



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

August 20, 2014

KRONUS Market Development Associates, INC.
C/O Tanis Jimenez
Quality Control and Regulatory Compliance Manager
170 S. Seneca Springs Way, Suite 105
Star, ID 83669

Re: DEN140001
KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 866.5670
Regulation Name: Zinc Transporter 8 Autoantibody immunological test system
Regulatory Classification: Class II
Product Code: PHF
Dated: June 13, 2014
Received: June 16, 2014

Dear Ms. Jimenez:

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 KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay, a prescription device under 21 CFR Part 801.109. The intended use of the KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay is

The KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay is for the semi-quantitative determination of autoantibodies to Zinc Transporter 8 (ZnT8) in human serum. The KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay may be useful as an aid in the diagnosis of Type 1 diabetes mellitus (autoimmune mediated diabetes). The ZnT8Ab assay is not to be used alone and is to be used in conjunction with other clinical and laboratory findings.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay, and substantially equivalent devices of this generic type, into class II under the generic name, “Zinc Transporter 8 Autoantibody immunological test system.”

FDA identifies this generic type of device as: Zinc Transporter 8 Autoantibody immunological test system.

A Zinc Transporter 8 Autoantibody immunological test system is a device that consists of reagents used to measure, by immunochemical techniques, the autoantibodies in human serum samples that

react with Zinc Transporter 8 (ZnT8). The measurements aid in the diagnosis of Type 1 diabetes mellitus (autoimmune mediated diabetes) in conjunction with other clinical and laboratory findings.

Section 513(f)(2) of 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 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 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 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 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.

In accordance with section 513(f)(1) of the FD&C Act, FDA issued an order on May 21, 2014 automatically classifying the KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay into class III, because it was not within a type of device which was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, nor which was subsequently reclassified into class I or II. On June 16, 2014, FDA filed your *de novo* request for classification of the KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay into class II. The petition was submitted under section 513(f)(2) of the FD&C Act. In order to classify the KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay 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 KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay intended for use as follows

The KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay is for the semi-quantitative determination of autoantibodies to Zinc Transporter 8 (ZnT8) in human serum. The KRONUS Zinc Transporter 8 Autoantibody (ZnT8Ab) ELISA Assay may be useful as an aid in the diagnosis of Type 1 diabetes mellitus (autoimmune mediated diabetes). The ZnT8Ab assay is not to be used alone and is to be used in conjunction with other clinical and laboratory findings.

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, provide reasonable assurance of the safety and effectiveness of the device type.

Table – Identified Risks and Required Mitigations

Identified Risks	Required Mitigations
Inaccurate test results that provide false positive or false negative results can lead to improper patient management.	Special controls (1), (2), and (3)
Failure to correctly interpret test results can lead to false positive or false negative results.	Special controls (1) (iii), (2), and (3)

In combination with the general controls of the FD&C Act, the Zinc Transporter 8 Autoantibody immunological test system is subject to the following special controls:

- 1) Premarket notification submissions must include the following information:
 - i.* A detailed description of the device that includes:
 - A) A detailed description of all components in the test system, including a description of the assay components in the kit and all required ancillary reagents.
 - B) A detailed description of instrumentation and equipment, and illustrations or photographs of non-standard equipment or methods if applicable.
 - C) Detailed documentation of the device software, including, but not limited to, standalone software applications and hardware-based devices that incorporate software where applicable.
 - D) A detailed description of appropriate internal and external quality controls that are recommended or provided. The description must identify those control elements that are incorporated into the recommended testing procedures.
 - E) Detailed specifications for sample collection, processing and storage.
 - F) A detailed description of methodology and assay procedure.
 - G) Detailed specification of the criteria for test results interpretation and reporting.
 - ii.* Information that demonstrates the performance characteristics of the device, including:
 - A) Device precision/reproducibility data generated from within-run, between-run, between-day, between-lot, between-operator, between-instruments, between-site, and total precision for multiple nonconsecutive days as applicable. A well characterized panel of patient samples or pools from the intended use population that covers the device measuring range must be used.
 - B) Device linearity data generated from patient samples covering the assay measuring range if applicable.
 - C) Information on traceability to a reference material and description of value assignment of calibrators and controls if applicable.
 - D) Device analytical sensitivity data, including limit of blank, limit of

- detection and limit of quantitation if applicable.
- E)* Device analytical specificity data, including interference by endogenous and exogenous substances, as well as cross-reactivity with samples derived from patients with other autoimmune diseases or conditions.
 - F)* Device instrument carryover data when applicable.
 - G)* Device stability data including real-time stability under various storage times and temperatures.
 - H)* Specimen stability data, including stability under various storage times, temperatures, freeze-thaw and transport conditions where appropriate.
 - I)* Method comparison data generated by comparison of the results obtained with the device to those obtained with a legally marketed predicate device with similar indication of use. Patient samples from the intended use population covering the device measuring range must be used.
 - J)* Specimen matrix comparison data if more than one specimen type or anticoagulant can be tested with the device. Samples used for comparison must be from patient samples covering the device measuring range.
 - K)* A description of how the assay cut-off (the medical decision point between positive and negative) was established and validated as well as supporting data.
 - L)* Clinical performance must be established by comparing data generated by testing samples from the intended use population and the differential diagnosis groups with the device to the clinical diagnostic standard. The diagnosis of Type 1 diabetes mellitus must be based on clinical history, physical examination, and laboratory tests, such as one or more pancreatic or insulin autoantibody test. Because the intended use population for Type 1 diabetes mellitus includes subjects less than 18 years old, samples from representative numbers of these subjects must be included. Representative numbers of samples from all age strata must be also be included. The differential diagnosis groups must include, but not be limited to the following: Type 2 diabetes mellitus; metabolic syndrome; latent autoimmune diabetes in adults; other autoimmune diseases such as celiac disease (without a concomitant diagnosis of Type 1 diabetes mellitus), systemic lupus erythematosus, rheumatoid arthritis, and Hashimoto's thyroiditis; infection; renal disease; and testicular cancer. Diseases for the differential groups must be based on established diagnostic criteria and clinical evaluation. For all samples, the diagnostic clinical criteria and the demographic information must be collected and provided. The clinical validation results must demonstrate clinical sensitivity and clinical specificity for the test values based on the presence or absence of Type 1 diabetes mellitus. The data must be summarized in tabular format comparing

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 Therese Datiles at 301-796-6166.

Sincerely yours,

Maria M. Chan -S

Maria M. Chan, Ph.D.

Director

Division of Immunology and Hematology Devices

Office of *In Vitro* Diagnostics and

Radiological Health

Center for Devices and Radiological Health