4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 862, 866, 876, 880, and 884

[Docket No. FDA-2017-N-1129]

Medical Devices; Exemptions From Premarket Notification: Class II Devices

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is publishing an order to exempt a list of class II devices from premarket notification (510(k)) requirements, subject to certain limitations. This exemption from 510(k), subject to certain limitations, is immediately in effect for the listed class II devices. This exemption will decrease regulatory burdens on the medical device industry and will eliminate private costs and expenditures required to comply with certain Federal regulations. FDA is also amending the codified language for the listed class II devices to reflect this final determination. FDA is publishing this order in accordance with the section of the Federal Food, Drug, and Cosmetic Act (FD&C Act) permitting the exemption of a device from the requirement to submit a 510(k).

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

FOR FURTHER INFORMATION CONTACT: Scott McFarland, Center for Devices and Radiological Health (CDRH), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4676, Silver Spring, MD 20993-0002, 301-796-6217.

SUPPLEMENTARY INFORMATION:

I. Statutory Background

Section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and the implementing regulations, 21 CFR part 807, subpart E, require persons who intend to market a new device to submit and obtain clearance of a premarket notification (510(k)) containing information that allows FDA to determine whether the new device is "substantially equivalent" within the meaning of section 513(i) of the FD&C Act (21 U.S.C. 360c(i)) to a legally marketed device that does not require premarket approval.

On December 13, 2016, the 21st Century Cures Act (Cures Act) (Pub. L. 114-255) was signed into law. Section 3054 of the Cures Act amended section 510(m) of the FD&C Act. As amended, section 510(m)(2) provides that, 1 calendar day after the date of publication of the final list under section 510 (1)(B), FDA may exempt a class II device from the requirement to submit a report under section 510(k) of the FD&C Act, upon its own initiative or a petition of an interested person, if FDA determines that a 510(k) is not necessary to provide reasonable assurance of the safety and effectiveness of the device. This section requires FDA to publish in the *Federal Register* a notice of intent to exempt a device, or of the petition, and provide a 60-calendar-day comment period. Within 120 days of publication of such notice, FDA shall publish an order in the *Federal Register* that sets forth its final determination regarding the exemption of the device that was the subject of the notice.

II. Criteria for Exemption

There are a number of factors FDA may consider to determine whether a 510(k) is necessary to provide reasonable assurance of the safety and effectiveness of a class II device. These factors are discussed in the January 21, 1998, *Federal Register* notice (63 FR 3142) and subsequently in the guidance the Agency issued on February 19, 1998, entitled "Procedures for

Class II Device Exemptions from Premarket Notification, Guidance for Industry and CDRH Staff" ("Class II 510(k) Exemption Guidance"). That guidance can be obtained through the internet at https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080199.pdf or by sending an email request to CDRH-Guidance@fda.hhs.gov to receive a copy of the document. Please use the document number 159 to identify the guidance you are requesting.

Accordingly, FDA generally considers the following factors to determine whether premarket notification is necessary for class II devices: (1) the device does not have a significant history of false or misleading claims or of risks associated with inherent characteristics of the device; (2) characteristics of the device necessary for its safe and effective performance are well established; (3) changes in the device that could affect safety and effectiveness will either (a) be readily detectable by users by visual examination or other means such as routine testing, before causing harm, or (b) not materially increase the risk of injury, incorrect diagnosis, or ineffective treatment; and (4) any changes to the device would not be likely to result in a change in the device's classification. FDA may also consider that, even when exempting devices, these devices would still be subject to the limitations on exemptions.

III. Comments on the Proposed Exemption and FDA Response

In the *Federal Register* of November 7, 2017 (82 FR 51633), FDA published a notice ("November 2017 notice") announcing its intent to exempt, upon its own initiative, certain class II devices listed in table 1 from 510(k) requirements, subject to certain limitations, and provided opportunity for interested persons to submit comments by January 8, 2018. After reviewing comments received, FDA is now providing its final determination on exempting the certain class

II devices listed in table 1 from 510(k) requirements, subject to certain limitations as identified in this order. FDA is also amending the codified language for the classification regulations for the certain class II devices listed in table 1 to reflect this final determination. Persons with pending 510(k) submissions for devices that are now exempt from 510(k), subject to the limitations, should withdraw their submissions.

In response to the November 2017 notice announcing FDA's intent to exempt those device types from 510(k) requirements, FDA received a submission from one commenter--a professional organization--opposing an exemption from 510(k) for the genetic health risk assessment test device type.

To make it easier to identify comments and our responses, the word "Comment" appears in parentheses before the comment's description, and the word "Response" in parentheses precedes the response. Specific issues raised by the comment and the Agency's response follows.

(Comment) The commenter recommended FDA not exempt one-time FDA reviewed genetic health risk assessment system devices from the 510(k) requirement because there would be insufficient oversight to ensure the analytical and clinical validity of these tests, consumers would be misled regarding which tests FDA has affirmed are scientifically valid, and concerns that, if one-time FDA reviewed genetic health risk assessment system devices were exempted, consumers would not be assured of being adequately informed about test quality. The commenter believed it is not possible to assess the analytical and clinical validity of all genetic health risks a company might offer by conducting a one-time review of its 'assessment system', as proposed by FDA. Such oversight, it is argued, will only allow FDA to assess the analytical and clinical validity, and 'mitigate the risks of false negatives and positives', for tests initially

proposed by the company during this one-time review. The commenter believed that it does not appear that there will be assessment of the analytical or clinical validity of subsequent tests offered, nor any assessment of the risks to the consumer of an incorrect result. This commenter believed that FDA's proposal to exempt one-time FDA reviewed genetic health risk assessment system devices will not prevent scientifically invalid tests from being marketed to the public and lacks a comprehensive assessment. Further, the commenter argued that, after undergoing the one-time FDA review for genetic health risk assessment tests, companies would be able to market subsequent tests to the public as part of the same system and declare that the tests meet FDA's standards. Such tests would not be held to any specific standards of analytical or clinical validity. The public would likely assume (and purveyors would likely advertise) that FDA had reviewed and approved such tests as valid even though they had not been reviewed by the Agency. The commenter also argued that there is a vast range of quality (i.e., scientific merit) of direct-to-consumer (DTC) genetic health risk assessment tests on the market. The commenter argued that the market's current mixing of entertainment tests, which make claims unsubstantiated by the scientific literature, with those tests which have a clinical utility, are clinically valid, and can be supported by current scientific literature, is particularly confusing for the average consumer.

(Response) We agree that the concerns raised above are important. These concerns were considered during our review and development of the initial classification regulation for genetic health risk assessment system devices and in our consideration of whether to exempt one-time FDA reviewed genetic health risk assessment system devices from the 510(k) requirement. We believe these concerns have been addressed and accounted for in our determination that the

510(k) requirement is not necessary to provide a reasonable assurance of safety and effectiveness for these devices. We outline our rationale below.

Consumer understanding of genetic risk is clearly an important issue that was considered extensively by FDA in the context of genetic health risk assessment system devices. This issue was balanced with the increasing desire from the public to learn more about one's own genetic makeup and how it affects genetic risk for health conditions. To ensure that the tests and test reports are presented to the lay consumer in a manner that is understandable, we employed several requirements. Consumer understanding of the tests and associated test reports is assured by user comprehension study requirements, specific labeling requirements for these over-the-counter (OTC) tests, and general requirements for devices. The special labeling requirements for these devices under § 866.5950(b) (21 CFR 866.5950(b)) include providing information on the manufacturer's website about frequently asked questions, available professional guidelines, and how to obtain access to a genetic counselor.

A. User Comprehension Study

A user comprehension study is required under § 866.5950(b)(3)(iii)(M). The required user comprehension study must assess comprehension of the test process and results by potential users of the test with pre- and post-test user comprehension studies. This study must be conducted on a statistically sufficient sample size of non-trained individuals who represent the demographics of the United States as well as a diverse range of age and educational levels. The study must include directly evaluating a representative sample of the material being presented to the user during use of the test. The test that is given to the participants must be informed by a physician and/or genetic counselor that identifies the appropriate general and variant-specific concepts contained within the material being tested in the user comprehension study to ensure

that all relevant concepts are incorporated in the study as well as having included the definition of the target condition being tested and related symptoms, explain the intended use and limitations of the test, explain the relevant ethnicities in regard to the variant tested, explain genetic health risks and relevance to the user's ethnicity, and assess participants' ability to understand the following comprehension concepts: the test's limitations, purpose, appropriate action, test results, and other factors that may have an impact on the test results. The outcome of this study has to meet rigorous standards, including meeting predefined primary endpoint criteria, including a minimum of a 90 percent or greater overall comprehension rate (i.e., selection of the correct answer) for each comprehension concept. In addition, the testing must follow a format where users have limited time to complete the studies (such as an onsite survey format and a one-time visit with a cap on the maximum amount of time that a participant has to complete the tests). From our experience with user comprehension studies, the Agency believes that meeting or exceeding these user comprehension study requirements ensures that the materials presented to the user are adequate for OTC use. The information the test provider must provide on its website includes a summary table of comprehension rates regarding comprehension concepts (e.g., purpose of test, test results, test limitations, ethnicity relevance for the test results, etc.) for each study report.

B. Frequently Asked Questions

The manufacturer's website must have a frequently asked questions section in the summary and technical information sections under § 866.5950(b)(3)(ii)(C)(*3*) and (b)(3)(iii)(L)(*3*). For the frequently asked questions sections, information must be included that is specific for each variant/disease pair that is reported and scientifically valid and supported by corresponding publications. Further information must be included that explains the health

condition/disease being tested, the purpose of the test, the information the test will and will not provide, the relevance of race and ethnicity on the test results, information about the population to which the variants in the test is most applicable, the meaning of the result(s), other risks factors that contribute to disease, appropriate followup procedures, how the results of the test may affect the user's family, including children, and links to resources that provide additional information.

C. Resources

Likely the test labeling information provided by the test manufacturer will not be the sole source of information that the consumer is seeking or even requires. For this reason, there are requirements under § 866.5950(b)(3)(ii)(C)(*2*) and (b)(3)(iii)(L)(*2*) that the manufacturer of the test provide a pre-purchase page in the summary and technical information sections that includes information regarding professional guidelines for testing specific genes and variants. Similar information must be provided in the frequently asked questions section found in the summary and technical information sections on the manufacturer's website, under § 866.5950(b)(3)(ii)(C)(*3*) and (b)(3)(iii)(L)(*3*). These frequently asked questions sections must include a statement about the current professional guidelines for testing these specific gene(s) and variant(s) and, if guidelines do not exist for certain genes or variants being tested for, then this information must be provided as well. Further, to facilitate more personalized support, under § 866.5950(b)(1)(i)(E), test manufacturers are required to provide information in the § 809.10 (21 CFR 809.10) compliant labeling and any pre-purchase page and test report generated regarding how a user obtains access to a genetic counselor, board-certified clinical molecular geneticist, or equivalent healthcare professional regarding the results of a user's test.

D. Genetic Health Risk Assessment System Tests

The tests that fall under the genetic health risk assessment system regulation are identified in the regulation in § 866.5950(a) as a qualitative in vitro molecular diagnostic system used for detecting variants in genomic deoxyribonucleic acid (DNA) isolated from human specimens that will provide information to users about their genetic risk of developing a disease to inform lifestyle choices and/or conversations with a healthcare professional. This assessment system is for OTC use. This device does not determine the person's overall risk of developing a disease.

The limitations that are most important for lay users to know about the intended use of these tests that fall under this device type are conveyed via the limiting statements required, under § 866.5950(b)(1)(i), to be provided on the § 809.10 compliant labeling and any pre-purchase page and test report generated. One of these limiting statements must explain that this test is not intended to diagnose a disease, tell you anything about your current state of health, or be used to make medical decisions, including whether or not you should take a medication or how much of a medication you should take. The limitations that are most important for healthcare professionals to know about the intended use of tests that fall under this device type are, under § 866.5950(b)(1)(ii), required to be provided in the § 809.10 labeling and any test report generated. These limitations include that the test is intended to provide users with their genetic information to inform lifestyle decisions and conversations with their doctor or other healthcare professional and that any diagnostic or treatment decisions should be based on testing and/or other information that a healthcare professional determines to be appropriate for a patient.

E. Rigorous Validation Requirements

FDA believes the analytical validation requirements are sufficiently detailed in the special controls under § 866.5950(b)(3)(iii)(J) that test providers will have no difficulty in

appropriately following these requirements. A high accuracy requirement is necessary for tests that are provided under this regulation and accuracy point estimates for all variants is required to be 99 percent or higher under § 866.5950(b)(3)(iii)(J)(*1*)(*vii*) or else they cannot be claimed or reported. Once FDA has reviewed one test that demonstrates this level of accuracy, then the test provider has demonstrated an ability to meet the accuracy requirements for additional similar tests offered.

F. Four Important Limitations on the Scope of the Classification Regulation

FDA agrees that there are four important express limitations to the types of tests that can be offered under this classification regulation even when these special controls are met. Tests cannot be offered under this classification regulation that are indicated for prenatal testing; predisposition for cancer where the result of the test may lead to prophylactic screening, confirmatory procedures, or treatments that may incur morbidity or mortality to the patient; assessing the presence of genetic variants that impact the metabolism, exposure, response, risk of adverse events, dosing, or mechanisms of prescription or OTC medications; or assessing the presence of deterministic autosomal dominant variants.

G. False or Misleading Claims

It is a prohibited act for devices to have labeling that is false or misleading in any particular manner, and thus FDA would deem such device to be misbranded under section 502(a) of the FD&C Act (21 U.S.C. 352(a)). This prohibition would include prohibiting the manufacturer of a genetic health risk assessment test device from falsely or misleadingly representing a test as having been part of an original FDA cleared device when it was added subsequently to FDA clearance. This prohibition would also include falsely or misleadingly representing the analytical or clinical validity of one of its tests. In addition, under section

502(c) of the FD&C Act, it is a prohibited act and thus FDA would deem a device to be misbranded if any information required on the labeling of a device by FDA by or under the FD&C Act is not placed prominently thereon with such conspicuousness and in such terms, as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use. Thus, a genetic health risk assessment test device for which a manufacturer later modified the formerly compliant labeling to make the labeling such that the labeling was not likely to be read and understood by the ordinary individual under customary conditions of purchase and use would be a misbranded device.

H. Conclusion

In summary, all tests that are marketed under this classification regulation must meet the general controls and the special controls that are specified in the regulation. Ability of a manufacturer to meet these special controls is demonstrated during the one-time review. Even after the one-time review, the general controls and special controls must continue to be met, including for all tests added or modified after the one-time review of a manufacturer's device.

IV. Limitations on Exemptions

FDA has determined that 510(k) is not necessary to assure the safety and effectiveness of the class II devices listed in table 1. This determination is based, in part, on the Agency's knowledge of the device, including past experience and relevant reports or studies on device performance (as appropriate), the applicability of general and special controls, and the Agency's ability to limit an exemption.

A. General Limitations of Exemptions

FDA's exemption from 510(k) for class II devices listed in table 1 applies only to those devices that have existing or reasonably foreseeable characteristics of commercially distributed

devices within that generic type, or, in the case of in vitro diagnostic devices, for which a misdiagnosis, as a result of using the device, would not be associated with high morbidity or mortality. A manufacturer of a listed device is still required to submit a 510(k) to FDA before introducing a device or delivering it for introduction into commercial distribution when the device meets any of the conditions described in §§ 862.9 to 892.9 (21 CFR 862.9 to 21 CFR 892.9).

B. Partial Limitations of Exemptions

In addition to the general limitations, FDA may also partially limit an exemption from 510(k) requirements to specific devices within a listed device type when initial Agency assessment determines that the factors laid out in the Class II 510(k) Exemption Guidance do not weigh in favor of exemption for all devices in a particular group. In such situations where a partial exemption limitation has been identified, FDA has determined that premarket notification is necessary to provide a reasonable assurance of safety and effectiveness for these devices. In table 1, for example, FDA is listing the exemption of the genetic health risk assessment system, but limits the exemption to such devices that have received a first-time FDA marketing authorization (e.g., 510(k) clearance) for the genetic health risk assessment system (a "one-time FDA reviewed genetic health risk assessment system"). FDA has determined that a one-time FDA review (e.g., premarket notification) of a genetic health risk assessment system is necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined that a one-time FDA review of a genetic health risk assessment system is necessary to mitigate the risk of false negatives and false positives by ensuring that certain information be submitted to FDA to allow the Agency to assess the safety and effectiveness of the devices as well as to ensure the devices perform to acceptable standards.

Exemption from the requirement of 510(k) does not exempt a device from other applicable regulatory controls under the FD&C Act, including the applicable general and special controls. This exemption from 510(k), subject to the limitations described above, is immediately in effect for the device types identified in table 1. This exemption will decrease regulatory burdens on the medical device industry and will eliminate private costs and expenditures required to comply with Federal regulations.

V. List of Class II Devices

FDA is identifying the following list of class II devices that will no longer require premarket notification under section 510(k) of the FD&C Act, subject to the general limitations to the exemptions found in §§ 862.9 to 892.9 and any partial exemption limitations identified in table 1:

Table 1.--Class II Devices

21 CFR Section	Device Type	Product Code	Partial Exemption Limitation (if applicable)
862.1840	Total 25-hydroxyvitamin D Mass Spectrometry Test System	PSL	
866.5950	Genetic Health Risk Assessment System	PTA	Exemption is limited to a genetic health risk assessment system that has received a first-time FDA marketing authorization (e.g., 510(k) clearance) for the genetic health risk assessment system (a "one-time FDA reviewed genetic health risk assessment system").
876.1500	Endoscope Disinfectant Basin	PUP	
880.6710	Purifier, Water, Ultraviolet, Medical	KMG	
884.5960	Vibrator for Therapeutic Use, Genital	KXQ	

FDA is revising the name of product code PUP to further clarify the device type that this product code is intended to represent. The device type was previously "Endoscope Maintenance System." To more accurately reflect the devices which fall within this device type (product code PUP), the device type has been renamed "Endoscope Disinfectant Basin." Specifically, these devices are described as "Wall-mounted tube(s) for holding disinfectant solution and endoscope

insertion tubes and accessories." This description has not changed since publication of the November 2017 notice.

VI. Analysis of Environmental Impact

The Agency has determined under 21 CFR 25.30(h) 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.

VII. Paperwork Reduction Act of 1995

This final order refers to previously approved collections of information found in other FDA regulations and guidance. These 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. 3501-3520). The collections of information in part 807, subpart E, regarding premarket notification submissions, have been approved under OMB control number 0910-0120; and the collections of information in 21 CFR parts 801 and 809, regarding labeling, have been approved under OMB control number 0910-0485.

List of Subjects

21 CFR Part 862

Medical devices.

21 CFR Part 866

Biologics, Laboratories, Medical devices.

21 CFR Parts 876, 880, and 884

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 862, 866, 876, 880, and 884 are amended as follows:

PART 862--CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES

1. The authority citation for part 862 continues to read as follows:

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

2. In § 862.1840, revise paragraph (b) introductory text to read as follows:

§ 862.1840 Total 25-hydroxyvitamin D mass spectrometry test system.

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(b) *Classification*. Class II (special controls). The device is exempt from the premarket notification procedures in part 807, subpart E, of this chapter subject to the limitations in § 862.9. The device must comply with the following special controls:

* * * * *

PART 866--IMMUNOLOGY AND MICROBIOLOGY DEVICES

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

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

4. In § 866.5950, revise paragraph (b) introductory text to read as follows:

§ 866.5950 Genetic health risk assessment system.

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(b) *Classification*. Class II (special controls). The genetic health risk assessment system device, when it has previously received a first-time FDA marketing authorization (e.g., 510(k) clearance) for the genetic health risk assessment system (a "one-time FDA reviewed genetic health risk assessment system"), is exempt from the premarket notification procedures in part

807, subpart E, of this chapter subject to the limitations in § 866.9. The device must comply with the following special controls:

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PART 876--GASTROENTEROLOGY-UROLOGY DEVICES

5. The authority citation for part 876 continues to read as follows:

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

6. In § 876.1500, revise paragraph (b)(1) to read as follows:

§ 876.1500 Endoscope and accessories.

* * * * *

(b) * * *

(1) Class II (performance standards). The device, when intended as an endoscope disinfectant basin, which consists solely of a container that holds disinfectant and endoscopes and accessories, is exempt from the premarket notification procedures in part 807, subpart E, of this chapter subject to the limitations in § 876.9.

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PART 880--GENERAL HOSPITAL AND PERSONAL USE DEVICES

7. The authority citation for part 880 continues to read as follows:

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

8. In § 880.6710, revise paragraph (b) to read as follows:

§ 880.6710 Medical ultraviolet water purifier.

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(b) *Classification*. Class II (performance standards). The device is exempt from the premarket notification procedures in part 807, subpart E, of this chapter subject to the limitations in § 880.9.

PART 884--OBSTETRICAL AND GYNECOLOGICAL DEVICES

9. The authority citation for part 884 continues to read as follows:

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

10. In § 884.5960, revise paragraph (b) to read as follows:

§ 884.5960 Genital vibrator for therapeutic use.

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(b) *Classification*. Class II (performance standards). The device is exempt from the premarket notification procedures in part 807, subpart E, of this chapter subject to the limitations in § 884.9.

Dated: May 29, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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