ViroLogic

2001 SEP 19 P2:50

September 18, 2001

BY OVERNIGHT MAIL

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Comments Regarding Analyte Specific Reagent Language Included in FDA's Draft Guidance - Premarket Notifications [510(k)s] for In Vitro HIV Drug Resistance Genotype Assays, Docket Number 01D-0286

To Whom It May Concern:

On August 29, 2001, the Food and Drug Administration announced the availability of and requested comments regarding a draft" guidance document, entitled "Premarket Notifications [510(k)s] for In Vitro HIV Drug Resistance Genotype Assays" under Docket Number 01D-0286. 1/ As a clinical laboratory that develops and conducts assays, including human immunodeficiency virus ("HIV"] drug resistance genotype assays, ViroLogic, Inc. ("ViroLogic" or the "company"), is providing with this letter our comments

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1/ Draft "Guidance for Industry: Premarket Notifications [5 10(k)s] for In Vitro HIV Drug Resistance Genotype Assays;" Availability, 66 Fed. Reg. 45,682 (August 29, 2001).

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regarding specific statements in the draft guidance that pertain to analyte specific reagents ("ASRs").

ViroLogic respectfully disagrees with the conclusion as stated in the draft guidance that FDA "consider(s) commercially distributed ASRs used in genotyping systems to detect HIV mutations to be class III devices requiring premarket approval." 2/ Specifically, the conipany submits that such reagents, if purchased from commercial sources for use in HIV drug resistance genotypic tests, are class I ASRs as defined by FDA regulations (2 1 C.F.R. §864.4020) and described in greater detail below. Accordingly, ViroLogic recommends that the draft guidance document be revised to include a statement that the guidance "applies to HIV Drug Resistance Assays, but not to Analyte Specific Reagents (ASRs)" and that all additional text regarding ASRs currently included in the draft guidance be deleted. The company's full rationale for the recommendation is set forth below.

I. FDA REGULATION OF ANALYTE SPECIFIC REAGENTS AND THEIR CLASSIFICATION (21 C.F.R. § 864.4020)

FDA published the current ASR regulation on November 23, 1997, 21 C.F.R. Parts 809 and 864. The regulation, which became effective on

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2/ Premarket Notifications [510(k)s] for In Vitro HIV Drug Resistance Genotype Assays, Draft Guidance for Industry (August 2001), at page 2.

November 23, 1998, addresses the agency's position regarding the sale of chemical or biological reagents with analyte specific binding or detection characteristics for use in the development of "home brew" assays, manufacture of in vitro diagnostic ("IVD") products, or for nondiagnostic, educational, or forensic testing.

All ASRs, unless provided for use in tests that have specific intended uses as described below for class II and class III ASRs, are regulated as class.1 medical devices that FDA has determined to be exempt from the agency's premarket notification requirements. Id, § 864.4020(b)(1). Manufacturers, however, are subject to FDA's postmarket requirements, including establishment- registration, device listing (id. Part 807) and compliance with FDA's quality system regulation ("QSR") (id. Part 820), medical device reporting ("MDR") requirements (id. Part 803), and ASR labeling/distribution requirements (id. §§ 809.10(e) and 809.30).

ASRs are, regulated as class II devices if measurement or detection of the analyte is used. for blood banking tests that have been classified as class II devices, such as certain cytomegalovirus serological tests and Treponema pallidum nontreponemal tests. Id. § 864.4020(b)(2). Class' II ASRs are subject to FDA's 510(k) premarket notification requirements as well as to postmarket requirements, including the agency's establishment registration, device listing,

QSR, and MDR regulations. Class II ASRs also are subject to the requirements set forth in various guidance documents listed in the ASR regulations. Id.

ASRs are regulated as class III devices when:

i) The analyte is intended as a component in a test intended for use in the diagnosis of a contagious condition that is highly likely to result in a fatal outcome and prompt, accurate diagnosis offers the opportunity to mitigate the public health impact of the condition; (e.g., human immunodeficiency virus (HIV/AIDS) or tuberculosis (TB)); or

ii) The analyte is intended as a component in a test intended for use in donor screening for conditions for which FDA has recommended or required testing in order to safeguard the blood supply or estabhsh the safe use of blood and blood products (e.g., tests for hepatitis or tests for identifying blood groups)"

Id. § 864.4020(b)(3).

Class III ASRs, unless marketed prior to 1976 as preamendment medical devices, require approval of a premarket approval ("PMA") application to be legally marketed in the United States and are subject to FDA's postmarket requirements. FDA anticipates that most class, II and class III ASRs will not be marketed as' independent components separate from the test

in which they are used. Accordingly, FDA undertakes premarket review of the performance of the class II and class III ASRs when the agency reviews the 510(k) notice or PMA for the test in which the ASR is used. See 62 Fed. Reg. at 62245.

II. INTENDED USE OF HIV DRUG RESISTANCE GENOTYPIC ASSAYS

FDA has defined HIV drug resistance genotypic tests as "in vitro diagnostic device[s] (IVD) intended for clinical laboratories to use in detecting HIV genomic mutations that confer resistance to specific anti-retroviral drugs, as an aid in monitoring and treating HIV infection"3/ (emphasis added). HIV drug resistance tests are not: (1) blood banking tests which FDA has classified as class II devices; (2) intended for use in the diagnosis of HIV; or (3) intended for use in donor screening or to establish the safe use of blood and blood products. Rather, the tests are intended as an aid in monitoring drug therapy for individuals who have already been diagnosed as HIV antibody positive or HIV antigen positive by FDA approved or licensed diagnostic tests. The drug therapy they are receiving, and for which the HIV drug resistance test has been requested, is intended to mitigate the public health impact of their condition.

3/ *See supra* Note 2, at page 1.

III. CONCLUSION

ASRs used in HIV drug resistance tests do not meet the definition of class II or class III ASRs as set forth in FDA's regulations. HIV drug resistance tests that may employ such ASRs are not class II blood banking devices,, Similarly, HIV drug resistance tests are not intended for use in the diagnosis of a conmgious condition or in donor screening/blood safety, testing. Therefore, ASRs used in HIV drug resistance tests meet FDA's definition of class I ASRs and should be regulated as such.

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We would be happy to discuss, our recommendations and the underlying support for ViroLogic's position if the agency feels this would be helpful. Feel free to call me directly at (650) 624-4243 if further information is needed or you would like to explore- our recommendations further.

Sincerely,

Kathy Hibbs,
General Counsel

cc: Jonathan S. Kahan, Esq.

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