February 14, 2001 Re: Document 1147

Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
Food and Drug Administration
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Rockville, MD 20852

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Comments on Draft Criteria for CLIA Waivers:

The proposal correctly quotes the statute regarding the waiver criteria, but then ignores part of the statute. There are two ways for a test to be "waived" if they are not published in the regulation. The FDA may approve tests for home use; or the Secretary may approve tests which are simple and have an insignificant risk of an erroneous result.

It would seem that this proposal is out of context without a side by side comparison of the criteria utilized to determine eligibility for home use. The two processes share many of the same criteria. Knowing that approval of a test for home use causes it to become waived should cause the FDA to be more cautious in examining the potential consequences of this action. Shouldn't a unified process (or "decision tree") be utilized for evaluation of tests for both home use and waiver? Shouldn't there also be input from both the public health folks at CDC and the lab standards folks with CLIA?

The document makes it sound as if the Secretary's decision is totally separate from the analysis that FDA does on tests submitted for waiver. Doesn't the FDA make recommendations to the Secretary, in addition to the analysis? Therefore, it is the FDA that makes the determination, presumably under delegation from the Secretary.

On page 3, Step 3, the proposal states that "If FDA determines the test is simple and has an insignificant risk of erroneous result, then it will not be waived unless the Secretary determines that it poses no reasonable risk of harm to the patient if performed incorrectly....." This makes it appear as if the FDA has no part in advising the Secretary on the proper decision. The reality is that CDRH/FDA, based upon their evaluations, makes recommendations. Indeed, the determination of simplicity, risk and accuracy is made by the FDA and is very clearly set out in your draft examples. But the statute imputes this responsibility to the Secretary to rule on risk of harm as well. Risk of harm must also be considered as part of the FDA evaluation or by some other public health entity; it is in the statute.

The logic of the statute seems plain.

Tests are waived that: are approved for home use by the FDA
Tests may become waived that: have an insignificant risk of erroneous results
Including those that: A) are simple and accurate, errors negligible or

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B) pose no unreasonable risk of harm if performed incorrectly

The proposal dwells on simplicity, insignificant risk of erroneous results and accuracy, but does not address risk of harm if performed incorrectly. This is a critical oversight, because the FDA is part of PHS and HHS, whose first responsibilities are to the public and public health. I fear that the traditional mindset at FDA, which requires fast processing and approval to manufacturers, may be contributing to some longer term health problems. There is not a shortage of testing available in the US. We can take the necessary and proper time to evaluate each test without causing a public health crisis.

If a test is performed incorrectly and an erroneous result is generated, the individual could be harmed in several ways. If a medication dosage depends on the result, an incorrect dosage could be taken, resulting in for example, a high glucose or insulin shock, or in the case of a prothrombin time, either increased risk of stroke or of having a serious bleed. In other cases, an individual could mistakenly think they did not have Streptococcus A or ulcers, failing to obtain proper treatment, with potentially serious sequelae. The potential for harm is exponentially greater when a test becomes waived, because instead of an individual testing him or herself, other individuals will be allowed to test anyone who comes to them, providing they hold a waiver certificate. They will escape any scrutiny by the CLIA program.

Has the FDA thought of doing a study of the effects of FDAMA's provision for waived status for tests approved for home use? Motivating factors and concern about accuracy are considerably different for a patient monitoring himself and an individual performing tests on others for pay. The fact that achieving waived status proclaims a test and its results "harmless" removes avenues of recourse to patients or families of patients who have been harmed. The same fact also removes cause for CLIA to conduct investigations of waived testing, because a critical factor in gaining access to facilities is the potential for harm to the public. Because of waiver classifications by FDA, CLIA would be handicapped in its ability to follow through in its responsibility to protect the public health.

Page 15. In the instructions for agreement studies for qualitative tests, an unfamiliar term appears. What is a "weak negative"? Either a reaction is negative or weakly positive or positive, or in rare cases "inconclusive." A survey of immunologists and package inserts did not disclose any familiarity with this term. In the distribution of aliquots for testing, those listed as weak negative should be moved to the weak positive column.

Page 18. Labeling should include a suggestion (requirement?) to participate in an approved proficiency testing program as a means of external validation of results.

Page 19. Each new operator. The definition is modified significantly from what is being utilized currently in laboratories. In the already waived coagulation testing, two levels of daily quality control are required with each operator running controls at least once a week.

With some of the strep kits, each new operator is required to do controls. A plain interpretation would mean this would be each day or each week, depending when a different operator performed testing. Consistency would be helpful, but we need to consider what's "out there" presently. There is confusion by users about QC requirements in general, depending on when a test was approved. Newer package inserts appear to give labs options which are not applicable in a waiver lab, but with side by side instructions for waived and moderate procedures, the facilities pick the process that is easiest for them, not necessarily the correct one.

Page 20. Manufacturers should be required to take action when their test demonstrates poor performance (as defined in the "Performance Targets" in this document) in any CLIA approved proficiency testing program {example: current Zstat Flu performance in CAP proficiency testing is below 40% accuracy for positive tests}. In addition they should be required to disclose all complaints and "technical issues" raised on their hot lines, preferably to the public and other users, not just the FDA. The internet would provide a perfect means of accomplishing this. In addition, to protect the public from erroneous testing, none of the proposed "Voluntary Safeguards" should be voluntary.

(Zstat Flu would be a good example to put through the proposed process. Their own data show that the test is really very accurate for negative tests. But the studies in their brochures show only about 65% accuracy [sensitivity] on average for positive tests. The water is muddied with discussion of prevalence rates compared to cultures. The analysis is flawed because they compare prevalence rates for the general population, not the relative sensitivity of their method. Their chart shows an approximate 10% difference between methods. But more critical analysis would show that their method misses about 33% of the positive tests! How did this test become waived?)

Tests that are waived should be more accurate (held to a higher standard) than non-waived test because there is no required professional oversight. And the public is trusting us to protect them.

Please don't let them down.

Sincerely

Ed Prichard

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