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OUR FILE NUMBER

60445

July 6, 2001

Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA – 305)
Rockville, MD 20852

RE: Docket No. 01D-0044

Dear Ladies and Gentlemen:

Please find enclosed the Comments of Dr. Richard Ferrans to the Guidance for Clinical Laboratory Improvement Act CLIA; Criteria for Waiver and Draft Guidance for Industry and FDA released for comment on March 1, 2001. The notice of this Guidance document was published in the Federal Register, Vol. 66, No. 41, Thursday, March 1, 2001, on p. 12939. These comments were previously transmitted by e-mail. Please file these Comments of Record.

With kindest regards,

Sincerely,

Anthony M. DiLeo

AMD:jma
Enclosure

cc: Dr. Richard Ferrans (with Enclosure)

01D-0044

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Comments on Guidance for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Criteria for Waiver; Draft Guidance for Industry and FDA

Richard Ferrans, M.D.
Senior Vice President, Labnetics

Labnetics would like to applaud the FDA's efforts towards reforming the CLIA waiver process. The draft guidance represents an important step towards regulatory reform for diagnostic laboratory technology. We are especially encouraged that the agency decided to change the regulations within months of beginning its role as overseeing CLIA complexity categorization, and immediately sought public testimony to quickly formulate this guidance.

Labnetics believes that the four-step process for meeting waiver criteria is an appropriate one to ensure device safety.

We wish to comment on these four steps and suggest reasonable modifications. We suggest these modifications in the spirit of our August testimony that described how technology had outpaced the original CLIA regulations. In that testimony, we stated our belief that the original regulations accurately carried out the legislative intent, but that regulation was focused on documenting processes (Qa and Qc programs) to provide quality control and quality assurance. It was not envisioned at that time that those processes could be automated.

In the process of developing the final rule, we believe the FDA should modify this industry guidance to accommodate multianalyte device technologies that are here today and those that are just over the horizon. Specifically, the FDA should modify its four step process to accommodate what will constant new analyte submissions for previously 510K approved devices that have had other analytes already waived. At the August hearings, several members of the panel publicly acknowledged that the "future is in point of care devices". As a manufacturer of a point of care diagnostic laboratory device in development, Labnetics believes that the four-step process spans both the device and the assay, and should be rationalized to recognize this fact. The FDA should clarify the process for adding new analytes to a device in a manner that reduces redundancy and ensures safety.

The first part of the new CLIA waiver process is to determine whether or not the device is a simple device. Under the guidance document, each time a device manufacturer creates a new assay for their multianalyte platform, that assay is treated as a new device, when in effect, the simplicity is a function inherent of the device itself, not of the new assay for that device.

Therefore, we recommend that multianalyte point of care device manufactures should submit data regarding device simplicity once to the agency (for example, in the first assay(s) submission), then refer to it in their subsequent assay submissions for CLIA waiver.

The second part of the process under the new CLIA guidance is the likelihood of erroneous results. The FDA requires a hazard analysis to be submitted that identifies potential sources of error and processes used to minimize the likelihood of erroneous result. Unlike simplicity, which can be inherent to the device itself rather than the individual assays, the sources of error fall into two categories; those inherent to the multianalyte platform device, and those that are a function of the assay itself. For example, operator procedures for two different assays may be identical on a multianalyte device other than selecting the test to be performed on the display; reagent stability may be entirely different.

Therefore, we recommend that a multianalyte device manufacturer be required to submit a complete hazard analysis for new assays on a previously 510K approved device that has one or more assays that have been previously CLIA waived. For sources of error identified from the hazard analysis that are inherent to the device (for example, hardware and electronics integrity), the manufacturer should be able to use previous validation data from its original submission, rather than having to repeat Qc validation studies for device related sources of error.

The third part of the process for waiver is the process of determining accuracy. We believe that accuracy is a function of the assay itself, and that accuracy data should be submitted each time a new assay is added to the platform. We question the need for 300 untrained users in the untrained user/ professional agreement study for Qualitative Tests section: we believe this should be a much smaller number of users making more observations, such as 50 users making 6 observations.

In summary, if a device manufacturer wishes to market a multianalyte device platform, the manufacturer should obtain 510K premarket clearance for the device and first analyte or first group of analytes (such as a Chem 8), then request CLIA waiver by submitting its data for simplicity, minimal risk of erroneous results, accuracy, and labeling to the FDA. Upon receiving waiver, the manufacturer should use the following process for adding more analytes to the platform:

1. Submit a 510K for the new analyte/ group of analytes
2. Upon receipt of 510K approval, the manufacturer should be able to submit *relevant* new hazard analysis information and Qc validation studies, accuracy study data, and labeling information to the FDA. It should also refer to or resubmit previous hazard analysis data and Qc validation data that are multianalyte device inherent, not analyte inherent.

Because the FDA has created objective criteria for meeting waiver (i.e. validation studies based on hazard analysis, and specific confidence limits for accuracy), it should be apparent to the manufacturer whether or not CLIA waiver will be granted for subsequent analytes on a 510K approved platform that already has one or more analytes waived. Therefore, we believe that upon submission, new assays should be able to be used in CLIA waived settings if

a) Risk of erroneous result does not materially differ from the original assays, and
b) Accuracy data indicates accuracy levels at the level predetermined by the FDA in the guidance.

We recommend that manufacturers submit CLIA waiver data for new analytes on a previously CLIA waived multianalyte platform, rather than seek CLIA waiver for additional analytes. In other word, waiver is implicitly granted for subsequent analytes on a platform that already has waiver for use with its initial analytes, so long as the same level of Qc and accuracy are present for the new analyte.

Finally, we believe that they agency should publish timelines as to how quickly it will review CLIA waiver applications. For example, the 90 day guideline for the agency to respond to a 510K application has led to the perception that the FDA is serious about getting approvals done in a timely fashion. A similar published guideline or goal would be very helpful for the CLIA program, especially in light of its history under other agencies.

FIRST CLASS MAIL

FROM: 60445/AMD/jma

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