4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 878

[Docket No. FDA-2022-N-0794]

General and Plastic Surgery Devices; Reclassification of Optical Diagnostic Devices for Melanoma Detection and Electrical Impedance Spectrometers, To Be Renamed Software-Aided Adjunctive Diagnostic Devices for Use on Skin Lesions by Physicians Trained in the Diagnosis and Management of Skin Cancer

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final order reclassifying optical diagnostic devices for melanoma detection (product code OYD) and electrical impedance spectrometers (product code ONV), both postamendments class III device types, into class II (special controls), subject to premarket notification. FDA is also renaming and codifying these devices under the new classification regulation named "software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer." FDA is also establishing the special controls necessary to provide a reasonable assurance of safety and effectiveness of these devices.

DATES: This order is effective [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

FOR FURTHER INFORMATION CONTACT: Jessica Carr, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4522, Silver Spring, MD 20993, 301-796-5997, Jessica.Carr@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 premarket approval, unless and until (1) the Food and Drug Administration (FDA, the Agency, or we) 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.

FDA relies upon "valid scientific evidence," as defined in section 513(a)(3) of the FD&C Act and 21 CFR 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 premarket approval application (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 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.

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 30, 2022, FDA published a proposed order[1] in the *Federal Register* to reclassify optical diagnostic devices for melanoma detection and electrical impedance spectrometers (product codes OYD and ONV, respectively) from class III to class II subject to premarket notification (87 FR 39025, the "proposed order").[2] FDA has considered the information available to the Agency, including the deliberations of the General and Plastic Surgery Devices Advisory Panel convened on July 28-29, 2022 (the "Panel") to discuss software-aided[3] adjunctive

---

[1] The "ACTION" caption for this 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 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.

[2] In the proposed order, FDA proposed to reclassify optical diagnostic devices for melanoma detection and electrical impedance spectrometers under a new device classification regulation with the name "computer-aided devices which provide adjunctive diagnostic information about lesions suspicious for melanoma." In this final order, FDA is renaming these devices with the name "software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer," to better describe the devices that fit within this generic device type and are subject to this reclassification order.

[3] FDA regulates software that meets the definition of a device, which is defined in section 201(h)(1) of the FD&C Act as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is – recognized in the official National

diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer and the proposed reclassification (as discussed in section II of this document), as well as comments from the public docket on the proposed order (as discussed in section III 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 IV 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 software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer from class III to class II (special controls).[4] Absent the special controls identified in this final order, general controls applicable to the device type are insufficient to effectively mitigate the risks identified for this device type, such as the risk of incorrect or delayed diagnosis of skin cancer from false negative results, and therefore insufficient to provide reasonable assurance of the safety and effectiveness of these devices. FDA expects that the reclassification of these devices will enable more manufacturers to develop these types of devices such that patients will benefit from increased access to adjunctive diagnostics for which there is a reasonable assurance of safety and effectiveness.

For these class II devices, instead of a PMA, manufacturers may submit a premarket notification and obtain FDA clearance of the devices before marketing them. This action will

---

Formulary, or the United States Pharmacopeia, or any supplement to them, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term 'device' does not include software functions excluded pursuant to section 520(o)" of the FD&C Act.

[4] 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.

decrease regulatory burden on industry, as manufacturers will no longer have to submit a PMA for these types of devices 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 these types of devices.

II. Deliberations of the Panel Meeting

A. Panel Discussion

On July 28, 2022, the Panel met to discuss the general topic of skin lesion analyzer technology and its application to detecting skin cancers in various patient care settings (the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer was discussed on the second day of the Panel meeting, as described later in this section). The Panel members were asked questions regarding the diagnosing standard, or ground truth, used to confirm lesion diagnosis in clinical testing of device accuracy; the acceptable sensitivity and specificity thresholds for different diagnoses and users; and patient characteristic considerations based on variable incidence of skin lesions in the U.S. population (Ref. 1).

The Panel generally advised that the diagnostic standard, or ground truth, for algorithm validation studies should be histological diagnosis, while some Panel members believed alternative approaches could be valuable depending on lesion type (such as consensus of a group of experts in certain benign lesion cases).

The Panel advised that the applicable thresholds for performance criteria, such as sensitivity and specificity, should be evaluated for specific skin lesion types (e.g., melanoma, basal cell carcinoma, and squamous cell carcinoma), intended users (e.g., dermatologist, primary care physician, lay user), and device type, and should show that the device improves the performance of the clinical user or improves patient outcomes (i.e., earlier diagnosis). The Panel also discussed that the sensitivity and specificity threshold should be higher for standalone

devices compared to devices intended for adjunctive use. Some Panel members commented on the importance of prospective data or post-market surveillance of real-world use to confirm device benefit. The Panel agreed that the selection of performance thresholds should take into account not only the risks of false negatives but also the risks of false positives, including psychological impacts and other effects.

Regarding patient characteristics that should be evaluated in clinical testing, the Panel advised that all patient skin phototypes should be studied with some flexibility in the data collection for low-incidence populations, such as by balancing premarket data with post-market study requirements and requiring transparency in the demographics and prevalence data in the studied populations.

On July 29, 2022, the Panel met to discuss and make recommendations regarding the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer from class III to class II (Ref. 1). In particular, the Panel discussed the proposed reclassification of MelaFind, a device that uses multispectral imaging and that was approved by FDA in 2011 (PMA P090012) (Ref. 2). The Panel also discussed the proposed reclassification of Nevisense, a device that measures electrical impedance and that was approved by FDA in 2017 (PMA P150046) (Ref. 3). Both MelaFind and Nevisense are intended for use on cutaneous lesions suspicious for skin cancer when a dermatologist chooses to obtain additional information when considering biopsy. At the Panel meeting, FDA presented the risks, mitigations, and special controls identified in the proposed reclassification order for a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer.

The Panel agreed with inclusion of the risks identified by FDA, but suggested additional risks be included, as detailed in section II.B.1.

The Panel agreed that general controls alone are not sufficient to provide a reasonable assurance of safety and effectiveness for this device type. The Panel had varying opinions on

whether the devices are life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, and whether or not these devices present a "potential unreasonable risk of illness or injury" considering, among other factors, that the devices are intended to be used adjunctively to standard of care but, in the opinion of some Panel members, have a potentially high risk associated with false negative output.

Some Panel members agreed that sufficient information exists to establish special controls for this device type, though most Panel members disagreed, suggesting more information is needed to understand device performance and device benefits and risks in real-world use. Several Panel members recommended additional clarity or detail in the proposed special controls. Some believed that FDA's proposed special controls were appropriate but not sufficient, recommending additional controls such as requirements for post-market surveillance, metrics to evaluate patient benefits and risks in addition to sensitivity and specificity, evaluation of specific patient populations and subtypes, prospective real-world use studies, and transparency regarding algorithm development. Various Panel members believed that this device type should not be reclassified from class III to class II.

B. FDA Responses to Panel Deliberations and Changes in the Final Order

FDA's responses to the recommendations of the Panel deliberations are detailed in this section. As discussed in section III, FDA also considered comments that were received from industry members, professional societies, and other interested parties in developing this final order. However, here in section II, we specifically address the Panel recommendations and FDA's responses.

1. Risks to Health

The Panel suggested that additional risks to health presented by software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer be included in FDA's overall assessment of the risks to health, such as device bias in different populations, psychological impact of false positives and false

negatives, risks associated with specific locations of device use, risks associated with inadequate user training, and risks associated with algorithm performance drift in real-world use.

FDA recognizes the potential psychological impact of inaccurate device output and considers this to be encompassed within the risks of false negative results, false positive results, use error or improper device use, and device failure or malfunction listed in table 1. FDA also agrees that there are risks associated with inadequate user training and considers these to be included in the risks of false negative results, false positive results, and use error or improper device use listed in table 1.

FDA agrees that devices may perform differently in different patient sub-populations due to several factors, including bias in training, tuning, and/or validation datasets. Likewise, FDA agrees that device use on different anatomical locations may result in different device performance. FDA considers these sources of performance variability to be encompassed within the risks of false negative results and false positive results listed in table 1. In response to the Panel discussion, FDA has made several additions to the special controls regarding clinical performance testing and labeling to mitigate these specific sources of performance variability and their contribution to device risk. These additions include requiring that clinical testing evaluate patients across risk factors that represent the intended patient population, including age, body site, skin phototype, and other clinical factors as applicable; requiring that labeling include a description of the patient population that was used in development or training of the device algorithm; and requiring that labeling include information related to the limitations of device performance or subpopulations for which the device may not perform as expected or for whom the device has not been validated.

Some Panel members also emphasized that interference with implants could pose risks to patients, including device interference that affects the implant performance, or interference of the implant that affects the device performance. FDA agrees, and notes that the risk of interference with other devices, including implants, was included among the risks to health identified in the

proposed order (87 FR 39025). FDA also considers these risks to be encompassed within the risks of false negative results, false positive results, and device failure or malfunction listed in table 1.

Regarding the Panel's comments on algorithm performance drift in real-world use, FDA notes that MelaFind and Nevisense have fixed algorithms which do not change or adapt over time or with exposure to lesions during clinical use. Devices with algorithms other than fixed algorithms would represent a change in technology from the existing devices, and would very likely raise different questions of safety and effectiveness than the predicate device, which would preclude a finding of substantial equivalence under 21 CFR 807.100(b). Such devices would need to be evaluated according to 21 CFR 807.100(b)(2) to determine whether such a device could be found substantially equivalent to a predicate device within this classification regulation.

In addition, when a manufacturer of a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer that has been cleared by FDA intentionally changes the algorithm of its device, FDA would review the change in a premarket submission if the change exceeds the regulatory threshold of 21 CFR 807.81(a)(3) for submission and clearance of a new 510(k). FDA acknowledges that the device-aided user's accuracy may change over time or may differ from that demonstrated in premarket clinical studies with a retrospective design. FDA considers risks to health related to the accuracy of the device-aided user to be encompassed within the risk to health of false results due to use error or improper device use listed in table 1. In response to the Panel discussion, FDA has made several additions to the special controls regarding clinical performance testing to mitigate these risks to health. These additional special controls include requiring data obtained from both premarket clinical performance validation testing and post-market surveillance acquired under anticipated conditions of use, unless FDA determines based on the totality of the premarket data that data from post-market surveillance is not required.

2. Special Controls

FDA appreciates the perspective of various Panel members that more information is necessary to understand the device performance and its benefits and risks in real-world use. However, FDA believes that sufficient information exists and is available to FDA through the MelaFind PMA and associated panel considerations of that PMA,[5] published peer-reviewed literature (as discussed in the proposed order (87 FR 39025))[6], and information collected from FDA's publicly available Medical Device Report (MDR) database, Manufacturer and User Facility Device Experience (MAUDE) database, and Medical Device Recall database since this device type was first introduced to the market, to understand the benefits and risks of this device type and establish special controls that effectively mitigate those risks. FDA reviewed certain real-world data, as discussed above, and does not agree that additional data from real-world use is necessary prior to establishing special controls (we note that data from real-world use is not a prerequisite to establishing special controls), or that special controls cannot be established based on current information, particularly as the intended use of the devices is limited to adjunctive use (rather than standalone use, which would present greater risks). For example, in response to feedback from the Panel, the special controls have been revised to require a high sensitivity (>90 percent for lesions with high metastatic potential, or a clinically justified alternative), which can effectively mitigate the risk of false negatives. See section IV for additional discussion of the mitigation measures for the risks to health identified for this device type. Some of the panel's concerns regarding real-world use appeared to relate to uncertainty about adaptive algorithms, but as noted above, devices with algorithms other than fixed algorithms are very likely to raise different questions of safety and effectiveness from the devices being reclassified here. In addition, to the extent there is concern about FDA relying on data from only two authorized devices, FDA notes that the statute contemplates that data from just one device could provide

[5] The FDA General and Plastic Surgery Devices Panel reviewed the MelaFind PMA at a meeting on November 18, 2010. Meeting materials are available at available at https://wayback.archive-it.org/7993/20170403223449/https:/www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/GeneralandPlasticSurgeryDevicesPanel/ucm205684.htm.

[6] Such literature included the pivotal study for Nevisense, see Ref. 9 in the proposed order.

sufficient information to establish special controls for a device type under the de novo provisions (see 21 U.S.C. 360c(f)(2)).

In addition, although FDA appreciates that this technology may continue to evolve, the potential for such evolution does not suggest that there is insufficient information to establish special controls for the current device type. Future devices would only fall within this device type, and thus be classified into class II subject to the special controls established in this final order, if the device is found to be "substantially equivalent" to a predicate software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer, which requires that the device have the same intended use and the same technological characteristics as the predicate device, or, if the device has different technological characteristics, the device must be as safe and effective as a legally marketed device and not raise different questions of safety and effectiveness. A future device that raises different questions of safety or effectiveness would not fall within the device type being reclassified into class II in this final order.

As noted in section II.B.1, FDA has made several additions to the clinical performance testing and labeling special controls in response to the deliberations of the Panel. FDA has also revised and added other special controls in response to recommendations from the Panel.

The Panel stated concerns regarding potential differences in device performance as observed in retrospectively designed premarket studies versus real-world device use. To partially address this concern, the revised special controls require data obtained from both premarket clinical performance validation testing and post-market surveillance acquired under anticipated conditions of use, unless FDA determines based on the totality of the premarket data that data from post-market surveillance is not required. The post-market surveillance data may provide additional information regarding device performance in the overall patient population, as well as in low-incidence patient sub-populations for whom relatively limited data was available at the time of premarket review.

As identified in the proposed order, and consistent with the recommendations of the Panel, the special controls allow for flexibility in the endpoints used to demonstrate patient benefits and risks in addition to sensitivity and specificity. The revised special controls require demonstration of "superior accuracy" of device-aided users' diagnostic characterization of the indicated lesions compared to the accuracy of unaided users, but do not specify a particular endpoint that must be used to evaluate accuracy. Additionally, to mitigate the high risk of false negatives identified by the Panel, the revised special controls require standalone device performance testing to demonstrate at least 90 percent sensitivity of the device output for lesions with high metastatic potential, or an alternative clinical consideration must be provided to justify lower sensitivity. The special controls also require that clinical justification be provided for the reported specificity. In addition, consistent with Panel feedback that applicable thresholds for performance criteria are dependent, in part, on the intended user, the labeling special controls require statements that the device is intended to be used by a physician trained in the clinical diagnosis and management of skin cancer (e.g., a dermatologist) and that the device is not intended for use as a standalone diagnostic.

FDA agrees with the Panel recommendation that device evaluation should consider specific patient populations and lesion subtypes. The revised special controls require clinical testing and standalone testing to evaluate patients across risk factors (including age, body site, skin phototype, and other clinical factors as applicable) that represent the intended patient population. Analysis of standalone performance must include subgroup analysis by relevant risk factors. Moreover, and in response to the Panel's feedback regarding transparency, the revised special controls require device labeling to include a description of the patient population that was used in development or training of the device algorithm. The labeling must also include a summary of the standalone and clinical performance testing conducted with the device, including performance of the device for all clinically relevant subgroups within the intended patient population, and information related to the limitations of device performance or subpopulations

for which the device may not perform as expected or for whom the device has not been validated.

FDA believes that these labeling special controls, along with other special controls such as those requiring human factors testing, device precision testing, the inclusion of information about device outputs in device labeling, and the inclusion of information about user qualifications in device labeling, will help to mitigate the risk of false results due to use error and changes in performance of the device in real-world use.

3. Reclassification from Class III to Class II

Under section 513(a)(1)(C) of the FD&C Act (21 U.S.C. 360c(a)(1)(C)), class III devices are those devices for which, among other things, insufficient information exists to determine that general controls and special controls would provide a reasonable assurance of safety and effectiveness. In contrast, under section 513(a)(1)(B) of the FD&C Act, class II devices are those which cannot be classified into class I because general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, but for which there is sufficient information to establish special controls to provide such assurance. FDA agrees with the Panel members that general controls are not sufficient to provide reasonable assurance of the safety and effectiveness of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. However, as noted above, FDA believes that sufficient information exists and is available to FDA through the MelaFind PMA and associated panel considerations of that PMA, published peer-reviewed literature, and FDA's publicly available MDR database, MAUDE database, and Medical Device Recall database to establish special controls that effectively mitigate the risks to health identified for this device type. Accordingly, FDA has determined that software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer should be reclassified from class III to class II.

III. Comments on the Proposed Order and Panel

A. Introduction

FDA received comments from more than 50 commenters on the proposed order (87 FR 39025) published in the Federal Register on June 30, 2022, and for the subsequent Panel meeting held on July 28-29, 2022. The comment period on the proposed order closed on August 29, 2022, and the docket for the Panel meeting also closed on August 29, 2022. The majority of the comments received by the close of the comment periods were from individual medical professionals. Professional societies and members of the medical device industry also provided comments. Some of the comments contained one or more comments on one or more issues. We received comments providing support for the proposed reclassification as well as comments recommending against the proposed reclassification. Many comments also included technical considerations for assessing the safety and effectiveness of the devices subject to the proposed reclassification.

We describe and respond to the comments in section III.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) Multiple comments supported the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. Commenters stated that reclassification into class II would be appropriate based on the device risks, that reclassification would support patient access to dermatological care, and that special controls could be established to provide a reasonable assurance of safety and effectiveness, with some commenters emphasizing the need to communicate risks due to false positives or false negatives. One commenter stated that there has

been widespread use of physician adjunctive-use skin lesion analyzers in Europe for several years and the commenter was unaware of any meaningful negative impacts associated with such use. Many commenters also specified that reclassification of these devices into class II would be appropriate as these devices are intended to provide adjunctive information, not intended for use as standalone diagnostic devices. Some of these commenters also expressed that it would be appropriate to use these devices for general screening or triage.

(Response 1) FDA agrees with the comments supporting reclassification. Based on the available information, as discussed in the proposed order and in section II of this document, and in consideration of the comments received on the proposed order and the Panel meeting, FDA has determined that reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer into class II is appropriate. FDA made this determination because there is sufficient information to establish special controls that together with general controls will provide a reasonable assurance of safety and effectiveness for these devices when used adjunctively by physicians trained in the diagnosis and management of skin cancer (including requirements that the device labeling provide information regarding performance measures, including sensitivity, specificity and statistical confidence intervals, and an identification of risks associated with misinterpretation of the device outputs).

FDA also agrees with the comments that state that reclassification is appropriate based on the intended use of these devices to provide adjunctive information to aid in the evaluation of lesions suspicious for skin cancer following identification of a suspicious skin lesion, and not as a standalone diagnostic or for use to confirm a clinical diagnosis. Based on the totality of information available, FDA believes that general controls and special controls can provide a reasonable assurance of safety and effectiveness for these devices when they are intended to provide adjunctive information, not a diagnosis, and the intended users are physicians trained in the diagnosis and management of skin cancer. However, use of these devices as general

screening tools or for triage falls outside the approved intended uses for the devices being reclassified, and hence is outside the scope of this final order. FDA would need additional data and information to address those uses.

The Agency believes that reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer under this final order will increase access to devices for which there is a reasonable assurance of safety and effectiveness by reducing the regulatory burden on manufacturers, while still providing reasonable assurance of safety and effectiveness. Specifically, reclassifying this type of device from class III into class II will reduce regulatory burdens on industry because instead of submitting a PMA, manufacturers may submit a less burdensome 510(k) to obtain FDA clearance of the device before marketing it. The Agency also agrees with commenters that this reclassification may have a positive impact on dermatological care.

(Comment 2) Multiple comments disagreed with the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. Some commenters stated that it would be inappropriate, difficult, or impossible to develop a uniform non-clinical and clinical testing paradigm that can be applied to every device of this type. Some commenters expressed concern that reclassification would reduce FDA's ability to provide input on non-clinical or clinical study design. Many commenters also indicated that each specific device should be assessed to ensure appropriate device performance and clinical validity catered to the device's specific technological characteristics, intended users, and lesion types, and that these devices should be maintained in class III to maintain the strictest level of FDA premarket review of device safety, performance, and labeling. Some commenters stated that there is not sufficient information or experience with this device type to support reclassification and the establishment of special controls to provide a reasonable assurance of safety and effectiveness, or that the consequences

of an inaccurate diagnosis could result in unnecessary procedures (such as biopsies and surgeries) or are too severe to support reclassification.

(Response 2) FDA disagrees that reclassification would be inappropriate based on the need for device-specific non-clinical and clinical assessments or premarket review for the specific device. FDA agrees that a uniform approach to non-clinical and clinical performance testing is not appropriate for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer, and there is no single clinical study design that would be appropriate for all devices of this type. The special controls for this device type outlined in this final order include controls for non-clinical and clinical testing that could support unique study designs that are appropriate for the specific indications for use and technological characteristics for each device that would be reviewed in a premarket notification. While every clinical study developed to support a premarket submission for a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer should be designed to demonstrate that the device performs as intended when used by the intended user in the intended patient population, the final special controls for these devices allow for customized study designs tailored specifically for each device considering the device technology and indications for use. Reclassification of these devices from class III to class II does not exclude device-specific non-clinical and clinical testing. Rather, the special controls establish requirements for non-clinical and clinical testing that is necessary to support reasonable assurance of safety and effectiveness for the device. The substantial equivalence framework in the 510(k) review paradigm permits potential clearance of devices of the same device type even when supported by data from different types of studies, consistent with FDA's least burdensome provisions.[7]

[7] *See* sections 513 and 515 of the FD&C Act. *See also* FDA's guidance, "The Least Burdensome Provisions: Concepts and Principles; Guidance for Industry and Food and Drug Administration Staff," Feb. 5, 2019. Available at https://www.fda.gov/media/73188/download.

FDA also agrees that these devices require appropriate regulatory oversight through premarket review, but disagrees that classification in class III and PMA approval is necessary to provide such oversight for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. For example, PMA approval requires, among other things, the submission of a complete description of the methods used in, and the facilities and controls used for, the manufacture, processing, packing, storage, and, where appropriate, installation of the device (21 CFR 814.20(b)(4)(v)), and FDA often conducts inspections prior to PMA approval. PMA requirements also include annual reporting requirements, and requirements regarding the submission and approval of PMA supplements. As discussed in more detail in response to Comment 8, FDA does not believe that compliance with such requirements is necessary to provide a reasonable assurance of safety and effectiveness for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. This final reclassification order establishes that instead of submission and approval of a PMA, submission and clearance of a 510(k) will be required prior to legally marketing these devices. FDA reviews the non-clinical and clinical data and related valid scientific evidence included in a 510(k) to assess substantial equivalence to a legally marketed predicate device, including, as appropriate, conformance to special controls. FDA will also evaluate device labeling to ensure that labeling is consistent with the labeling requirements established in the special controls. Clearance of a 510(k) reflects FDA's determination that the device has the same intended use and technological characteristics as the predicate, or, if the device has different technological characteristics, that the device is as safe and as effective as a legally marketed device and does not raise different questions of safety and effectiveness than the predicate device (see section 513(i) of the FD&C Act).

Additionally, some commenters expressed concern that reclassification would reduce FDA's ability to provide input on non-clinical or clinical study design. However, regardless of whether a device is classified in class III or class II, FDA may provide input on non-clinical or

clinical study design. A manufacturer may seek FDA input on non-clinical or clinical study design by utilizing our Q-Submission program, through which FDA may provide input on device-specific requirements and recommendations for non-clinical and clinical studies intended to support device-specific indications for use. Additional information regarding the Q-Submission program can be found in FDA's final guidance document entitled "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program" (Ref. 4). In addition, reclassification does not change the regulatory requirements related to clinical study oversight and investigational device exemptions (IDEs). FDA may provide specific feedback and study design considerations for clinical trials as a part of IDE review for significant risk studies. The special controls also require that specific study design elements consider the indicated lesions, intended patient population, and intended users to provide a reasonable assurance of safety and effectiveness.

Ultimately, as discussed in section II.B.2 of this document, FDA believes there is sufficient information and experience available to support the reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer into class II, including sufficient information to establish special controls for these devices such that general controls and special controls together provide a reasonable assurance of safety and effectiveness. Considering the intended use of these devices as an adjunctive source of information for clinical decision making (rather than to provide a diagnosis), FDA believes these controls effectively mitigate the potential negative consequences of an incorrect diagnosis based on the adjunctive information from the device.

(Comment 3) Multiple comments disagreed with the proposed reclassification based on the concern that software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer may be used by the general public (as an over-the-counter device) or by other unqualified users to assess skin lesions (their own or others'), or based on the concern that these devices may be used as standalone diagnostic

devices in the absence of a clinical assessment by a physician trained in the clinical diagnosis and management of skin cancer (e.g., a dermatologist). Some of these commenters indicated that use by untrained users, including non-dermatologist medical providers and/or lay users, would likely increase the risk of device misuse and result in unacceptable rates of false positive and false negative results, leading to patient harm (such as delay in diagnosis of skin cancer and/or unnecessary procedures and patient anxiety) or increased demand for dermatological services. Commenters stated that diagnosis by a medical professional trained in the diagnosis and management of skin cancer is the gold standard for skin cancer diagnosis and that a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer is not a substitute for a clinician's diagnosis and histopathology.

(Response 3) FDA agrees that software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer are not a substitute for diagnosis of skin lesions by a trained clinician and would present different risks if intended for use by untrained users. The devices being reclassified in this final order are identified as being intended for prescription use only and for use by a physician trained in the clinical diagnosis and management of skin cancer (e.g., a dermatologist) as an adjunctive device following identification of a suspicious skin lesion. These devices are not intended to be used by the general public or by medical personnel untrained in the clinical diagnosis and management of skin cancer, and are not intended for use as a standalone diagnostic or to confirm a clinical diagnosis.

FDA agrees that the expertise of a trained clinician is needed to appropriately select lesions for assessment consistent with the intended use and instructions for use for these devices, and consistent with the clinical studies that validate device performance. As such, the intended users of these devices are physicians trained in the clinical diagnosis and management of skin cancer. The clinical performance validation testing special controls require that lesions used in clinical testing must be selected by representative users (e.g., dermatologists) and a justification

must be provided for the quantity and range of mimic lesions per diagnosis, which is intended to ensure that the device works safely and effectively on the lesions that a user (e.g., a dermatologist) would choose to use the device on. Additionally, the labeling special controls require that the labeling include a statement that the device is not intended for use as a standalone diagnostic and include the user qualifications needed for safe use of the device, including a description of required user training and a statement that the device is intended to be used by a physician trained in the clinical diagnosis and management of skin cancer.

(Comment 4) Some commenters stated that reclassified software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer should include devices intended for use by non-specialists and by general practitioner care providers.

(Response 4) FDA disagrees with these comments and believes that physicians trained in the clinical diagnosis and management of skin cancer are the appropriate intended users of these devices based on the intended use, performance testing for the devices, and the expertise and training needed to utilize these devices as adjunctive sources of information for clinical decision making for suspicious skin lesions. This is consistent with the indications for use of approved software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer (see Refs. 2 and 3). While different types of skin lesion analyzers may have different intended users,[8] different users present different risks, and the Agency believes that the assessment of a clinician trained in the diagnosis and management of skin cancer is important for the safe and effective use of this device type.

(Comment 5) Several commenters provided feedback on what may be considered the ground truth as a comparator for device performance in clinical studies for a software-aided

[8] FDA has separately classified "software-aided adjunctive diagnostic device[s] for use by physicians on lesions suspicious for skin cancer" into class II under 21 CFR 878.1830. Please see De Novo classification order DEN230008, available at https://www.accessdata.fda.gov/cdrh_docs/pdf23/DEN230008.pdf. The publication of this classification in the Federal Register and codification in the Code of Federal Regulations are currently pending at the time of publication of this final order.

adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. Other commenters provided feedback on what type of data should be considered as an input for these devices. These comments generally agreed that histologically confirmed diagnosis of biopsied tissue assessed by a trained dermatopathologist or a panel of trained dermatopathologists would be appropriate as a ground truth comparator for clinical studies, though one comment noted that biopsy of non-suspicious lesions may not be needed to establish ground truth in a clinical trial because a large number of benign lesions are already considered suspicious enough to biopsy and can be used to form a ground truth for benign lesions. Some commenters stated that dermoscopic images should be used as inputs for these devices, rather than standard images or other types of input data.

(Response 5) FDA agrees that in many cases, histologically confirmed diagnosis by a trained dermatopathologist or a panel of trained dermatopathologists provides an appropriate ground truth comparator for use in clinical studies of a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer, though the exact source of information used in clinical trials as a comparator may be specific to each clinical trial design, including the range and number of suspicious and non-suspicious lesions sampled for the trial. FDA also believes that it is important to consider that, as technology and clinical practices evolve, additional comparators may be possible with appropriate justification and supportive valid scientific evidence. To that end, the clinical performance special controls include a requirement that justification must be provided for the determination of ground truth.

FDA also acknowledges that dermoscopic images may be used as inputs for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. However, we note that current devices utilize other types of inputs, including multispectral images or electrical impedance measurements, and as discussed

elsewhere in this document, FDA has determined that general controls and the special controls established in this final order effectively mitigate the risks to health identified for these devices.

(Comment 6) Multiple comments provided input regarding statistical performance targets and study endpoints for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer, including the extent to which such targets and endpoints should be specified in special controls. Generally, these comments indicated that sensitivity, specificity, accuracy, and other indicators of statistical performance and validity should be assured to be appropriate for each device based on the intended use and intended user, and that there is not a single set of statistical performance targets that would be appropriate for every device and every indication, though some commentators suggested that the special controls should include specific targets for statistical performance requirements. Some commenters emphasized the importance of ensuring that performance goals and study requirements are achievable for each type of study conducted to support device performance, and that use of a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer should improve physicians' ability to detect skin cancer without causing an unacceptable increase in systemic care burden, particularly if the care burden is unnecessary biopsies.

Specific feedback regarding statistical performance included a recommendation that suitable studies of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer should demonstrate sensitivity with a lower bound of the confidence interval greater than 90 percent. One commenter recommended that device sensitivity for the indicated skin cancer(s) should be superior to unaided providers in the study or in literature, and that the sum of device sensitivity and specificity should be greater than one to demonstrate that the device performance is statistically meaningful and is a beneficial adjunct to inform dermatologist decision making. Another commenter recommended that, ultimately, the primary effectiveness criterion should be that use

of the device improves dermatologists' correct assessment of whether to biopsy a lesion suspicious for skin cancer.

(Response 6) FDA agrees that the device, when used by a provider trained in the diagnosis and management of skin cancer as an adjunctive device to aid in the evaluation of lesions suspicious for skin cancer following identification of a suspicious skin lesion, should enable superior accuracy in the provider's decision-making process for assessing skin lesions compared to unaided providers. FDA also agrees that the performance goals and study endpoints for clinical studies used to test these devices should be reasonable and achievable. The performance special controls established in this final order therefore include clinical testing with clinically justified endpoints for device sensitivity and specificity relative to ground truth for a representative range of individuals with different risk factors and a justified quantity and range of mimic lesions, which are benign skin lesions that are visually very similar to malignant lesions. Performance data must also demonstrate superior accuracy of device-aided users' diagnostic characterization of lesions compared to that of unaided users. For lesions with high metastatic potential, FDA believes that a sensitivity of at least 90 percent, or a clinically justified alternative, is necessary to mitigate the risks related to false negatives, and as such has established requirements in the special controls to that effect. Device specificity and other endpoints should be clinically justified and appropriate for the specific indications and labeling to mitigate the risks related to false positives, which may also reduce any potential increase in care burden such as from unnecessary biopsies.

(Comment 7) Multiple comments provided recommendations for study design considerations related to patient demographics and lesion selection. Specific recommendations included that there should be a sufficient number of subjects across multiple clinical sites in studies to allow for subgroup analysis. Demographic considerations recommended in these comments included ethnicity, sex, age, low/intermediate/high-risk populations, and Fitzpatrick

skin type[9] of the intended patient population. Some comments noted that patients with darker Fitzpatrick skin types (IV-VI) are often underserved in dermatology and underrepresented in clinical studies related to assessing skin lesions; these comments supported that clinical trials should utilize investigational patient populations representative of the intended patient population of the device. Some comments further stated that software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer ought to be effective at assessing lesions in patients with darker Fitzpatrick skin types, while other comments stated that a phased approach to considering different skin types would be appropriate. One comment asserted that special controls addressing labeling may be used to minimize risk in underrepresented populations. Comments also recommended that a broad range of lesion types, sizes, and anatomic sites should be included in clinical studies. Additionally, commenters stated that the classification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer should reflect the difference in risk associated with devices indicated for use for melanoma as compared to devices indicated for use for other types of lesions and skin cancers.

(Response 7) FDA believes that clinical studies supporting the safety and effectiveness of a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer should consider patient populations representative of the intended patient population for the device and a wide variety of lesions to support the specific indication(s) and intended patient population for the device. The special controls state that clinical testing must evaluate patients across risk factors (including age, body site, skin

[9] The Fitzpatrick skin type classification scale is a recognized standard in dermatology used to estimate the response of different types of skin to ultraviolet (UV) light. Fitzpatrick skin types range from Type I to VI where individuals with Type I always burn and never tan (pale white skin; blond or red hair; blue eyes; freckles) and individuals with Type VI never burn (deeply pigmented skin; dark hair and eyes). Fitzpatrick skin type is an independent risk factor for skin cancer, notably melanoma, basal cell carcinoma, and squamous cell carcinoma. *See* National Cancer Institute, "Genetics of Skin Cancer (PDQ) – Health Professional Version," available at https://www.cancer.gov/types/skin/hp/skin-genetics-pdq (last updated on May 9, 2025); Fitzpatrick, T.B., "The Validity and Practicality of Sun-Reactive Skin Types I Through VI," Arch Dermatol, 124(6):869-71, 1988, available at https://doi.org/10.1001/archderm.124.6.869.

phototype, and other clinical factors as applicable) that represent the intended patient population and that analysis of standalone performance must include subgroup analysis by relevant risk factors to help demonstrate that the device performs as intended in the intended patient population. The special controls require both premarket clinical performance validation testing and post-market surveillance, in part to provide a reasonable assurance of safety and effectiveness in patients with relatively lower incidence of skin cancer, unless FDA determines based on the totality of the premarket data that data from post-market surveillance is not required. The clinical performance special controls also state that a justification must be provided for the quantity and range of mimic lesions per diagnosis used in testing, that data must demonstrate superior accuracy of device-aided users' diagnostic characterization of the indicated lesions compared to the accuracy of unaided users, and that testing must demonstrate at least 90 percent sensitivity of the device output for lesions with high metastatic potential (or an alternative clinical consideration must be provided to justify lower sensitivity), thereby contributing to the risk mitigation for higher risk types of skin cancers, and different types of skin cancers and lesions. The special controls established in this final order therefore mitigate the risk associated with use for different lesion types, including lesions with high metastatic potential such as melanoma.

Additionally, FDA agrees that labeling special controls, among the other special controls established in this final order, are necessary to provide a reasonable assurance of safety and effectiveness of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. The labeling special controls state that device labeling must include, among other things, information about device performance for all clinically relevant subgroups within the intended patient population(s), a description of the patient population that was used in development or training of the device algorithm, and information about subpopulations for which the device may not perform as expected or for whom the device has not been validated.

(Comment 8) Multiple comments stated that FDA should conduct premarket inspections and establish post-market requirements for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer including post-market surveillance studies, manufacturing facility inspections, and annual reports. One comment stated that databases should be maintained to help ensure the safety of patients on which software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer are used. Some commenters raised concerns regarding how future changes to device hardware or software, especially artificial intelligence and machine learning (AI/ML) algorithms, might be managed under the 510(k) paradigm and suggested that PMA annual reporting requirements or PMA supplement requirements may be the only way to provide appropriate oversight of such changes, and that such changes may need to be supported by additional clinical data. Another commenter supported the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer and suggested that special controls should require adequate documentation on AI/ML data management, training, and validation.

(Response 8) FDA agrees with parts of these comments. The special controls established in this final order include a requirement that data obtained from post-market surveillance demonstrate that the device performs as intended in the intended patient population and under anticipated conditions of use, unless FDA determines based on the totality of the premarket data that data from post-market surveillance is not required. For any such required post-market surveillance, FDA believes that to conduct the surveillance in a timely fashion, a manufacturer generally should submit a complete study protocol for the post-market surveillance study consistent with the special control requirements within 30 days of receipt of a 510(k) decision letter finding the device substantially equivalent to a predicate device. FDA generally expects to work with the manufacturer to approve the study protocol within 90 days of that letter. In

addition, to ensure the surveillance is conducted in a timely fashion, FDA believes that from the date of protocol approval, the first study subject should generally be enrolled within 6 months; 20 percent of subjects should generally be enrolled within 12 months; 50 percent of subjects should generally be enrolled within 24 months; and 100 percent of subjects should generally be enrolled within 36 months. FDA also believes that manufacturers should generally submit post-market study progress reports every year until subject enrollment has been completed, and annually thereafter, from the date of the 510(k) decision letter; that if any enrollment milestones are not met, manufacturers should generally submit enrollment status reports every 6 months in addition to the annual post-market study progress reports, until FDA notifies the manufacturer otherwise; and that manufacturers should generally submit a final post-market study report 3 months from study completion (i.e., last subject's last follow-up date). FDA anticipates that specific timelines may be discussed with the manufacturer at the time of and/or following receipt of the 510(k) decision letter.

FDA also maintains the MDR database, MAUDE database, and Medical Device Recall database, which allows for additional post-market surveillance of these devices and helps to ensure continued safety for marketed devices.

FDA does not agree that premarket site inspections are necessary to provide reasonable assurance of safety and effectiveness for these devices. There is a low risk of batch variability in the manufacturing of these devices, and the hardware of these devices can generally be characterized with well-established methods and standards. The special controls identified in this final order establish requirements for validating both software and hardware components of the devices premarket, including that testing must include a description of compatible hardware and processes, pre-specified compatibility testing protocols, and dataset(s). The special controls also establish requirements relating to device precision, electromagnetic compatibility, and electrical, mechanical, and thermal safety, biocompatibility, and software verification, validation, and hazard analysis. Additionally, routine or for-cause inspections, which may consider compliance

with quality management system requirements[10] applicable to the manufacturing of the device, allow for post-market oversight of these devices with respect to inspections.

FDA also disagrees that the PMA annual reporting requirements (distinct from annual reporting associated with a post-market surveillance study) or PMA supplement requirements are necessary to ensure that changes to a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer that has received marketing authorization have appropriate oversight. Under the 510(k) paradigm, a new 510(k) is required for any change or modification to a cleared device that could significantly affect the safety or effectiveness of the device, or for a major change or modification in intended use.[11] Information on more minor changes, such as might be submitted in a PMA supplement or reported in a PMA periodic report, is not needed for reasonable assurance of safety and effectiveness here considering that the intended use of the devices being reclassified is limited to adjunctive use after a provider has identified a suspicious skin lesion and is not for use to confirm a clinical diagnosis, and because, as discussed in section IV, the special controls established in this final order, in addition to general controls, are sufficient to mitigate the risks to health that may be associated with the use of a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer.

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

[10] On February 2, 2024, FDA issued a final rule amending the device Quality System Regulation, 21 CFR part 820, to align more closely with international consensus standards for devices (89 FR 7496). This final rule took effect on February 2, 2026. This rule withdrew the majority of the previous requirements in part 820 and instead incorporated by reference the 2016 edition of the International Organization for Standardization (ISO) 13485, Medical devices – Quality management systems – Requirements for regulatory purposes, in part 820. As stated in the final rule, the requirements in ISO 13485 are, when taken in totality, substantially similar to the requirements of the previous part 820, providing a similar level of assurance in a firm's quality management system and ability to consistently manufacture devices that are safe and effective and otherwise in compliance with the FD&C Act.

[11] In accordance with 21 CFR 807.81(a)(3), a 510(k) is required for significant changes or modifications to a device in design, components, method of manufacture, or intended use, which include: (1) a change or modification that "could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process," or (2) "a major change or modification in the intended use of the device."

new 510(k) for each significant change or modification[12] while continuing to provide a reasonable assurance of device safety and effectiveness.[13] 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 significant change or modification described in the PCCP. When used appropriately, PCCPs authorized by FDA are expected to be least burdensome for manufacturers and FDA.[14]

Based on all available information, including feedback from the July 2022 reclassification panel meeting, the Agency believes it likely that changes to the AI/ML algorithm in a software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer could significantly impact device effectiveness or safety. As such, these changes would likely require a new 510(k) (unless the changes are implemented consistent with a cleared PCCP), as would changes to device hardware (including signal capturing hardware), the device output, or other software aspects that could significantly impact device safety or effectiveness. Examples of such changes include expansion or modification of the AI/ML algorithm training data, modification to cut-off values or thresholds used to determine device output, and addition, removal, or modification of device outputs. It is important to note that the devices subject to this reclassification do not utilize adaptive algorithms (i.e., algorithms that evolve dynamically due to continuous learning while they are used). FDA also notes that FDA's quality management system requirements include

---

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

[13] Section 3308 of the Food and Drug Omnibus Reform Act of 2022, Title III of Division FF of the Consolidated Appropriations Act, 2023, Pub. L. No. 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 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.

[14] Sections 513 and 515 of the FD&C Act. *See also* FDA's guidance, "The Least Burdensome Provisions: Concepts and Principles; Guidance for Industry and Food and Drug Administration Staff," Feb. 5, 2019. Available at https://www.fda.gov/media/73188/download.

documentation requirements related to, among other things, device modifications and validation (see 21 CFR part 820).

FDA agrees that some changes to device software or hardware may require new clinical data, which may require premarket review within the context of a new premarket submission.

(Comment 9) Several comments expressed concerns related to layperson use of mobile phone-based software applications intended to provide information about or diagnose skin lesions. Commenters stated that these devices have different risks and may have greater risks than the software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer being reclassified in this order, and stated that such mobile phone-based software applications intended for use by lay persons should not be a part of this reclassification. Others expressed a concern that reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer might be interpreted as indicating an Agency position on layperson, mobile phone-based devices with similar intended uses. Some commenters provided input regarding requirements that should be established for mobile phone-based software applications intended for use by lay persons on skin lesions, such as that they should use digital dermoscopy images, not smartphone images.

(Response 9) FDA agrees that mobile phone-based or other web-based software applications intended for use by lay users to provide information about or diagnose skin lesions have different risks than the devices being reclassified in this final order. The devices subject to this reclassification order are not mobile phone or web-based applications available to lay users. At the time of publication of this final order, FDA has not classified, cleared, approved, or granted authorization for a layperson use mobile phone-based or web-based application intended to provide diagnostic or adjunctive information about skin lesions, and layperson, mobile phone-based or web-based devices are not within the scope of this final order. Comments related to the

technological characteristics of mobile phone applications intended for use by lay users are outside the scope of this reclassification order.

(Comment 10) One comment stated that FDA's method of notifying the dermatologic community about the opportunity for public comment on the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer was inadequate, noting that certain interested persons were not informed that the topic was under discussion.

(Response 10) FDA disagrees that its method of informing interested persons of the opportunity for public comment on the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer was inadequate. FDA's procedures were conducted consistent with the Agency's regulations under 21 CFR 860.134 and section 513(f)(3) of the FD&C Act, including publication of a proposed order in the Federal Register (87 FR 39025), provision of a 60-day comment period for interested persons to submit comments to a public docket, and the convening of a meeting of the appropriate classification panel to discuss the proposed reclassification (including the establishment of an additional docket for public comment and opportunities for interested persons to attend and/or present data, information, or views at the Panel meeting). These procedures provided meaningful opportunity for public comment; FDA received comments from more than 50 commenters on the proposed order and Panel meeting, including comments from a variety of entities such as individual medical professionals, professional societies, and members of the medical device industry. FDA therefore believes that the Agency provided sufficient opportunity for interested parties to comment on the proposed reclassification of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer.

IV. Changes in the Final Order

As described in sections II and III of this document, FDA has made revisions in this final order in response to feedback from the Panel and comments regarding the proposed reclassification order that were submitted to public dockets.

Based, in part, on the Panel feedback and comments regarding the proposed reclassification order, FDA has revised the list of risks to health associated with the use of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer, the special controls that FDA has determined will mitigate these risks, and Table 1, "Risks to Health and Mitigation Measures for Software-Aided Adjunctive Diagnostic Devices for Use on Skin Lesions by Physicians Trained in the Diagnosis and Management of Skin Cancer".

FDA has identified the following risks to health associated with the use of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer:

- *False negative results or false positive results:* False negative results could result in incorrect or delayed diagnoses and delays in skin cancer treatment. These delays may allow an undetected condition to worsen and potentially increase skin cancer associated morbidity and mortality. False positive results may result in complications such as incorrect management of the patient, including unnecessary invasive biopsy procedures and more frequent screenings, as well as the potential administration of inappropriate treatments and/or the withholding of appropriate treatments, with possible adverse effects.
- *Use error or improper device use*: Use error or improper device use could lead to false results or failure to generate a result. The device could be misused to analyze data from an unintended patient population, an unintended anatomical site, or lesions having an unintended attribute, or to analyze data acquired with incompatible hardware or incompatible acquisition settings, potentially resulting in the device not operating at its expected

performance level. The device could also be misused if the user does not follow the appropriate use protocol for using the device to assess lesions of interest. Examples of not following the appropriate use protocol include overreliance on the device output or not using the device in an adjunctive manner, i.e., using the device output alone to make a patient management decision, which may lead to lower accuracy. Inaccurate results may result in the same complications associated with false negative or false positive results as previously discussed.

- *Device failure or malfunction*: Device failure or malfunction could result in the absence or delay of device output, or incorrect device output, which could lead to inaccurate patient assessment. Inaccurate results may result in the same complications associated with false negative or false positive results as previously discussed.
- *Electrical, thermal, mechanical, or light exposure-related injury*: While in operation, the device may discharge electricity that could shock the user or patient. Electrical discharge or exposure to device-generated heat may cause thermal injury or discomfort. Moving parts may cause mechanical injury. For devices that utilize energy (e.g., light) to provide adjunctive diagnostic information, accidental eye exposure to the energy source could cause eye injury.
- *Interference with other devices*: Individuals with electrically powered implants could experience an adverse interaction with the device due to electromagnetic interference or radiofrequency interference.
- *Adverse tissue reaction*: A patient could experience skin irritation and/or allergic reaction associated with non-biocompatible materials in patient-contacting components of the device.
- *Infection and cross contamination*: If components of the device that must be sterile are not adequately sterilized or if reusable components are not adequately reprocessed (i.e., are not cleaned and sterilized or disinfected) between uses, the device may introduce pathogenic organisms to patients which may result in an infection.

FDA has determined that the following special controls will mitigate these risks to health, and that these special controls, in addition to general controls, will provide a reasonable assurance of safety and effectiveness for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer:

- The risk of false negative results or false positive results can be mitigated through clinical performance testing – including standalone testing that demonstrates at least 90 percent sensitivity of the device output for lesions with high metastatic potential (or an alternative clinical consideration must be provided to justify lower sensitivity), and with a clinical justification provided for the reported specificity – as well as non-clinical performance testing and post-market surveillance (unless FDA determines based on the totality of the premarket data that data from post-market surveillance is not required). The clinical performance testing must demonstrate superior accuracy of device-aided users' diagnostic characterization of the indicated lesions compared to the accuracy of unaided users. The non-clinical performance testing, among other information, must demonstrate that the device performs as intended under anticipated conditions of use, including a description of compatible hardware and processes, pre-specified compatibility testing protocols, and dataset(s). In addition, post-market surveillance data may address potential differences in device performance as observed in retrospectively designed premarket studies versus real-world device use and provide additional information regarding device performance in the overall patient population, including in low-incidence patient sub-populations for whom relatively limited data was available at the time of premarket review. The risk of false positive results and false negative results can be further mitigated by special controls that require information in labeling to provide detailed instructions for use and inform the user of the expected device performance for all clinically relevant subgroups within the intended patient population.

- The risk associated with use error or improper device use can be mitigated by performance testing that demonstrates device precision, including repeatability and reproducibility of device performance, across operators and challenging use conditions. In addition, this risk can be mitigated by requiring that the device labeling include information regarding performance of the device for all clinically relevant subgroups within the intended patient population, as well as a description of the patient population that was used in development or training of the device algorithm. This risk can be further mitigated by special controls that require the device labeling to include information related to the limitations of device performance or subpopulations for which the device may not perform as expected or for whom the device has not been validated. The risk resulting from not following the device instructions for use can be mitigated by special controls that require a human factors assessment to demonstrate that intended users can correctly use the device according to the intended use. This risk can be further mitigated by requiring that the device labeling include information needed to facilitate interpretation of all device outputs and identification of the risks associated with misinterpretation of the device outputs, and by special controls requiring that the device labeling provide a description of user training required prior to use and a statement that the device is not intended for use as a standalone diagnostic.
- The risk of device failure or malfunction can be mitigated by requiring non-clinical performance testing and software verification, validation, and hazard analysis, and by requiring performance testing that demonstrates device precision, including repeatability and reproducibility of device performance, across operators and challenging use conditions. This risk can be further mitigated by requiring that instructions for device maintenance and validated methods and instructions for reprocessing of any reusable components be included in the labeling.
- The risk of electrical, thermal, mechanical or light-related hazards leading to user injury or discomfort can be mitigated by special controls that require testing that demonstrates

electrical, mechanical, and thermal safety; software verification, validation and hazard analysis; and device labeling that includes instructions on appropriate usage and maintenance of the device. The risk of eye injury due to energy (e.g., light) exposure can be mitigated by special controls that require labeling that warns users about exclusion of lesions close to the eye and unsafe exposure to any energy-emitting components of the device.

- The risk that the device may interfere with other devices due to radiofrequency or electromagnetic interference can be mitigated by requiring testing that demonstrates electromagnetic compatibility.
- The risk of adverse tissue reaction for patient-contacting devices can be mitigated by special controls that require elements of the device that may contact the patient to be demonstrated to be biocompatible and labeling that includes, in addition to user qualifications needed for safe use of the device, instructions for device maintenance and validated methods and instructions for reprocessing of any reusable components.
- The risks of infection and cross contamination for patient-contacting components can be mitigated by special controls that require sterilization validation, shelf-life testing, and labeling that includes validated methods and instructions for reprocessing of any reusable components (i.e., cleaning and sterilization or disinfection).

Table 1.--Risks to Health and Mitigation Measures for Software-Aided Adjunctive Diagnostic Devices for Use on Skin Lesions by Physicians Trained in the Diagnosis and Management of Skin Cancer

Identified Risk to Health	Mitigation Measures
False negative results or false positive results	Clinical performance testing Post-market surveillance Non-clinical performance testing Labeling
Use error or improper device use	Precision testing Human factors testing Labeling
Device failure or malfunction	Non-clinical performance testing Precision testing Software verification, validation, and hazard analysis Labeling

Electrical, thermal, mechanical, or light exposure-related injury	Electrical, mechanical, and thermal safety testing Software verification, validation, and hazard analysis Labeling
Interference with other devices	Electromagnetic compatibility testing
Adverse tissue reaction	Biocompatibility evaluation Labeling
Infection and cross contamination	Sterilization validation Shelf-life testing Cleaning and disinfection validation Labeling

V. The Final Order

In this final order, FDA is adopting relevant findings from the June 30, 2022, proposed order (87 FR 39025). FDA has made revisions in this final order in response to the Panel deliberations (see section II) and comments received (see section III). FDA is issuing this final order to reclassify optical diagnostic devices for melanoma detection and electrical impedance spectrometers from class III into class II under a new device classification regulation with the name software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer, and to establish special controls by revising 21 CFR part 878 (adding 21 CFR 878.1820). The identification for § 878.1820(a)(1) has been revised to provide a more accurate description of the devices in this classification regulation.

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 software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. In this final order, the Agency has made refinements to the special controls as previously described in the proposed order to further mitigate the risks to health associated with the use of software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer. Specifically, and among other things, FDA added new special controls requiring that data from post-market surveillance demonstrate that the device performs as intended in the

intended patient population and under anticipated conditions of use (unless FDA determines based on the totality of the premarket data that data from post-market surveillance is not required); requiring that standalone testing demonstrate at least 90 percent sensitivity of the device output for lesions with high metastatic potential (or an alternative clinical consideration must be provided to justify lower sensitivity), and that a clinical justification be provided for the reported specificity; requiring that clinical testing evaluate patients across risk factors that represent the intended patient population, including age, body site, skin phototype, and other clinical factors as applicable; requiring that performance testing demonstrate device precision, including repeatability and reproducibility of device performance, across operators and challenging use conditions; and requiring that labeling include a description of the patient population that was used in development or training of the device algorithm.

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).[15] FDA has not made this determination for software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer 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 software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer that they intend to market and must obtain FDA clearance of the device prior to marketing it.

[15] 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" 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 878.9.

Under this final order, software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer are prescription use devices under § 801.109 (21 CFR 801.109). Prescription devices are exempt from the requirement for adequate directions for use for the layperson under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)) and 21 CFR 801.5, as long as the conditions of § 801.109 are met. The device would continue to be 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 (21 CFR part 807).

VI. Effective Date

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

VII. Analysis of Environmental Impact

The Agency has 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.

VIII. 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 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 812 (Investigational Device Exemptions) have been approved under OMB control number 0910-0078; the collections of information in part 807, subpart E (Premarket Notification Procedures), have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 822 (Postmarket Surveillance) have been approved under OMB control number 0910-0449; and the collections of information

under 21 CFR part 801 (Device Labeling) have been approved under OMB control number 0910-0485.

IX. 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 software-aided adjunctive diagnostic devices for use on skin lesions by physicians trained in the diagnosis and management of skin cancer in the new § 878.1820, under which these devices are reclassified from class III into class II.

X. 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, July 28-29, 2022, Meeting of the General and Plastic Surgery Devices Panel Meeting Materials (available at https://www.fda.gov/advisory-committees/advisory-committee-calendar/july-28-29-2022-general-and-plastic-surgery-devices-panel-medical-devices-advisory-committee-meeting).

2. P090012 Approval Order, available at https://www.accessdata.fda.gov/cdrh_docs/pdf9/P090012A.pdf.

3. P150046 Approval Order, available at https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150046A.pdf.

4. 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.

List of Subjects in 21 CFR Part 878

Medical devices.

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 878 is amended as follows:

PART 878—GENERAL AND PLASTIC SURGERY DEVICES

1. The authority citation for part 878 continues to read as follows:

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

2. Add § 878.1820 to subpart B to read as follows:

§ 878.1820 Software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer.

(a) *Identification*. A software-aided adjunctive diagnostic device for use on skin lesions by physicians trained in the diagnosis and management of skin cancer is a device that uses a software algorithm to analyze optical or other physical properties of a skin lesion and returns a classification of the skin lesion. The device is intended for prescription use by a physician trained in the clinical diagnosis and management of skin cancer (e.g., a dermatologist) as an adjunctive device to aid in the evaluation of lesions suspicious for skin cancer following identification of a suspicious skin lesion. The device is not intended for use as a standalone diagnostic and is not for use to confirm a clinical diagnosis.

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

(1) Data obtained from premarket clinical performance validation testing, or a combination of premarket clinical performance validation testing and post-market surveillance (in accordance with paragraph (b)(2) of this section), must:

(i) Demonstrate superior accuracy of device-aided users' diagnostic characterization of the indicated lesions compared to the accuracy of unaided users in the intended patient population and under anticipated conditions of use;

(ii) Include an evaluation of patients across risk factors (including age, body site, skin phototype, and other clinical factors as applicable) that represent the intended patient population under anticipated conditions of use; and

(iii) Include standalone device performance testing that demonstrates the accuracy of the device output relative to ground truth in the intended patient population and under anticipated conditions of use, including the following:

(A) Testing must demonstrate at least 90% sensitivity of the device output for lesions with high metastatic potential, or an alternative clinical consideration must be provided to justify lower sensitivity. Clinical justification must be provided to support the reported specificity.

(B) Lesions must be selected by representative users (e.g., dermatologists) and a justification must be provided for the quantity and range of mimic lesions per diagnosis.

(C) Justification must be provided to support the determination of ground truth.

(D) Testing must include a representative range of individuals with different risk factors (including age, body site, skin phototype, and other clinical factors as applicable), and analysis of standalone performance must include subgroup analysis by relevant risk factors.

(2) Data obtained from post-market surveillance must demonstrate, in consideration of the premarket data obtained in accordance with paragraph (b)(1) of this section, that the device performs in accordance with paragraph (b)(1) of this section, unless FDA determines, based on the totality of the premarket data, that data from post-market surveillance is not required to demonstrate that the device performs as intended. Such post-market surveillance must be

conducted per a protocol determined appropriate by FDA to demonstrate that the device performs as intended (in consideration of the premarket data obtained in accordance with paragraph (b)(1) of this section), and must include initiation, enrollment, and reporting requirements to ensure timely periodic updates to FDA on post-market surveillance progress and outcomes.

(3) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including compatibility testing of the device software with specific signal or image acquisition hardware. Testing must include a description of compatible hardware and processes, pre-specified compatibility testing protocols, and dataset(s).

(4) Performance testing must demonstrate device precision, including repeatability and reproducibility of device performance, across operators and challenging use conditions.

(5) Performance testing must demonstrate electromagnetic compatibility, and electrical, mechanical, and thermal safety of any electrical components of the device.

(6) Performance testing must validate reprocessing instructions for reusable components of the device.

(7) Sterilization validation must be conducted for components that must be sterile. Performance testing must also demonstrate continued sterility and package integrity of components that must be sterile, as well as continued device functionality, over the identified shelf life of the device.

(8) The patient-contacting components of the device must be demonstrated to be biocompatible.

(9) Software verification, validation, and hazard analysis must be performed.

(10) A human factors assessment must demonstrate that the device can be safely used by intended users.

(11) Labeling must include:

(i) A summary of standalone and clinical performance testing conducted with the device. The summary must describe performance measures, including sensitivity and specificity, and statistical confidence intervals, as well as performance of the device for all clinically relevant subgroups within the intended patient population;

(ii) A description of the patient population that was used in development or training of the device algorithm;

(iii) Information related to the limitations of device performance or subpopulations for which the device may not perform as expected or for whom the device has not been validated;

(iv) Information needed to facilitate interpretation of all device outputs, and identification of the risks associated with misinterpretation of the device outputs;

(v) A statement that the device is not intended for use as a standalone diagnostic and is not for use to confirm a clinical diagnosis;

(vi) User qualifications needed for safe use of the device, including a description of user training required prior to use, and a statement that the device is intended to be used by a physician trained in the clinical diagnosis and management of skin cancer (e.g., a dermatologist);

(vii) Warnings to avoid unsafe exposure to any energy-emitting components of the device (e.g., excluding use of the device on lesions close to the eye); and

(viii) Instructions for device maintenance and validated methods and instructions for reprocessing of any reusable components.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2026-05772 Filed: 3/24/2026 8:45 am; Publication Date: 3/25/2026]