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K042259/



Diagnosics

Document Mail Center, ODE, (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
9200 Corporate Blvd.  
Rockville, Maryland 20850  
December 17, 2004

FDA RECEIVED  
DEC 20 11:22  
FEDERAL BUREAU OF INVESTIGATION

**Re: K042259, AmpliChip CYP450 (2D6) Test Request for Evaluation of Automatic Class III Designation under 513(f)(2)**

Dear FDA:

**510(k) Number for NSE finding:**

Roche Molecular Systems, Inc. respectfully requests that premarket notification K042259 be considered for a risk-based classification of the AmpliChip CYP450 Test (2D6). A "not substantially equivalent" decision was rendered for K042259 on December 17, 2004.

**Statement of Cross Reference to 510(k)**

Roche Molecular Systems, Inc. hereby cross-references information contained in K042259.

**Classification being Recommended:**

Roche Molecular Systems, Inc. believes the documentation presented in premarket notification K042259 is sufficient to substantiate an order classifying the AmpliChip CYP450 Test (2D6) as Class II (general and special controls) pursuant to section 513 of the Federal Food, Drug and Cosmetic Act.

**Potential benefits**

In individualized medicine, selection of appropriate therapies may help assure desired therapeutic outcome in the safest and most cost-effective manner. Genotyping of polymorphic CYP450 genes will allow physicians to individualize treatment and dose of certain medications according to the genetic profile.

The consequence of incorrectly predicting a phenotype depends on the particular CYP450 allele combination (genotype) present. Failure to correctly identify the presence of two null activity alleles associated with the poor metabolizer phenotype could result in the incorrect phenotype assignment of extensive metabolizer or intermediate metabolizer. In this situation a patient might be prescribed a normal drug dose with concomitant increased risk of adverse reactions due to decreased drug metabolism. Failure to determine directly that a reduced or null activity CYP2D6 allele has been duplicated would lead to incorrect assignment of the ultrarapid metabolizer phenotype. In such subjects, prescription of higher than normal drug doses based on the assignment of ultrarapid metabolizer phenotype could lead to an increased risk of adverse drug reaction.

2005N-0067

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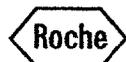
The benefits derived from testing outweigh the possible risks associated with use of the product as the information provided in this genetic test supplements therapeutic decision-making and presents a low risk for introducing a novel genetic assay in the market. These data will only be used in conjunction with routine monitoring by a physician.

**Proposed General and Special Controls:**

Roche Molecular Systems, Inc. believes that general controls and special controls in accordance with FDA's draft Class II Special Control Guidance Document: **Guidance for Industry and FDA Staff Class II Special Controls Guidance Document: CYP2D6 Genotype Detection System** constitute adequate information to ensure reasonable assurance of the safety and effectiveness of the AmpliChip CYP450 Test (2D6) and K042259 via the premarket notification process 21 CFR 807. These controls parallel the safety and effectiveness information provided in K042259 for its intended use in identifying a patient's CYP2D6 genotype from genomic DNA extracted from a whole blood sample. Information about the CYP2D6 genotype may be used as an aid to clinicians in determining therapeutic strategy and treatment dose for therapeutics that are metabolized by the CYP2D6 gene product.

If there are any questions regarding this submission, please contact me by phone at 925-730-8180 or by fax at 925-225-0207, or by mail at the address given below.

Yours Sincerely



**James F. Kelly, Ph.D**  
**Roche Molecular Systems**  
**Director, Regulatory Affairs**  
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DEC 23 2004

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Re: k042259  
Evaluation of Automatic Class III Designation  
Roche AmpliChip CYP450 Test  
Regulation Number: 21 CFR 862.3360  
Classification: Class II  
Product Code: NTI

Dear Dr. Kelly:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your petition for classification of the Roche AmpliChip CYP450 Test that is intended to identify a patient's CYP2D6 genotype from genomic DNA extracted from a whole blood sample. Information about CYP2D6 genotype may be used as an aid to clinicians in determining therapeutic strategy and treatment doses for therapeutics that are metabolized by the CYP2D6 gene product. FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Roche AmpliChip CYP450 Test, and substantially equivalent devices of this generic type into class II under the generic name, Drug Metabolizing Enzyme Genotyping System. This order also identifies the special controls applicable to this device.

FDA identifies this generic type of device as:

21 CFR §862.3360 – Drug Metabolizing Enzyme Genotyping System. A drug metabolizing enzyme genotyping system is intended for use in testing DNA to identify the presence or absence of human genotypic markers encoding a drug metabolizing enzyme. The device is used as an aid in determining treatment choice and individualizing treatment dose for therapeutics that are metabolized primarily by the specific enzyme about which the system provides genotypic information.

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360c(f)(1)) (the act), devices that were not in commercial distribution prior to May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976 (the amendments)), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III and require

premarket approval, unless and until the device is classified or reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and Part 807 of the FDA regulations (21 CFR 807).

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) for a device 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, within 60 days of receiving such a request classify the device. This classification 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** classifying the device type.

On December 20, 2004, FDA filed your petition requesting classification of the Roche AmpliChip CYP450 Test into class II. The petition was submitted under section 513(f)(2) of the act. In accordance with section 513(f)(1) of the act, FDA issued an order on December 17, 2004, automatically classifying the Roche AmpliChip CYP450 Test in 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, which was subsequently reclassified into class I or class II. In order to classify the Roche AmpliChip CYP450 Test 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 petition, FDA has determined that the Roche AmpliChip CYP450 Test can be classified in class II with the establishment of special controls. FDA believes that class II special controls provide reasonable assurance of the safety and effectiveness of the device.

FDA has identified no direct risks to health related to use of drug metabolizing enzyme genotyping systems. However, failure to correctly identify a drug metabolizing enzyme genotype, or failure to properly interpret genotyping results, could lead to incorrect patient management decisions. The measures FDA recommends to mitigate these risks are described in the guidance documents, "Class II Special Controls Guidance Document: Drug Metabolizing Enzyme Genotyping System", which includes recommendations for performance validation and labeling.

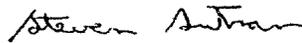
In addition to the general controls of the act, the Roche AmpliChip CYP450 Test is subject to the following special controls: "Class II Special Controls Guidance Document: Drug Metabolizing Enzyme Genotyping System." Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined

premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the device is not exempt from the premarket notification requirements. Thus, persons who intend to market this device type must submit to FDA a premarket notification submission containing information on the Drug Metabolizing Enzyme Genotyping System they intend to market 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 begin marketing your device subject to the general control provisions of the act, and the special controls identified in this order. If you have questions concerning this classification order, please contact Courtney Harper at (240) 276-0443.

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.  
Director  
Office of *In Vitro* Diagnostic Device  
Evaluation and Safety  
Center for Devices and  
Radiological Health