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May 29, 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

Please accept the following comments relevant to Docket No 1147, *Guidance for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Criteria for Waiver; Draft Guidance for Industry and FDA*

General Comment: Upon review of the document, it is clear that the draft document uses many of the existing "waiver criteria" instituted under the prior CDC controlling guidelines. The current draft does make an effort to standardize the actual data required to prove simple and accurate test systems, terminology previously characterized by the CDC as "accurate and precise" testing. None-the-less, for both clinical users and for the manufacturers, a clearer definition of "operators" and a better qualified objective evidence for "accuracy and agreement" would help to ensure that test candidates can evaluated appropriately for "waived categorization". The comments below are drawn from our recent experience in working with the FDA to gain a CLIA waiver for a point-of-care (POC) prothrombin time (PT) test. Our request had begun with the CDC while they still maintained control of the categorization process and continued once the Agency took over the process.

Specific Comments

Page 4, Operator status as used under "Terms used in the Document". The guidance document continues the operator terminology established years earlier by the CDC. The segregation of "untrained users " and laboratory professionals", without regard for the target "user group", serves to potentially ignore those individuals most likely to perform the test once commercially available. The clinical reality is there exists a considerable gradient between untrained users and trained professionals. The guidance procedure should focus on the "intended user" to provide accuracy data. For example, nurses (RN) are excluded from the untrained user category because they have had college level laboratory training. Not only does college lab experience not reflect true clinical laboratory experience, as practiced by MLTs and MTs, but in most POC clinical settings the RN represents the most likely operator. Accuracy assessment would be better served by defining the intended user population and conducting studies in that arena.

Page 12, Untrained/Professional Precision Study for Quantitative Tests. The document states a need for professional testing at each study site. However, it is not intuitive as to the merits of conducting multiple professional evaluations rather than performing the evaluation at a central location. Precision assessments would be equally accurate by comparing 20 operators at each of 3 test sites to a mean, standard deviation and CV of professional determinations performed at a central site.

Page 13, Precision Targets for Quantitative Tests. Relying upon a ratio of the SD of the untrained users and the trained professional would appear to overly burden a highly reproducible professional assessment in which the SD was very small, while favoring a professional test in which the SD is larger. While a ratio is appropriate there should also be some absolute limits for cases in which professional precision is extremely tight and any untrained user variability is within acceptable clinical decision limits.

Page 13, Number and Type of "matched specimens" for Agreement Study. It is not clear why 300 matched specimens should be required. While there is an option to employ "contrived specimens" our experience while engaged in our current waiver request, has been that the FDA is not inclined to accept the "contrived specimens". From a clinical trial perspective, the problem is that many institutions frown upon "untrained users" handling potentially infectious patient blood. The acceptance of "safe contrived samples" could facilitate a more readily available substrate for agreement study conduct.

On a related issue, the guidance document makes no mention of comparison of the waived device result to an established laboratory standard. However, again under our current waived application the Agency was unwilling to accept a current laboratory test result when comparing a POC-PT result, preferring a WHO reference "tilt-tube" test, though it was universally accepted that it would be nearly impossible to get accurate "tilt-tube" results. While it is notable that the current guidance document does not require any "agreement to a laboratory standard" it would be worthwhile for the guidance document to address this issue either directly or through reference to current FDA 510(k) accuracy requirements.

Page 17, 7th Grade Reading Level. Based upon the earlier comment, it seems more worthwhile to prepare instructional documents relevant to the intended user. It is difficult to imagine any "untrained user" who can only read at a 7th grade level to understand the quality control requirements discussed in the guidance document as being integral to the conduct of the waived test.

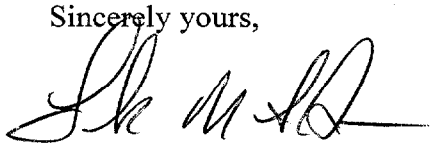
Page 19, QC Test Intervals. It would be ideal in this document to establish some general guidelines for QC test intervals. CDC had attempted to do so earlier, at one point considering a minimum regular requirement, i.e., once per month or per week, and NCCLS, with clinical, manufacturer and regulatory input has recommended a minimum

of one-tenth of the product shelf life as the minimum test frequency, i.e., every 5 weeks for one year shelf life (NCCLS Document EP-18).

Page 20-21, Post-marketing Surveillance Program. The current post-marketing surveillance program for our patient self-testing PT test is quite extensive. It is only practical due to the restricted nature of the product distribution. If the Agency intends to require post-market surveillance for all waived tests it must be more restricted, limited to customer complaints analysis, relevant device design changes and design control and customer (non-complaint) feed-back.

These brief comments are directed at those critical areas of operator selection and data analysis of the draft document. Clearly this guidance document is a laudable start on the part of the Agency to establish universal standards for CLIA waiver categorization request. Thank you for your attention to these comments.

Sincerely yours,



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[illegible] Olympian representing the United States in the 110-meter hurdles, Swift is training in the same event for the 2000 Olympic Games in Sydney, Australia. He has worked at UPS for 14 years and is currently in the human resources department in Oakland, California. He is a member of the global UPS Athlete Training Assistance Program (ATAP), which provides employee-athletes with the support they need to pursue their Olympic dreams.