



Food and Drug Administration  
10903 New Hampshire Avenue  
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Silver Spring, MD 20993-0002

May 23, 2013

Roche Diagnostics Corporation  
c/o Ms. Susan Hollandbeck  
Regulatory Affairs Consultant  
9115 Hague Road  
Indianapolis, IN 46256

Re: K121291- Order for Granting the Request for De Novo Classification  
COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay  
Evaluation of Automatic Class III Designation-*De Novo* Request  
Regulation Number: 21 CFR 862.1373  
Regulation Name: Hemoglobin A1c Test System  
Regulatory Classification: Class II  
Product Code: PDJ  
Dated: March 22, 2013  
Received: March 29, 2013

Dear Ms. Hollandbeck:

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 COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay. The assay is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. It is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche COBAS INTEGRA 800 clinical chemistry analyzer. The COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay is a prescription device under 21 CFR Part 801.109. FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay into class II under the generic name, "Hemoglobin A1c test system."

FDA identifies this generic type of device as follows: Hemoglobin A1c test system

A hemoglobin A1c test system is a device used to measure the percentage concentration of hemoglobin A1c in blood. Measurement of hemoglobin A1c is used as an aid in the diagnosis of diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus.

Section 513(f)(2) of the FD&C Act provides that any person who submits a premarket notification under section 510(k) for a type of device that has not been previously classified may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1), request FDA to classify the device under the criteria set forth in section 513(a)(1). FDA shall by order classify the device, which shall be the initial classification of the device type. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

In accordance with section 513(f)(1) and 513(i) of the FD&C Act, FDA issued an order on March 14, 2013, finding the COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay not substantially equivalent to any device within a type that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or that was subsequently reclassified into class I or class II, which means this device is automatically in class III under section 513(f)(1). On March 29, 2013, FDA filed your de novo request for classification of the COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay into class II. The petition was submitted under section 513(f)(2) of the FD&C Act. In order to classify the COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 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 COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay indicated as follows:

The test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. It is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche COBAS INTEGRA 800 clinical chemistry analyzer.

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- Potential Risks and Required Mitigations

Identified Potential Risk	Mitigation Measure
False negative or false positive test results due to inadequate device performance.	<ul style="list-style-type: none"><li>• The device must have initial and annual standardization verification by a certifying glycohemoglobin standardization organization deemed acceptable by FDA.</li><li>• The premarket notification submission must include performance testing to evaluate precision, accuracy, linearity and interference, including the following:<ul style="list-style-type: none"><li>○ Performance testing of device precision must, at a minimum, use blood samples with concentrations near 5.0%, 6.5%, 8.0% and 12% hemoglobin A1c. This testing must evaluate precision over a minimum of 20 days using at least 3 lots of the device and 3 instruments, as applicable.</li><li>○ Performance testing of device accuracy must include a minimum of 120 blood samples that span the measuring interval of the device and compare results of the new device to results of a standardized test method. Results must demonstrate little or no bias versus the standardized method.</li><li>○ Total error of the new device must be evaluated using single measurements by the new device compared to results of the standardized test method, and this evaluation must demonstrate a total error less than or equal to 6%.</li><li>○ Performance testing must demonstrate that there is little to no interference from common hemoglobin variants, including Hemoglobin C, Hemoglobin D, Hemoglobin E, Hemoglobin A2 and Hemoglobin S.</li></ul></li></ul>
Use of the test for patients with hemoglobin variants that may interfere with the test system, and lead to incorrect results.	<ul style="list-style-type: none"><li>• When assay interference from Hemoglobin F or interference with other hemoglobin variants with low frequency in the population is observed, a warning statement must be placed in a black box and must appear in all labeling material for these devices describing the interference and any affected populations.</li></ul>

In addition to the general controls of the FD&C Act, a hemoglobin A1c test system is subject to the following special controls:

- 1) The device must have initial and annual standardization verification by a certifying glycohemoglobin standardization organization deemed acceptable by FDA.
- 2) The premarket notification submission must include performance testing to evaluate precision, accuracy, linearity and interference, including the following:
  - i) Performance testing of device precision must, at a minimum, use blood samples with concentrations near 5.0%, 6.5%, 8.0% and 12% hemoglobin A1c. This testing must evaluate precision over a minimum of 20 days using at least 3 lots of the device and 3 instruments, as applicable.
  - ii) Performance testing of device accuracy must include a minimum of 120 blood samples that span the measuring interval of the new device and compare results of the new device to results of the standardized test method. Results must demonstrate little or no bias versus the standardized method.
  - iii) Total error of the new device must be evaluated using single measurements by the new device compared to results of the standardized test method, and this evaluation must demonstrate a total error less than or equal to 6%.
  - iv) Performance testing must demonstrate that there is little to no interference from common hemoglobin variants, including Hemoglobin C, Hemoglobin D, Hemoglobin E, Hemoglobin A2 and Hemoglobin S.
- 3) When assay interference from Hemoglobin F or interference with other hemoglobin variants with low frequency in the population is observed, a warning statement must be placed in a black box and must appear in all labeling material for these devices describing the interference and any affected populations.

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 hemoglobin A1c test system they intend to market and receive clearance to market from FDA prior to marketing the device.

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 market your device subject to the general control provisions of

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the FD&C Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Meshawn Payne at 301-796-6668.

Sincerely yours,

/s/

Courtney H. Lias, Ph.D.

Director

Division of Chemistry and Toxicology Devices

Office of *In Vitro* Diagnostics and

Radiological Health

Center for Devices and Radiological Health