

CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE MEETING

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PUBLIC COMMENT FORM

Waived Testing Criteria:

This discussion addresses criteria to be applied to decide which tests are to be placed in the waived category, rather than in the categories of moderate or high complexity. It is understood that tests in the waived category are exempt from CLIA oversight, including documentation that the test is being performed per manufacturer's directions.

AdvaMed has proposed that tests be waived if pre-market tests show that both trained and untrained users get the same answers when given the manufacturers directions, e.g. package insert. **This discussion provides examples of three categories of issues required for safe and effective performance of patient care tests that would not be covered by the approach suggested by AdvaMed.**

Issue 1:

The AdvaMed proposal presumes that in the real world, users will follow manufacturer's directions, as they do in the proposed assessment situation in which testers are provided the manufacturer's directions, and told to follow them. The studies of CMS of waived testing laboratories in 8 states, have documented that in the real world, at least 50% of laboratories **fail to follow manufacturer's directions.** (Other studies by OIG, by state oversight organizations, and others confirm this problem.)

A real-life example may be seen with urine dip-sticks—perhaps the simplest, and longest practiced waived test. Surveys of users asked when the tests on the stick should be read, predictably report that they should be read at one minute. In truth, to be accurate, the timing for different tests on the stick ranges between 30 seconds and two minutes. One physician at my institution with responsibility for training residents and fellows indicated that they were well trained because they only looked at two tests with their one minute reading, e.g. leukocyte esterase and nitrate reductase. He was astonished to learn that these two are the tests that require two minute incubations for accuracy.

Issue 2:

A key requirement for waived tests is that it be not only simple to perform, but also unlikely to cause harm if misread. There are 4 inherent causes of high risk for patient harm when tests are waived: 1) Risks of harm inherent in the test itself; (this will not be discussed); 2) Risks due to failure to follow manufacturer's directions; 3) Judgment failures caused by lack of training, and 4) Off label use.

Risks due to failure to follow manufacturer's directions leading to erroneous results: A real-world example pertains to direct observation of the ability of a group of skilled nurses to perform hemaglobin measurements in a labor and delivery suite. Despite the fact that the waived test involved only finger-stick blood and an excellent, simple device, three successive nurses made very major mistakes. The first tested a specimen with a bubble in the cuvette, seriously risking unnecessary transfusion for the patient, the second tested a sample in which blood had spilled on all sides of the cuvette, contaminating the device, and risking erroneous values for all subsequent tests. The third nurse put in the cuvette upside down. Thus three sequential nurse users who were multi-tasking in a high intensity area, failed to follow

manufacturer's directions, and put patients at serious risk of harm, through exposure to possible transfusion of un-needed blood, and to potential failure to transfuse when warranted.

Risk of harm due to judgment calls: The untrained are unlikely to recognize when a test not performing properly. A real-world example is that of the excellent hemaglobin device described above. One entire lot of cuvettes proved defective. Our institution was the only user that recognized this fact, and worked with the manufacturer to identify the problem—all other waived users of the product had to have obtained highly erroneous values that varied with the individual cuvette used on a given patient. The users were not equipped to understand when or how to recognize a defective product or test run.

Risk of harm due to "off label" use: When a device is waived, it is used for any purpose, not just those for which it has been approved for the waived category. Although "off label use" is a recognized problem on the part of the FDA, such use has never been tracked, monitored, or appropriately re-classified and reviewed by CMS as a high complexity device (which it becomes, under CLIA, when manufacturer's directions are not being followed.) Thus a glucose meter waived for home use by a single patient, is used in hospitals to monitor insulin dosing in critically ill patients. Home use devices are not built to be as accurate as usual patient care chemistry devices, commonly having an accuracy of plus or minus 20% -- fine for at home monitoring, not fine for hospital uses. In the hospital, it has been shown that diabetic surgical patients heal most rapidly when their glucose level is maintained at 105 mg./dl, e.g. insulin is given for values above 105, or withheld below it. Untrained users do not understand the inability of these devices to achieve such accuracy, so that patients incur wide swings, and are at risk for inappropriate dosing. We have experienced patients put into coma through inappropriate insulin dosing for other reasons as well, including testing delays after finger sticks, inappropriate finger stick technologies including obtaining specimens from fingers coated with lotions, spilled fruit juice, etc, in which the error was not perceived by the operator. Similarly, devices approved to monitor anticoagulant levels on patients are designed to screen for abnormalities, with abnormal results to be checked in a standard laboratory. Known "off label use" includes monitor in patients to determine if they can have invasive procedures—a use for which the devices have not been designed, risking major harm.

Issue 3:

Failure to address pre-and/or post-analytical components of a test: The AdvaMed approach considers only the analytical part of a laboratory test, ignoring the pre-analytical factors such as patient identification, specimen procurement, etc., and the post-analytical component, e.g. the two components of a test shown by the Institute of Medicine study to be responsible for **70%** of fatal, avoidable errors in laboratory testing, the analytical component being responsible for only 30% of serious errors. Key pre-analytical considerations include problems with patient identification and specimen procurement. Key post-analytical errors include appropriate interpretation of the test, and failure by the care-giver to take required post-analytical actions. Real world examples include failure to follow a screening test with a confirmatory test, as well as failure to take appropriate clinical actions. An example of the latter problem is seen with waived tests for influenza A and B, for which sensitivity may be as low as 50%. Harm occurs for patients given a false negative result when they are denied appropriate anti-viral therapy when it would have been warranted. Harm occurs from a public health perspective when a patient with influenza is returned to a nursing home, or other health-related location where they can unknowingly spread the disease to fragile populations.

Conclusion: The AdvaMed recommendation that a working group be convened to assist in recommending straight forward policies to be used to classify tests for the waived category is an

important, thoughtful recommendation. Waived tests, using simple methods provide an important medical resource that must be protected, and appropriately advanced, and manufacturers must know in advance what criteria are to be used to classify their products.

The criteria, and follow-up monitoring if appropriate, must, however, understand and consider among other factors, those illustrated above, namely steps to ensure that manufacturer's directions will be used, assessments consider risk of harm in the real-life usage environment, including off label use monitoring, and that pre-and post analytical components of a test be addressed, not just the analytical component.