, are needed to assure the safety and effectiveness of oncology therapeutic ISH-based test systems, FDA

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

disagrees that the commenter's proposed edits to § 864.1890 are necessary. FDA believes the labeling special controls proposed by the Agency, in combination with the applicable general controls, which include general in vitro diagnostic (IVD) product labeling requirements under § 809.10, are sufficient for the labeling of this device type.

FDA declines to adopt the proposed revisions at § 864.1890(b) to the codified text. Much of this information is already required to be submitted to FDA under existing general controls. For example, § 809.10(b)(2) requires the type of procedure to be included in labeling (*e.g.,* qualitative or quantitative) and § 807.87(e) requires submission of the device's proposed labeling as part of a 510(k). FDA does not believe that an additional requirement mandating submission of all of this information is necessary for all devices in this device type. Moreover, and as discussed further below, FDA does not believe all of this information needs to be included in the device's intended use/indications for use statement found in the device's labeling to provide reasonable assurance of the safety and effectiveness of these devices. Accordingly, FDA is not adding the proposed paragraph to § 864.1890, nor is FDA renumbering the identification and classification paragraphs as proposed.

FDA also declines to incorporate the commenter's proposed edits to the labeling special control. The suggested revisions would require labeling to include an intended use statement referencing the commenter's proposed § 864.1890(b), which FDA is not adopting for the reasons described in the previous paragraph. Moreover, the commenter's suggested requirements duplicate or overlap with existing regulatory requirements under § 809.10 and part 801 (21 CFR part 801), as well as the labeling elements already encompassed by the Agency's proposed special controls. The Agency's proposed special controls, along with applicable statutory and regulatory requirements, address all of the necessary intended use statements and operational descriptions (*e.g.,* summary and explanation of the test) that are to be included in labeling, without the need for the additional codified requirements. FDA believes the special controls, as finalized, along with general controls, will ensure the device's risks to health are appropriately mitigated and provide a reasonable assurance of the safety and effectiveness of oncology therapeutic ISH-based test systems.

(Comment 6) One comment acknowledged the suitability of the analytical performance tests outlined in the proposed order but recommended that FDA consider incorporating surrogate samples for use in the precision/reproducibility data generation, where the sample type can be supported as representative. This would apply to situations where sufficient clinical specimens for the intended use specimen type(s) are unavailable for analytical validation testing. The comment stated that such an inclusion would facilitate manufacturers' ability to conduct adequate verification testing by using surrogate samples that are morphologically comparable to the intended-use clinical specimens.

(Response 6) Based on the information FDA considered and analyzed in proposing to reclassify these devices, as well as comments received in response to the proposed order, FDA acknowledges that certain exceptional clinical circumstances may warrant consideration of alternative approaches to the use of clinical specimens for the purpose of analytical validation testing (*e.g.,* rare cancer(s) or tumor type(s) where obtaining sufficient clinical specimens presents a significant challenge). However, FDA maintains that precision studies represent a fundamental device performance requirement that is essential for demonstrating analytical performance and ensuring consistent and reliable device function. Upon further consideration, FDA has decided to modify the special control related to this comment (see § 864.1890(b)(1)(v)) to consider surrogate samples that adequately represent the intended use specimen type(s) and intended use biomarker(s), as appropriate, as determined by FDA, to supplement clinical specimens. For example, FDA will determine the appropriateness of surrogate samples based on clinical and scientific data and/or justification available to the Agency.

In addition to the above modification, FDA, based in part on the comments received, has also removed the special control requiring device performance data demonstrating appropriate reagent stability. Upon further review of the information the Agency considered and analyzed in proposing to reclassify these devices, such as postmarket safety data from medical device reports and recalls, as well as comments received on the proposed special controls, FDA believes that a special control requiring reagent stability data is not necessary and that general controls, such as premarket notification (510(k)) requirements and quality system requirements set forth under part 820 (21 CFR part 820) are sufficient to ensure that reagents are appropriately assessed and labeled such that this special control is not necessary. As such, the Agency is removing proposed § 864.1890(b)(1)(viii).

(Comment 7) One comment recommended FDA revise the ''Identification'' language of proposed § 864.1890 to include the term ''companion.''

(Response 7) FDA disagrees with the recommended edit and is finalizing the identification language in this final order without change. The comment did not provide context to support the suggested revision, and FDA continues to believe that the identification, as proposed, provides an appropriate level of clarity regarding the type of device intended to fall within the scope of § 864.1890.

(Comment 8) One comment expressed a desire to work with the Agency to address nuanced clinical performance adequacy scenarios as potentially applicable to future devices either via a pre-submission route or alternative mechanism.

(Response 8) FDA agrees that questions of this nature may be appropriate topics to discuss with the Agency through the Q-Submission program. Prior to submission, a sponsor may seek FDA input on specific questions regarding review topics relevant to a planned marketing submission by utilizing our Q-Submission program. Through the Q-Submission program FDA may provide input on device-specific requirements and recommendations intended to support a marketing submission. Additional information regarding the Q-Submission program can be found in FDA's final guidance document titled ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program'' (Ref. 1).

Sponsors may also review information on FDA's Center for Devices and Radiological Health's (CDRH) website regarding previously approved oncology therapeutic ISH-based test systems, such as Summary of Safety and Effectiveness Data (SSED) documents available in FDA's Premarket Approval Database,[7] which detail the clinical evidence, risks, and benefits for medical devices. Additionally, sponsors may consider reviewing CDRH's 510(k) Decision Summaries, found in FDA's 510(k) Premarket Notification Database,[8] which summarize the information that informed the Agency's substantial

[7] *https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm.*

[8] *https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm.*

equivalence decision and that may help inform interested parties regarding FDA's thinking on the types of performance the Agency might expect for this type of device. Sponsors also should refer to the special controls codified at § 864.1890, established as part of this final order, which set forth requirements that are necessary to provide a reasonable assurance of safety and effectiveness for these devices. Comments related to a sponsor's study- or device-specific questions are outside the scope of this final order.

(Comment 9) One comment requested that FDA evaluate other devices and therapies with comparable risk profiles to determine whether reclassification may be appropriate, with the goal of broadening availability of such devices. The comment also requested that FDA review and update the special controls for oncology therapeutic ISH-based test systems on a regular basis and ensure that clinical data supporting the development and implementation of the special controls is transparent and readily available to interested parties.

(Response 9) The FDA periodically reviews the classification of devices to ensure they are being regulated in the appropriate class (class III, II, I) with the necessary level of regulatory controls. CDRH has previously undertaken reclassification efforts as part of the Center's systematic approach, including the 2014–2015 Strategic Priorities,[9] and as part of CDRH's regular due diligence in considering the specific classification for a particular device type. Additionally, in 2024, CDRH announced its intent to initiate the reclassification process for most high risk IVD devices, reflecting this ongoing, systematic approach to ensuring appropriate classification.[10] FDA intends to continue evaluating the classification of devices to ensure they are subject to the appropriate level of regulatory controls.

Further, FDA acknowledges the comment's request that the Agency regularly review and update the special controls and ensure transparency. For class II devices, special controls are established to provide reasonable assurance of safety and effectiveness for the device type and are developed based on the totality of available scientific evidence at the time of classification or reclassification. As new information becomes available, including advances in scientific knowledge and changes in device technology, FDA may evaluate whether such developments and device modifications give rise to new benefit-risk considerations such that new or different special controls, in addition to general controls, are needed to assure the safety and effectiveness for the device type.

With respect to transparency, FDA strives to make publicly available the scientific basis for its regulatory decisions, consistent with applicable statutes and regulations. In general, the clinical and scientific information that forms the basis of the special controls is included in the public docket associated with the classification or reclassification action, to the extent permitted by law. FDA, therefore, believes that the current regulatory framework provides an appropriate mechanism for ensuring the relevance of special controls and the availability of supporting information. No changes to the final order have been made in response to this comment.

(Comment 10) One comment proposed edits to Table 1. Risks to Health and Mitigation Measures in the proposed order. The comment proposed additional mitigation measures to each of the three identified risks to health to include, for example, the addition of ''*Device Description and Principle of Operation*'' and ''*Implementation of Controls, procedures and user training requirements.*''

(Response 10) As discussed in response to comment 5, FDA disagrees that such line edits or clarifications are needed to the mitigations identified in the proposed order. The mitigation measures proposed to be added to table 1 correspond to this commenter's proposed additions to the codified, as described in comment 5. As noted in response to comment 5, the language proposed by the commenter is generally already covered for oncology therapeutic ISH-based test systems by the regulatory requirements for IVDs under part 801 and § 809.10, as well as the Agency's proposed special controls. FDA believes that the special controls set forth in the proposed order with the changes identified in this final order (see comment 5 and the Agency's response), together with general controls, are sufficient to effectively mitigate the risks to health identified in section V of the proposed order and are necessary to provide a reasonable assurance of the safety and effectiveness of oncology therapeutic ISH-based test systems. For these reasons, we decline to incorporate the proposed edits.

With regards to the commenter's recommendation to include ''*Implementation of Controls, procedures and user training requirements*'' in table 1 of the proposed order, FDA also disagrees that this is necessary. FDA believes that the commenter's proposed requirement is already encompassed within the Agency's proposed special controls. Specifically, this proposed recommendation falls within certain design verification and validation activities required by the special controls under § 864.1890(b)(1)(i) which indicates that ''[s]*pecification for risk mitigation elements intended to mitigate risks associated with testing and results interpretation, including controls, procedures, and user training requirements, as appropriate.*''

(Comment 11) One comment requested clarification on how FDA's determination that devices under the relevant oncology therapeutic ISH-based test system product codes share similar purposes, designs, functions, and risk profiles would affect their use as predicate devices under the 510(k) pathway. The commenter also sought general guidance on how substantial equivalence would be evaluated in cases where a device's intended use or labeling is expanded, such as to include a new oncology therapeutic product, clinical indication, or clinical cut-off.

(Response 11) FDA acknowledges the commenter's request for clarification regarding the implications of this reclassification on the use of these devices as predicates under the 510(k) pathway. While the Agency has determined that devices within the relevant product codes share similar purposes, designs, functions, and overall risk profiles for purposes of reclassification, this determination does not alter the statutory and regulatory requirements applicable to demonstrating substantial equivalence. For a new device to be considered substantially equivalent to a predicate device, the new device must have the same intended use as the predicate device and the same technological characteristics or different technological characteristics that do not raise different questions of safety and effectiveness than the predicate device. Additional information can be found in FDA's final guidance ''The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]'' (Ref. 4).

In accordance with section 513(i) of the FD&C Act and part 807, substantial equivalence determinations are made on a case-by-case basis and depend on the specific intended use and technological characteristics of the device under review. Any oncology therapeutic ISH-based test system with a new intended use or technological characteristics that raise different questions of safety and

[9] See 81 FR 52445.

[10] See *https://www.fda.gov/medical-devices/medical-devices-news-and-events/cdrh-announces-intent-initiate-reclassification-process-most-high-risk-ivds.*

effectiveness compared to legally marketed devices would generally not be found to be substantially equivalent. However, devices could be used as predicate devices to support a substantial equivalence determination when a device has a new clinical cut-off or a new indication for use that includes a new therapeutic product if adequate data and information are provided to demonstrate the new indication(s) for use fall within the intended use of the predicate device and any technological differences do not raise different questions of safety and effectiveness. If a manufacturer has a question regarding a specific device for which they intend to seek marketing authorization, the manufacturer may choose to utilize the Q-Submission Program to seek feedback on the appropriate regulatory pathway for modified devices. Additional information regarding the Q-Submission program can be found in FDA's final guidance document titled ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program'' (Ref. 1).

(Comment 12) One comment requested that the Agency clarify that devices already on the market would be automatically reclassified into class II without the need for any additional premarket notification or submission, and that only future devices, or currently marketed devices with significant modifications, would be required to submit a premarket notification.

(Response 12) FDA appreciates the need to provide clarification on the implementation of this final order. To provide such clarification and assist in the efficient implementation of this final order, the Agency has added an implementation strategy in section IV of this final order. Among other things, section IV clarifies that upon its effective date the final order reclassifies devices that are oncology therapeutic ISH-based test systems as described within the scope of the proposed order and adopted as part of this final order, from class III (premarket approval) into class II (special controls). Oncology therapeutic ISH-based test systems with prior PMA approval may continue to be marketed per the previous marketing authorization and would not require an additional marketing application. For changes or modifications that could significantly affect the safety or effectiveness of such devices or a major change or modification in the intended use of such devices (see § 807.81(a)(3)), FDA expects that manufacturers will submit a 510(k) for the modified device.

(Comment 13) One comment encouraged FDA to issue a detailed guidance regarding the special controls described in the proposed order at the same time as the publication of this final order in the **Federal Register**.

(Response 13) At this time, FDA does not intend to issue a guidance document regarding compliance with the special controls identified in this final order. For the reasons discussed in the proposed order, the Agency believes that the special controls, as stated in § 864.1890(b), provide sufficiently clear and appropriate requirements, at a level of detail necessary to reasonably assure the safety and effectiveness of this device type. Should FDA determine in the future that further information is warranted, the Agency may consider issuing guidance. The Agency also believes information available to sponsors through other resources will be helpful in preparing 510(k)s for submission and complying with special controls. For example, sponsors may review information on CDRH's website regarding previously approved oncology therapeutic ISH-based test systems such as SSED documents available in FDA's Premarket Approval Database, which detail the clinical evidence, risks, and benefits for approved devices. In addition, the performance data and related valid scientific evidence included in 510(k)s reviewed by FDA may be a helpful resource. Once available, sponsors may consider reviewing the 510(k) Decision Summaries in FDA's 510(k) Premarket Notification Database to inform the types of performance the Agency expects for this type of device.

III. The Final Order

In this final order, FDA is adopting relevant findings, including the reasoning that supports those findings, from the June 11, 2025, proposed order. FDA has made revisions in this final order based, in part, on the comments received (see section II). FDA is issuing this final order to reclassify oncology therapeutic ISH-based test systems from class III into class II under a new device classification regulation with the name In Situ Hybridization Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product, and to establish special controls by revising 21 CFR part 864 (adding § 864.1890).

Further, in this final order, FDA has identified the special controls under section 513(a)(1)(B) of the FD&C Act that, along with general controls, provide a reasonable assurance of the safety and effectiveness for oncology therapeutic ISH-based test systems. As described in section II of this document, FDA has made revisions to the special controls as previously described in the proposed order. Based, in part, on comments regarding the proposed order, FDA has revised the design verification and validation special controls to add to the existing proposed § 864.1890(b)(1)(v) requirement the consideration of surrogate samples that adequately represent the intended use specimen type(s) and intended use biomarker(s), as appropriate, as determined by FDA, to supplement clinical specimens. Additionally, FDA has removed the proposed § 864.1890(b)(1)(viii) requiring device performance data demonstrating reagent stability.

Based on the information discussed in the preambles to the proposed order and this final order, including the comments received for the proposed order, FDA concludes that special controls, in addition to general controls, provide a reasonable assurance of the safety and effectiveness of oncology therapeutic ISH-based test systems. In this final order, the Agency has identified the special controls under section 513(a)(1)(B) of the FD&C Act that, along with general controls, provide a reasonable assurance of the safety and effectiveness of these devices. In addition, in this final order, to provide additional clarification and to efficiently implement this order, the Agency has added an implementation strategy in section IV.

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 under section 510(m).[11] FDA has not made this determination for oncology therapeutic ISH-based test systems and, therefore, this class II device type is not exempt from 510(k) requirements. Thus, under sections 510(k) and 513(f) of the FD&C Act, persons who intend to market this device type must submit a 510(k) containing information on the

[11] 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 63 FR 3142 (January 21, 1998) and further explained in FDA's guidance ''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,* to determine 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 864.9.

oncology therapeutic ISH-based test system that they intend to market and must obtain FDA clearance of the device prior to marketing it.

Under this final order, oncology therapeutic ISH-based test systems are prescription use IVD devices and as such, these tests must satisfy prescription labeling requirements for IVD products (see § 809.10(a)(4) and (b)(5)(ii)). This device type is subject to the submission and device clearance requirements of sections 510(k) and 513 of the FD&C Act and of part 807, subpart E, of FDA's regulations.

IV. Implementation Strategy

This final order is effective 30 days after the date of its publication in the **Federal Register**.

For oncology therapeutic ISH-based test systems that have not been offered for sale prior to the effective date of the final order, manufacturers must obtain 510(k) clearance before marketing the device (and for subsequent modifications to the device, as appropriate).

For oncology therapeutic ISH-based test systems that have been offered for sale prior to the effective date of the final order and have prior PMA approval, such devices may continue to be marketed under the previously issued PMA approval and do not require an additional marketing authorization.

For devices that have been legally marketed via PMA before the effective date of this final order, FDA expects that manufacturers will submit a 510(k) premarket notification when making a change or modification that could significantly affect the safety or effectiveness of the device or a major change or modification in the intended use of the device. See § 807.81(a)(3).

V. Analysis of Environmental Impact

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

VI. Paperwork Reduction Act of 1995

This final administrative order refers to previously approved collections of information found in FDA regulations. 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 (44 U.S.C. 3501–3521). The collections of information in part 820 (Quality Management System Regulation) have been approved under OMB control number 0910–0073; the collections of information in 21 CFR part 812 (Investigational Device Exemptions) have been approved under OMB control number 0910–0078; the collections of information in 21 CFR part 814, subparts A through E (Premarket Approval of Medical Devices) have been approved under OMB control number 0910–0231; the collections of information in part 807, subpart E (Premarket Notification Procedures) have been approved under OMB control number 0910–0120; and the collections of information in parts 801 and 809 (Device Labeling) have been approved under OMB control number 0910–0485.

VII. 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, we are codifying in this final order the classification of In Situ Hybridization Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product in the new § 864.1890, under which these oncology therapeutic ISH-based test systems are reclassified from class III into class II.

VIII. References

The following references are on display at the Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500, and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at *https://www.regulations.gov.* Although FDA verified the website addresses in this document, please note that websites are subject to change over time.

1. FDA, ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program; Guidance for Industry and Food and Drug Administration Staff,'' May 29, 2025. (Available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.*)
2. FDA, ''Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence-Enabled Device Software Functions; Guidance for Industry and Food and Drug Administration Staff,'' August 18, 2025. (Available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/marketing-submission-recommendations-predetermined-change-control-plan-artificial-intelligence.*)
3. FDA, ''Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices; Guidance for Industry and Food and Drug Administration Staff,'' August 17, 2022. (Available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/replacement-reagent-and-instrument-family-policy-in-vitro-diagnostic-devices.*)
4. FDA, ''The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]; Guidance for Industry and Food and Drug Administration Staff,'' July 28, 2014. (Available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k.*)

List of Subjects in 21 CFR Part 864

Blood, Medical devices, Packaging and containers.

Therefore, under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321 *et seq.,* as amended), and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 864 is amended as follows:

PART 864—HEMATOLOGY AND PATHOLOGY DEVICES

■ 1. The authority citation for part 864 continues to read as follows:

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

■ 2. Add § 864.1890 to subpart B to read as follows:

§ 864.1890 In situ hybridization test systems for use with a corresponding approved oncology therapeutic product.

(a) *Identification.* In situ hybridization (ISH) test systems indicated for use with a corresponding approved oncology therapeutic product are identified as prescription in vitro diagnostic devices consisting of nucleic acid probes intended for the qualitative or quantitative detection of specific nucleic acid sequences in human clinical specimens to provide information related to the use of a corresponding approved oncology therapeutic product as described in the corresponding approved oncology therapeutic product labeling.

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

(1) Design verification and validation must include:

(i) Specification for risk mitigation elements intended to mitigate risks

associated with testing and results interpretation, including controls, procedures, and user training requirements, as appropriate.

(ii) Specification of the criteria for test result interpretation and reporting, including device cut-off(s) (*i.e.,* clinical threshold(s) or the medical decision point(s) between positive and negative results) or other relevant criteria that distinguishes positive and negative or quantitative results. This information must include the rationale for the chosen cut-off(s) to include the upper reference of normal, or other relevant criteria and results supporting validation of the cut-off(s) evaluating borderline samples around the clinical threshold(s). Scoring criteria for all applicable signals must be included.

(iii) Device performance data demonstrating appropriate analytical sensitivity from studies using interphase nuclei from intended use specimen type(s) that are considered karyotypically normal, or through an alternative approach, as determined to be appropriate by FDA (*e.g.,* probe sensitivity and probe limits).

(iv) Device performance data demonstrating appropriate analytical specificity of the device for the intended use specimen type(s), as determined to be appropriate by FDA (*e.g.,* probe specificity, interference study, cross-reactivity and cross contamination testing).

(v) Device performance data demonstrating appropriate precision and reproducibility of the device using clinical specimens representing the intended use specimen type(s) and intended use biomarker(s) from the intended use population and investigating major sources of variability (*e.g.,* multiple reagent lots, operators, instruments over multiple days, and inter- and intra-reader precision). Surrogate samples that adequately represent the intended use specimen type(s) and intended use biomarker(s) may be appropriate, as determined by FDA, to supplement clinical specimens. If the device will be used at more than one site, data must demonstrate adequate reproducibility across multiple intended use sites. Additionally, precision and reproducibility of the device must be evaluated with specimens near the clinical decision threshold(s) and near the limits of reportable range. Additionally, device performance data demonstrating appropriate precision must be included from studies evaluating the different signals and associated cut-offs and controls, as determined to be appropriate by FDA. Furthermore, precision of the device must be evaluated per specimen and in aggregate.

(vi) Device performance data demonstrating appropriate device robustness, as determined to be appropriate by FDA. The study must assess the tolerance ranges for various critical test and specimen parameters, as applicable.

(vii) Device performance data demonstrating linearity of quantitative results using samples covering the device measuring range, as applicable.

(viii) Device performance data demonstrating appropriate specimen stability based on the intended use specimen type(s) of the device, as applicable.

(ix) Clinical data generated using well-characterized clinical specimens representative of the intended use population demonstrating appropriate clinical performance of the device for its intended use, as determined to be appropriate by FDA.

(2) Labeling must include:

(i) An appropriate summary, as determined by FDA, of the performance studies performed and the results of those studies, including those that relate to all design verification and validation special controls.

(ii) A limiting statement, as appropriate, that explains that the test results are intended to be interpreted by a qualified or appropriately trained reader in conjunction with other diagnostic laboratory test results and/or pathology test results, relevant clinical information, and proper controls.

(iii) Language indicating that the test system is indicated for use with a corresponding FDA-approved oncology therapeutic product and device labeling must be consistent with the information set forth in the corresponding FDA-approved oncology therapeutic product labeling.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2026–16727 Filed 8–14–26; 8:45 am]

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DEPARTMENT OF THE TREASURY

Alcohol and Tobacco Tax and Trade Bureau

27 CFR Part 9

[Docket No. TTB–2024–0007; T.D. TTB–206; Ref: Notice No. 235]

RIN 1513–AD08

Establishment of the Columbia Hills Viticultural Area

AGENCY: Alcohol and Tobacco Tax and Trade Bureau, Treasury.

ACTION: Final rule; Treasury decision.

SUMMARY: The Alcohol and Tobacco Tax and Trade Bureau (TTB) establishes the 29,387-acre ''Columbia Hills'' American viticultural area (AVA) in Klickitat County, Washington. The newly established AVA is located entirely within the existing Columbia Valley viticultural area. TTB designates viticultural areas to allow vintners to better describe the origin of their wines and to allow consumers to better identify wines they may purchase.

DATES: This final rule is effective September 16, 2026.

FOR FURTHER INFORMATION CONTACT: Karen A. Thornton, Regulations and Rulings Division, Alcohol and Tobacco Tax and Trade Bureau, 1310 G Street NW, Box 12, Washington, DC 20005; phone 202–453–1039, ext. 175.

SUPPLEMENTARY INFORMATION: In accordance with 5 U.S.C. 553(b)(4), a summary of this rule may be found at *https://www.regulations.gov/docket/TTB-2024-0007.*

Background on Viticultural Areas

TTB Authority

Section 105(e) of the Federal Alcohol Administration Act (FAA Act), 27 U.S.C. 205(e), authorizes the Secretary of the Treasury (Secretary) to prescribe regulations for the labeling of wine, distilled spirits, and malt beverages. The FAA Act provides that these regulations should, among other things, prohibit consumer deception and the use of misleading statements on labels and ensure that labels provide the consumer with adequate information as to the identity and quality of the product. The Alcohol and Tobacco Tax and Trade Bureau (TTB) administers the FAA Act pursuant to section 1111(d) of the Homeland Security Act of 2002, codified at 6 U.S.C. 531(d). The Secretary has delegated certain administrative and enforcement authorities to the TTB Administrator through Treasury Order 120–01.