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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
Attention Docket Number 1147

May 24, 2001

Docket Manager:

We have reviewed the Agency's current thinking on "Guidance for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Criteria for Waiver; Draft Guidance for Industry and FDA" and make the following comments.

Comments regarding the demonstration of "SIMPLE":

Include within the type of samples, sweat and saliva in addition to finger stick, nasal swabs and urine as examples.

Comments regarding the demonstration of "ACCURATE":

The expected population demographics for the precision and agreement studies are unclear. The guidance indicates that the "professional" user should be a laboratory professional. While it is appropriate to have a clinical laboratory professional function as a professional user, the target demographics for the "untrained users" are defined only as "individuals who represent anticipated users". The guidance indicates that "the participant's occupations should be diverse". Maintaining a focus on "anticipated users" may result in a lack of diversity in the participants' occupations. The identification of a participant as an "untrained user" is a misnomer, since a laboratory professional that is performing a test for the first time can also be considered an "untrained user" for the test under study. The purpose of the precision and agreement studies is to evaluate the ability of the "untrained user" to obtain results comparable to those obtained by laboratory "professionals". Therefore, the guidance should refer to the participants not as "untrained users", but rather "non-laboratory professionals". The guidance should state that "non-laboratory professionals are defined as

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individuals not having education or experience in the clinical laboratory sciences" in order to better define the population used in the comparison.

Comments regarding the demonstration of "SIGNIFICANT RISK OF ERRONEOUS RESULT":

The rationale for using 300 specimens in the agreement study is also unclear. The specimens are to be equally distributed across the reportable range of the test. The data is to be presented primarily as a scatter plot with regression line, descriptive statistics, slope and intercept with 95% confidence intervals, mean and standard deviation for the individual specimens. The percent difference between the professional and untrained user results for each specimen is calculated. The purpose of this study is to determine the accuracy of the untrained users' results, compared to the professional users' results. It also will demonstrate the incidence of gross errors obtained by the untrained users. The use of 60 unique specimens equally distributed across the reportable range of the test should be sufficient for an accurate calculation of slope and intercept, allowing for the identification of a correlation coefficient of at least 0.5, which is much lower than the expected correlation. The use of 60 specimens should be sufficient to determine the frequency of gross errors and the ability of the "untrained user" to obtain accurate results. Sixty (60) unique specimens will allow the precision and agreement studies to be performed by the same individuals participating as "untrained users". This will make the overall effort of enrolling participants less burdensome. The use of 60 specimens instead of 300 will decrease the ability of the assay coefficient of variation to influence the agreement between the untrained users and the professional users.

The rationale for the presentation of descriptive statistics for the specimens to be tested is unclear. These specimens are to be equally distributed across the reportable range of the test. The statistics of median, minimum and maximum will not provide information that is more relevant than the mean and standard deviation for the individual specimens and the percent difference between the professional and untrained user results for each specimen.

Comments regarding the "Untrained/Professional Agreement Study"

The least burdensome approach for selecting specimens for the agreement study should be used. The guidance should indicate a preference for using contrived samples for the agreement studies, since they are not potentially as infectious or hazardous. The use of actual patient specimens is overly burdensome because the applicant must prospectively collect and evaluate each patient specimen until the appropriate concentrations of analyte are identified. This process would undoubtedly require collection of specimens from a total number of patients that is far greater than the number required for the agreement study. The use of contrived specimens will ensure that the reportable range is adequately challenged in the agreement study.

Comments regarding Waiver Labeling:

The suggested contents for the Quick Reference Instructions are too comprehensive. We presume that this Quick Reference and should be no more than one or two pages. Those items that address other than how to use the test system should be referenced to the Package Insert. These referenced items would include:

- ❑ Non- technical maintenance, such as cleaning.
- ❑ QC acceptable ranges (may vary lot to lot for control materials).
- ❑ Actions to be taken if the QC results are outside of the expected range.
- ❑ Actions to take if system is inoperable or requires trouble shooting.

Comments regarding the "Voluntary safeguards for waived test":

The use of proficiency testing may not be feasible and may be considered redundant. With proper data collection techniques, QC samples may serve the same purpose.

Sincerely

R.H. Davis Jr.

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