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

Re: Docket No. 2005D-0434: Draft Guidance for Industry and FDA Staff: Nucleic Acid Based In Vitro Diagnostic Devices for Detection of Microbial Pathogens

Dear Sir or Madam:

Gen-Probe is providing this response to the Food and Drug Administration's (FDA's) request for comments to the draft guidance entitled, "Draft Guidance for Industry and FDA Staff: Nucleic Acid Based In Vitro Diagnostic Devices for Detection of Microbial Pathogens."

GENERAL COMMENTS

Gen-Probe supports FDA's efforts to update guidance for nucleic acid amplification-based IVDs based on the recent changes in the technologies available for nucleic acid detection, as well as expanded use in clinical laboratories. Providing this guidance should greatly assist diagnostic companies in preparation for a successful premarket review of a nucleic acid-based device that detects microbial pathogens. However, Gen-Probe believes the restrictions imposed by not allowing the aforementioned diagnostic companies to implement the *Replacement Reagent and Instrument Family Policy* to self-validate interchanging device test systems is not the least burdensome approach for both FDA and industry.

SPECIFIC COMMENTS

Scope

Page 7, paragraph 1, sentence 2 states, "The guidance document, *Replacement Reagent and Instrument Family Policy*, (available at <http://www.fda.gov/cdrh/oivd/guidance/950.pdf>) does not apply to reagents or to instrumentation that are part of these device test systems, because we believe that interchanging different reagents with different instrument systems would significantly affect the safety and effectiveness of the device."

RECOMMENDATION: Gen-Probe recommends modifying the statement to allow diagnostic companies that manufacture nucleic acid based IVD test systems to utilize the guidance and direction provided in the *Replacement Reagent and Instrument Family Policy* (RRP). Gen-Probe would like to present an example of three separately cleared nucleic acid based IVD devices ("assays") that utilize the same specimen processing and assay technology to demonstrate that when one previously cleared assay receives a new clearance on a new automated analyzer, the

2005D-0434

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other two previously cleared assays should be able to follow the RRP by utilizing the same validation protocol to self-validate the instrument/reagent combination:

Three separate assays (e.g., Assays 1, 2, and 3) utilize the same specimen processing and assay technology and have received premarket clearances for use with general purpose, semi-automated laboratory instrumentation. Assay 1 has also been cleared for use with an automated analyzer.

As a result of the similarities in specimen processing steps and assay technology, the company wants to validate Assay 2 and 3 on the same automated analyzer using the same specimen types, assay processing steps, and analyzer software, all of which have been previously reviewed and cleared with Assay 1. Therefore, with the many similarities between the assays, a duplicate review is a burdensome approach for FDA and the validation protocol is the key factor in determining equivalent assay performance of Assays 2 and 3.

The validation protocol that was conducted, submitted and cleared to support the use of the Assay 1 on the automated analyzer is the model used to evaluate the Assay 2 and 3 on the automated analyzer. By having a scientifically sound validation protocol to evaluate the additional assays on the automated analyzer, in conjunction with a comprehensive Quality System, along with a detailed RRP guidance that requires a submission if the validation protocol fails, should alleviate FDA's concerns about the risks associated with validating appropriate instrument/reagent test systems.

Device Descriptive Characteristics

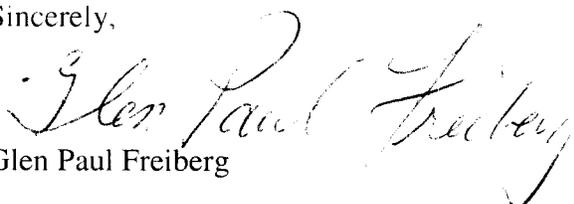
Technological Characteristics

Instrumentation and software components

Page 11, paragraph 4, sentence 4 states, "If an instrument is non-dedicated, you should cite the premarket notification (510k) submission, or PMA number of the instrument."

RECOMMENDATION: Gen-Probe recommends explaining further the rationale for this sentence. It is confusing to read that the RRP is not allowed for IVDs to detect microbial pathogens on page 7, and then read on page 11 that an instrument can be "non-dedicated." If an instrument can be non-dedicated, why does OIVD require that an automated analyzer have an assay associated to it within a submission? Is OIVD currently allowing non-dedicated automated analyzers to be cleared as instruments that are separate of specific assays? If an analyzer can be cleared as a non-dedicated instrument, and a company has a prior assay clearance, the RRP should be applicable because, according to RRP, the process would be taking a previously-cleared instrument and a previously-cleared assay and internally documenting the validation with no submission necessary if the validation protocol passes.

Sincerely,



Glen Paul Freiberg

cc Larry Kessler, Ph.D.