



March 12, 2019

HemoSonics, LLC
Anne Zavertnik
Sr. Director, Regulatory Affairs and Quality Systems
400 Preston Avenue, Suite 250
Charlottesville, Virginia 22903

Re: DEN180017

Trade/Device Name: The Quantra QPlus System
Regulation Number: 21 CFR 864.5430
Regulation Name: Coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients
Regulatory Class: Class II
Product Code: QFR
Dated: March 30, 2018
Received: April 2, 2018

Dear Anne Zavertnik:

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 The Quantra QPlus System, a prescription device with the following indications for use:

The Quantra QPlus System is composed of the Quantra Hemostasis Analyzer, QPlus Cartridge, and Quantra Quality Controls Level 1 and 2. The Quantra QPlus System is intended for in vitro diagnostic use.

The Quantra Hemostasis Analyzer uses Sonic Estimation of Elasticity via Resonance (SEER) Sonorheometry, an ultrasound-based technology, to measure the shear modulus of whole blood during coagulation. The QPlus Cartridge is a multi-channel cartridge that provides semi-quantitative indications of the coagulation state of a 3.2% citrated venous whole blood sample. The QPlus Cartridge includes tests to assess coagulation characteristics via the intrinsic pathway, via the extrinsic pathway, and includes tests with a heparin neutralizer.

The system is intended to be used by trained professionals at the point-of-care and in clinical laboratories to evaluate the viscoelastic properties of whole blood by means of the following functional parameters: Clot Time (CT), Clot Time with Heparinase (CTH), Clot Stiffness (CS), Fibrinogen Contribution to Clot Stiffness (FCS), Platelet Contribution to Clot Stiffness (PCS) and Clot Time Ratio (CTR).

The Quantra QPlus System is indicated for the evaluation of blood coagulation in perioperative patients age 18 years and older to assess possible hypocoagulable and hypercoagulable conditions in cardiovascular or major orthopedic surgeries before, during, and following the procedure.

Results obtained with the Quantra QPlus System should not be the sole basis for patient diagnosis.

For prescription use only.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov. FDA concludes that this device should be classified into Class II. This order, therefore, classifies the The Quantra QPlus System, and substantially equivalent devices of this generic type, into Class II under the generic name Coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients.

FDA identifies this generic type of device as:

Coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients. A coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients is an in vitro diagnostic device used to evaluate blood coagulation, fibrinolysis, or both, in perioperative patients, as an aid in the assessment of coagulopathies when used in conjunction with clinical signs and symptoms and other clinical and laboratory findings.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This 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 Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. 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 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 announcing the classification.

On April 2, 2018, FDA received your De Novo requesting classification of the The Quantra QPlus System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the The Quantra QPlus 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, for the previously stated indications for use, the Quantra QPlus System can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Identified Risks to Health	Identified Mitigations
Incorrect test results	Transparent device performance descriptions in labeling Transparent device limitations descriptions in labeling Certain precision, performance, interference, and specimen stability testing
Incorrect interpretation of test results	Transparent device performance descriptions in labeling Transparent device limitations descriptions in labeling Certain precision, performance, interference, specimen stability, and human factors testing
Cartridge malfunction	Transparent device performance descriptions in labeling Transparent device limitations descriptions in labeling Certain precision, performance, interference, and specimen stability testing

In combination with the general controls of the FD&C Act, the Coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients must comply with the following special controls:

- (1) Design verification and validation must include detailed documentation of, and results from, the following:
 - i. A study assessing precision using protocols determined to be acceptable by FDA, to cover the measurement range for each reported parameter (test output). Testing must include native specimens with coagulation profiles representative of the intended use population. In order to cover the measuring range, testing may include a limited number of contrived specimens, not to exceed 10–20%, or as otherwise deemed appropriate by FDA. The contrived specimens must be prepared to resemble clinical specimens. This testing must evaluate repeatability and reproducibility and provide assessments of within-run, within-day, between-run, between-day, between-reagent lot, between-instrument, between-site, and between-operator precision, as applicable to the system;
 - ii. Studies that demonstrate the performance of each parameter (test output) throughout the claimed measurement range, to include linearity studies or dose-response studies, as applicable to the parameter (test output);

- iii. Potential interferent study that includes evaluation of hemolyzed and lipemic samples as potential interferents; exogenous and endogenous interferents associated with each patient population intended for use with the device, and which might be expected to affect assay performance, must be evaluated; and potential interferents that are specific for, or related to, the technology or methodology of the device. Evaluation of all potential interferents must be performed using a protocol determined to be acceptable to the FDA (e.g., an FDA-recognized standard) and include both normal and abnormal specimens covering coagulation profiles representative of the intended use population;
- iv. A study that evaluates specimen stability under the intended conditions for specimen collection, handling, and storage, using samples that cover the coagulation profiles representative of the intended use population, and using protocols determined to be acceptable by FDA;
- v. A multi-site clinical study, determined to be acceptable by FDA, demonstrating performance, relative to clinically relevant and clinically validated laboratory test(s) for each parameter (test output). Further, the study must meet all of the following criteria:
 - A. The study must be performed in the intended use population and include representation from all patient populations for whom the device is intended to be used. Potential endogenous and exogenous interferents for each target patient population must be evaluated or known prior to the study;
 - B. The study must be conducted at a minimum of three external sites representative of the intended use setting by the intended operators;
 - C. Test samples must be collected at time intervals relevant to the device's use in the intended use population;
 - D. Clinical specimens, which cover coagulation profiles representative of the intended use population, must be evaluated at each of the three clinical sites in the study;
 - E. Analysis of the concordance of clinical interpretation of patient coagulation status made from individual test parameter (test output) results as compared to clinical interpretation of coagulation status from a clinically relevant laboratory test or tests (e.g., a comparative viscoelastic device or standard laboratory tests) must be conducted; and
 - F. Expected (reference) values for each parameter (test output) must be demonstrated by testing a statistically appropriate number of samples from apparently healthy normal individuals.
- vi. For a device with a user interface that has information that needs to be interpreted by the user in correctly using the device to achieve the intended test results or a device that does not provide a final output that is a comprehensive interpretation of all parameter (test output) results, a study evaluating the ability of device users to correctly interpret results;

- vii. For any device indicated to guide blood product use, a clinical outcome study determined to be acceptable by FDA that specifically validates the device's indicated use in guiding blood product use; and
- viii. For any device indicated to guide use of medication, a clinical outcome study determined to be acceptable by FDA that specifically validates the device's indicated use in guiding use of medication.

(2) The labeling required under 21 CFR 809.10(b) must include the following:

- i. A summary of results from the study required by paragraph (b)(1)(i), including repeatability, reproducibility, and assessments of within-run, within-day, between-run, between-day, between-reagent lot, between-instrument, between-site, and between-operator precision, as applicable to the system.
- ii. The claimed measurement range of each parameter (test output), as supported by demonstrated performance of the parameter (test output) throughout the claimed measurement range, including, but not limited to, studies required by paragraphs (b)(1)(i), (b)(1)(ii), (b)(1)(iii), (b)(1)(v), and, if applicable, (b)(1)(vii) and (b)(1)(viii).
- iii. Identification of known interferents, including all endogenous, exogenous, technology-specific, and patient population-specific interferents, specific to each parameter (test output). The information must include the concentration(s) or level(s) at which interference was found to occur and the concentration range or levels at which interference was not found to occur.
- iv. Information regarding the multisite clinical study required by paragraph (b)(1)(v), including:
 - a. Each patient population evaluated;
 - b. Each intended use setting and the operators;
 - c. A summary of the results, including the concordance analysis to clinically relevant laboratory test(s); and
 - d. Demonstrated expected (reference) values for each parameter (test output).

(3) The labeling required under 21 CFR 809.10 must include:

- i. A limiting statement that the result(s) from the device is(are) not intended to be used as the sole basis for a patient diagnosis.
- ii. Unless appropriate clinical outcome studies are done in accordance with (b)(1)(vii) that specifically validate an indication for the device's use in guiding blood product use, a limiting statement that the device has not been evaluated to guide blood product use.

- iii. Unless appropriate clinical outcome studies are done in accordance with (b)(1)(viii) that specifically validate an indication for the device's use in guiding use of medication, a limiting statement that the device has not been evaluated to guide use of medication.

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 Coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients they intend to market 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; 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.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/>) and CDRH Learn (<http://www.fda.gov/Training/CDRHLearn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<http://www.fda.gov/DICE>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Natasha Thorne at 240-402-0475.

Sincerely,

Lea Carrington
Director
Division of Immunology
and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health