



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

March 28, 2016

Food and Drug Administration  
10903 New Hampshire  
Avenue  
Document Control Center –  
WO66-G609  
Silver Spring, MD 20993-0002

Bio-Rad Laboratories  
Maria Zeballos  
Regulatory Affairs Representative IV, Quality Systems Division  
9500 Jeronimo Road  
Irvine, California 92614

Re: DEN150058  
Amplichek II  
Evaluation of Automatic Class III Designation – *De Novo* Request  
Regulation Number: 21 CFR 866.3920  
Regulation Name: Assayed quality control material for clinical microbiology assays.  
Regulatory Classification: Class II  
Product Code: PMN  
Dated: December 16, 2015  
Received: December 18, 2015

Dear Ms. Zeballos:

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 Amplichek II, a prescription device. The Amplichek II is indicated for use as follows:

Amplichek II is intended for use as an external assayed quality control material to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of Methicillin Resistant *Staphylococcus aureus*, Methicillin Sensitive *Staphylococcus aureus*, *Clostridium difficile* and Vancomycin-resistant *Enterococci* performed on Cepheid GeneXpert Systems. This product is not intended to replace manufacturer controls provided with the device. This product is only for use with assays and instruments listed in the Representative Results Chart in this labeling.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Amplichek II, and substantially equivalent devices of this generic type, into class II under the generic name, “Assayed quality control material for clinical microbiology assays.”

FDA identifies this generic type of device as: Assayed quality control material for clinical microbiology assays.

An assayed quality control material for clinical microbiology is a device indicated for use in a test system to estimate test precision or to detect systematic analytical deviations that may arise from reagent or analytical instrument variation. This type of device consists of single or multiple microbiological analytes intended for use with either qualitative or quantitative

assays.

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 December 18, 2015, FDA received your *de novo* request for classification of the Amplichek II. The petition was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Amplichek II 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 Amplichek II indicated for use as follows

Amplichek II is intended for use as an external assayed quality control material to monitor the performance of *in vitro* laboratory nucleic acid testing procedures for the qualitative detection of Methicillin Resistant *Staphylococcus aureus*, Methicillin Sensitive *Staphylococcus aureus*, *Clostridium difficile* and Vancomycin-resistant *Enterococci* performed on Cepheid GeneXpert Systems. This product is not intended to replace manufacturer controls provided with the device. This product is only for use with assays and instruments listed in the Representative Results Chart in this labeling.

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 the applicable general controls, including the design controls under 21 CFR part 820, provide reasonable assurance of the safety and effectiveness of the device type.

**Table – Identified Risks and Required Mitigations**

Identified Risks to Health	Required Mitigations
Incorrect use of the instrument for non-indicated samples resulting in a delay in diagnosis	Special Controls (1), (3), and (4)
Assessment performance error (false negative)	Special Control (1)

Incorrect results due improper or unexpected performance	Special Control (2) and (4)(iii)
Failure to correctly operate the instrument	Special Control (1)

In combination with the general controls of the FD&C Act, an assayed quality control material for clinical microbiology assays must comply with the following special controls:

- (1) Premarket notification submissions must include detailed device description documentation and information concerning the composition of the quality control material, including, as appropriate:
  - (i) Analyte concentration;
  - (ii) Expected values;
  - (iii) Analyte source;
  - (iv) Base matrix;
  - (v) Added components;
  - (vi) Safety and handling information; and,
  - (vii) Detailed instructions for use.
- (2) Premarket notification submissions must include detailed documentation, including line data as well as detailed study protocols and a statistical analysis plan used to establish performance, including:
  - (i) Description of the process for value assignment and validation.
  - (ii) Description of the protocol(s) used to establish stability.
  - (iii) Line data establishing precision/reproducibility.
  - (iv) Where applicable, assessment of matrix effects and any significant differences between the quality control material and typical patient samples in terms of conditions known to cause analytical error or affect assay performance.
  - (v) Where applicable, identify or define traceability or relationship to a domestic or international standard reference material and/or method.
  - (vi) Where applicable, detailed documentation related to studies for surrogate controls.
- (3) Premarket notification submissions must include an adequate mitigation (e.g., real-time stability program) to the risk of false results due to potential modifications to the assays specified in the device's 21 CFR 809.10 compliant labeling.
- (4) Your 21 CFR 809.10 compliant labeling must include the following:
  - (i) The intended use in your 21 CFR 809.10(a)(2) and 21 CFR 809.10(b)(2) compliant labeling must include the following:
    - (A) Assayed control material analyte(s);
    - (B) Whether the material is intended for quantitative or qualitative assays;
    - (C) Stating if the material is a surrogate control;
    - (D) The system(s), instrument(s), or test(s) for which the

quality control material is intended.

- (ii) The intended use in your 21 CFR 809.10(a)(2) and 21 CFR 809.10(b)(2) compliant labeling must include the following statement: “This product is not intended to replace manufacturer controls provided with the device.”
- (iii) A limiting statement that reads “Quality control materials should be used in accordance with local, state, federal regulations, and accreditation requirements.”

In addition, this is a prescription device. 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 has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the assayed quality control material for clinical microbiology they intend to market prior to marketing the device and receive clearance to market from FDA.

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 Stephanie Krmeneč at 240-402-4976.

Sincerely yours,

For Uwe Scherf, M.Sc., Ph.D.  
Director  
Division of Microbiology Devices  
Office of *In Vitro* Diagnostics and  
Radiological Health  
Center for Devices and  
Radiological Health