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Members of the Clinical Laboratory Improvement Advisory Committee
c/o Ms. Rhonda Whalen, Chief
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Dear CLIAC Members,

The Centers for Medicare and Medicaid Services (CMS) recently published a revision of Appendix C of the State Operations Manual: Interpretative Guidelines for CLIA. These guidelines set minimum standards for laboratory quality, generally interpret application of CLIA requirements and set the foundation for conducting compliance audits.

With the publication of these guidelines, CMS has introduced a new concept called "equivalent QC" without any formal public comment or input. The ostensible purpose of equivalent QC, which was recently described by Dr. Jim Westgard in one of his website articles as "fatally flawed," is to allow laboratories to reduce the amount of quality control testing within the framework of "minimal quality." While Bio-Rad supports the concept of "customizing" QC based on statistically and scientifically validated test performance, we feel equivalent QC as described by CMS is unscientific, unproven relative to patient outcomes, and based on three screening protocols that have no apparent statistical foundation. Consequently, we are concerned that some laboratories will adopt equivalent QC regardless of how this process may or may not affect quality, and we firmly believe that equivalent QC may put patients at risk under certain conditions.

Specifically, our concerns with equivalent QC are:

1. There is no scientific basis for equating a 10-day, 30-day or 60-day error-free process control period to reliable analytical performance and positive patient outcomes subsequent to the evaluation period.

2. Less frequent QC seems contradictory to other CLIA requirements designed to ensure and maintain laboratory quality. These requirements state that the laboratory must be able to identify system failures "when they occur."

3. None of the protocols account for presence of analytical bias. A laboratory may have a beautiful Levey-Jennings chart for the test with good distribution of QC values above and below the mean and tightly grouped data (low imprecision) during the qualifying period, and yet be sufficiently biased to affect patient test results. Under these circumstances, a laboratory that passes the equivalent QC protocol may implement once/week or once/month testing of QC but have potential problems with patient outcomes.

4. None of the protocols account for total analytical error. As in the case above, a laboratory that passes the protocol may implement less frequent testing of QC but may produce patient test results containing an unacceptable amount of error.

5. All the protocols assume that the laboratory has correctly calculated the standard deviation for the QC material used during the qualifying period. If the standard deviation is uncharacteristically large, the laboratory will likely have a 10 day/60 day error-free period. Under these circumstances, a laboratory that passes the protocol may implement less frequent testing of QC but have potential problems with patient outcomes.

6. None of the protocols account for the range of imprecision that may occur for a specific test on a specific platform among laboratories. Consequently, the protocol rewards laboratories with less precision (greater imprecision), making it potentially easier to pass the qualifying period while potentially penalizing those laboratories with very tight precision. That is, one group of laboratories must meet a higher performance standard than another group to pass the protocol.

7. All the protocols assume that the laboratory has set appropriate statistical controls for each test. Some laboratories may be too restrictive, some too flexible. Some laboratories may simply adjust limits or process control rules in order to pass. Laboratories with more conservative process control in place may find it harder to pass the protocol than other labs. Accordingly, the protocol has the potential to reward the less scrupulous laboratory. Determining the "appropriateness" of the statistical rules in place during the qualifying period will become the responsibility of the auditor, which requires a higher level of sophistication in the area of statistics and process control.

8. The protocols specifically allow the laboratory to use historical QC performance. That is, the laboratory could look at QC records for the past 10, 30 or 60 days and proclaim the test passes. The protocols should take the form of an experiment with a well-defined procedure, have a start date, an end date and a definition of what is and is not a failure. Furthermore, anecdotal evidence indicates that some laboratories make it a practice not to log the first outlier if the repeat is in control. Such a practice biases the outcome of the evaluation. The protocol should dictate that every result is to be accounted for, including outliers (failures) to avoid the practice of only recording acceptable results.

9. None of the protocols specifically require multiple system calibrations or reagent changes during the qualifying period, two events that can potentially result in process failure.

10. None of the protocols specifically tell the laboratory whether the protocol is system-oriented or test-oriented. The wording "test systems (with/without) internal/procedural controls..." combined with lack of specifics makes the protocol appear system-oriented, when it should be test-specific.

11. Laboratories should be advised that less frequent QC presents some unique challenges when a QC failure does occur, including:

- Access to patients or patient samples for retesting.

- What is to be done when retesting shows incorrect results have been reported in the days prior. CMS does not adequately define "extensive evaluation" in the phrase "…will require a more extensive evaluation of patient test results when a control failure occurs."

- The stability of analytes which may not match the period between QC testing events.

- The cost to the laboratory of retesting patient samples, which will likely be higher than if the laboratory were to run QC daily. That is, a laboratory that tests QC daily or more frequently may have to retest only a small number of samples, whereas a laboratory that tests only once per week (or once per month) may have to retest hundreds of samples. The laboratory that tests QC less frequently runs the risk of higher retest costs for reagents, consumables and labor.

13. None of the protocols make a distinction between in-kit, manufacturer, and third-party controls. There is ample evidence that in-kit controls and controls made by the kit or instrument manufacturer are often made from the same raw materials as the calibrators. This results in a control product that is less sensitive to system component deterioration. A laboratory using such controls runs the risk of missing system failures. Such risks may be compounded by allowing for less QC with in-kit controls or controls made by the manufacturer. Again, use of an in-kit control or one made by the manufacturer could create an artificially favorable situation during the qualifying period.

Anecdotal evidence suggests that many laboratories in this country will go beyond what is required to ensure the quality of the test results they report. Unfortunately, there are just as many laboratories where quality that "meets minimum" is considered acceptable. In view of the concerns we have presented in this letter, we ask your Committee to do the following:

1. Urge CMS to hold open public hearings to solicit input on "equivalent QC" and to implement new guidelines based on this input. Technically, a period of public comment is not required for guidelines, but the guidance on equivalent QC borders on setting regulatory policy outside the framework of the CLIA rule.

2. Urge CMS to modify the equivalent QC protocols and testing paradigms to reflect the concerns listed in this letter.

3. Urge CMS to devise an evaluation protocol that:

    - Is scientifically validated
    - Demonstrates stable analytical performance over time, and
    - Documents that total error, imprecision and/or bias for the test is acceptable for reporting test results.

4. Urge CMS to prescribe a protocol for retesting of patient samples when a QC failure occurs and failure is documented.

Bio-Rad Laboratories wishes to thank you for taking the time to consider these issues that can have a direct effect on the quality of care in this country. If we can provide any further information or assistance, please do not hesitate to contact us at your convenience.

Sincerely

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