



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
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May 18, 2017

AB SCIEX LLC  
% SHILPA SHARMA  
REGULATORY AFFAIRS ASSOCIATE  
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FRAMINGHAM, MA 01701 USA

Re: DEN170019  
Vitamin D 200M Assay for the Topaz System  
Evaluation of Automatic Class III Designation – *De Novo* Request  
Regulation Number: 21 CFR 862.1840  
Regulation Name: Total 25-hydroxyvitamin D Mass Spectrometry Test System  
Regulatory Classification: Class II  
Product Code: PSL  
Dated: March 17, 2017  
Received: March 20, 2017

Dear Shilpa Sharma:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your *de novo* request for classification of the Vitamin D 200M Assay for the Topaz System, a prescription device. The Vitamin D 200M Assay for the Topaz System is indicated for use as follows:

The Vitamin D 200M Assay for the Topaz System is intended for in vitro diagnostic use in the quantitative determination of total 25-hydroxyvitamin D (25-OH-D) through the measurement of 25-hydroxyvitamin D3 (25-OH-D3) and 25-hydroxyvitamin D2 (25-OH-D2) in human serum using LC-MS/MS technology by a trained laboratory professional in a clinical laboratory. The Assay is intended for use with the Topaz System. The Vitamin D 200M Assay for the Topaz System is intended to be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions in an adult population in the assessment of vitamin D sufficiency.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Vitamin D 200M Assay for the Topaz System, and substantially equivalent devices of this generic type, into class II under the generic name, “Total 25-hydroxyvitamin D Mass Spectrometry Test System.”

FDA identifies this generic type of device as: **Total 25-hydroxyvitamin D Mass Spectrometry Test System.**

A total 25-hydroxyvitamin D mass spectrometry test system is a device intended for use in clinical laboratories for the quantitative determination of total 25-hydroxyvitamin D (25-OH-D) in serum or plasma to be used in the assessment of vitamin D sufficiency.

Section 513(f)(2) of the Food, Drug & Cosmetic Act (FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This new law provides two options for *de novo* classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the FD&C Act may, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the FD&C Act. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the FD&C Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register classifying the device type.

On March 20, 2017, FDA received your *de novo* requesting classification of the Vitamin D 200M Assay for the Topaz System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Vitamin D 200M Assay for the Topaz System into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the *de novo* request, FDA has determined that the Vitamin D 200M Assay for the Topaz System indicated for use as follows:

The Vitamin D 200M Assay for the Topaz System is intended for *in vitro* diagnostic use in the quantitative determination of total 25-hydroxyvitamin D (25-OH-D) through the measurement of 25-hydroxyvitamin D3 (25-OH-D3) and 25-hydroxyvitamin D2 (25-OH-D2) in human serum using LC-MS/MS technology by a trained laboratory professional in a clinical laboratory. The Assay is intended for use with the Topaz System. The Vitamin D 200M Assay for the Topaz System is intended to be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions in an adult population in the assessment of vitamin D sufficiency.

can be classified in class II with the establishment of special controls for this type of device. FDA believes that the class II special controls identified later in this order, along with applicable general controls, including the design controls under 21 CFR part 820, provide reasonable assurance of the safety and effectiveness of the device type. The identified risks to health and identified mitigations associated with the device type are summarized in Table 1.

**Table 1 – Identified Risks to Health and Identified Mitigations**

<b>Identified Risks to Health</b>	<b>Identified Mitigations</b>
Clinical action based on falsely elevated inaccurate Vitamin D results may lead to unnecessary supplementation of Vitamin D	General controls and special controls (1) and (2)
Clinical action based on falsely low inaccurate Vitamin D results may lead to a delay in supplementation of Vitamin D	General controls and special controls (1) and (2)
Clinical action based on uninterpretable results due to lack of established device specific reference range values for the representative population	General controls and special control (3)
Clinical action based on the misinterpretation of Vitamin D2 or Vitamin D3 results as total Vitamin D results	General controls and special control (4)

In combination with the general controls of the FD&C Act, a Total 25-hydroxyvitamin D Mass Spectrometry Test System is subject to the following special controls:

- (1) The device must have initial and annual standardization verification by a certifying vitamin D standardization organization deemed acceptable by FDA.
- (2) The 21 CFR 809.10(b) compliant labeling must include detailed descriptions of performance testing conducted to evaluate precision, accuracy, linearity, interference, including the following:
  - (i) Performance testing of device precision must, at a minimum, use intended sample type with Vitamin D concentrations at medically relevant decision points. At least one sample in the precision studies must be an unmodified patient sample. This testing must evaluate repeatability and reproducibility using a protocol from an FDA-recognized standard.
  - (ii) Performance testing of device accuracy must include a minimum of 115 serum or plasma samples that span the measuring interval of the device and compare results of the new device to results of a reference method or a legally marketed standardized mass spectrometry based vitamin D assay. The results must be described in the 21 CFR 809.10(b)(12) compliant labeling of the device.
  - (iii) Interference from vitamin D analogs and metabolites including vitamin D2, vitamin D3, 1-hydroxyvitamin D2, 1-hydroxyvitamin D3, 3-Epi-25-Hydroxyvitamin D2, 3-Epi-25-Hydroxyvitamin D3, 1,25-Dihydroxyvitamin D2, 1,25-Dihydroxyvitamin D3, 3-Epi-1,25-Dihydroxyvitamin D2, and 3-Epi-1,25-Dihydroxyvitamin D3, 25, 26-Dihydroxyvitamin-D3, 24 (R), 25-dihydroxyvitamin-D3, 23 (R), 25-dihydroxyvitamin-D3 must be described in the 21 CFR 809.10(b)(7) compliant labeling of the device.

(3) The 21 CFR 809.10(b) compliant labeling must be supported by a reference range study representative of the performance of the device. The study must be conducted using samples collected from apparently healthy male and female adults at least 21 years of age and older from at least 3 distinct climatic regions within the United States of America in different weather seasons. The ethnic, racial, and gender background of this study population must be representative of the US population demographics.

(4) The results of the device as provided in the 21 CFR 809.10(b) compliant labeling and any test report generated must be reported as only total 25-hydroxyvitamin D.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA believes premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, is planning to exempt the device from the premarket notification requirements of the FD&C Act. Accordingly, FDA intends to issue a notice of intent to exempt a Total 25-hydroxyvitamin D Mass Spectrometry Test System under Section 510(m) of the FD&C Act. If there are questions about 510(k) submission prior to finalization of the 510(k) exemption, you should contact FDA at the number provided below. Once finalized, persons who intend to market this device type need not submit a 510(k) premarket notification containing information on the Total 25-hydroxyvitamin D Mass Spectrometry Test System prior to marketing the device.

Please be advised that FDA's decision to grant this *de novo* request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD&C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the **Federal Register**. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the *de novo* request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Matthew Humbard at [matthew.humbard@fda.hhs.gov](mailto:matthew.humbard@fda.hhs.gov) or (240) 402-2155.

Sincerely,

Courtney H. Lias, Ph.D.  
Director  
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