DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

September 26, 2001

Dr. Gillian Morgan
Visible Genetics, Inc.
700 BAY Street, Suite 1000
Toronto, Ontario M5G 1Z6
Canada

Re: Docket No. 01D-0286
Product: TRUEGENE HIV Genotyping Kit and OpenGene DNA Sequencing System
Classification: II

Dear Dr. Morgan:

The Center for Biologics Research and Review (CBER) of the Food and Drug Administration (FDA) has completed its review of your petition for classification of the TRUGENE HIV-1 Genotyping Kit and OpenGene DNA Sequencing System that is intended for use in detecting HIV genomic mutations (in the protease and part of the reverse transcriptase regions of HIV) that confer resistance to specific types of anti-retroviral drugs, as an aid in monitoring and treating HIV infection. FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the TRUGENE HIV-1 Genotyping Kit and OpenGene DNA Sequencing System, and substantially equivalent devices of this generic type into class II under the generic name, In Vitro HIV Drug Resistance Genotype Assay.

This order also identifies the special controls applicable to this device as the procedures identified in the FDA draft guidance document "Guidance for Industry - Premarket Notifications [510(k)s] for In Vitro HIV Drug Resistance Genotype Assays: Special Controls." The August 2001 guidance is available on the FDA web site at http://www.fda.gov/cber/blood/bldguid.htm.

FDA identifies this generic type of device as: In Vitro HIV Drug Resistance Genotype Assay.

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. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register classifying the device.

On July 13, 2001, FDA filed your petition requesting classification of the TRUGENE HIV-1 Genotyping Kit and OpenGene DNA Sequencing System 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 June 27, 2001 automatically classifying the device 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 device 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.

FDA reviewed the information submitted in the petition, the scientific literature concerning HIV drug resistance, and the recommendation of the Blood Products Advisory Committee (BPAC) sitting as a device panel, and has determined that the TRUGENE HIV-1 Genotyping Kit and OpenGene DNA Sequencing System intended for use in detecting HIV genomic mutations (in the protease and part of the reverse transcriptase regions of HIV) that confer resistance to specific types of anti-retroviral drugs, as an aid in monitoring and treating HIV infection, can be classified in class II with the establishment of special controls. FDA believes that class II special controls established in the draft guidance document provide reasonable assurance of the safety and effectiveness of the device.

FDA identified risks to health associated with use of the device. These risks include inaccurate detection of resistance mutations present in a patient's viral swarm that can result in continuance of therapies that are no longer appropriate or changes to new, inadequate therapies. In both cases the patient's viral load may increase, worsening the clinical prognosis and accelerating the development of drug resistant viruses. Patients may be needlessly subjected to serious, deleterious side effects of inappropriate anti-viral drugs. Furthermore, failure of the assay to give any results at all (sequence failure) can deny or delay beneficial, appropriate therapies, which may also result in high viral loads and their attendant morbidity.

FDA believes that these risks can be controlled by adherence to the procedures identified in the FDA draft guidance document. The draft guidance document describes a flexible set of design guidelines and analytical and clinical studies which are sufficient to determine the

sensitivity, reproducibility and accuracy of detecting, reporting and interpreting sequences of HIV genomes present in the blood of patients already known to be infected with HIV when HIV drug resistance genotype assays are used by qualified personnel.

BPAC sat as a medical device panel to consider the reclassification of Human Immunodeficiency Virus (HIV) drug sensitivity assays from Class III to Class II medical devices at their meeting on September 17, 1999. The Committee voted to support the reclassification of HIV genotype drug resistance assays from Class III medical devices to Class II medical devices. The transcripts of this meeting are available on the FDA web site at http://www.fda.gov/ohrms/dockets/ac/99mtbc.htm.

In addition to the general controls of the act, the device is subject to the special controls of the procedures described in the draft guidance. 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 must submit to FDA a premarket notification submission containing information on the In Vitro HIV Drug Resistance Genotype Assay 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 immediately market this device, subject to the general control provisions of the Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Dr. Sayah Nedjar at 301-827-3524.

Sincerely,

Jay S. Epstein, M.D.
Director
Office of Blood Research and Review
Center for Biologics
Evaluation and Research