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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket No. FDA-2010-N-0274

Dear Sir or Madam:

Following are the comments of the American Association of Bioanalysts (AAB), a national association of clinical laboratory directors, owners, managers, supervisors, technologists and technicians, concerning FDA's request for comments on the "Oversight of Laboratory Developed Tests" published June 17, 2010, in Vol. 75, No. 116, of the Federal Register.

Recently there have been a number of highly publicized situations in which Laboratory Developed Tests (LDTs) played a prominent role, including:

1. Quest's LDT for Vitamin D utilizing LC-MS/MS;
2. Ovasure's IVDMIA for Ovarian Cancer;
3. Georgetown University Hospital's genetic analysis for breast cancer patients;
4. Direct-To-Consumer Genetic Laboratories [e.g., 23andMe].

Some of the regulatory actions involving these cases resulted in significant civil money penalties, shutting down laboratories, and pulling products off the market.

AAB recognizes that these are very serious problems that create significant risks for patients. Therefore, AAB supports efforts to eliminate, or at the very least reduce, the occurrence of these problems.

One possible solution is to require LDTs to undergo formal FDA review as medical devices. AAB believes this is a possible solution for high frequency, high dollar volume tests offered by large, publicly traded laboratories, especially if the FDA has already approved a test

kit for that particular purpose. However, many LDTs are developed by research and smaller laboratories for rare and unusual diseases or conditions. The cost and time required to undergo FDA's formal medical device review is prohibitive for many of these laboratories. Therefore, requiring all LDTs to undergo FDA's formal medical device review would restrict laboratories offering LDTs to large, publicly traded laboratories that have the financial resources to undergo FDA's medical device review process. But these are the very laboratories that have been involved in several of the problems enumerated above.

However, even for low volume LDTs designed for rare or unusual diseases, patients need to be assured that the tests are accurate, reliable, and reproducible.

Therefore, AAB suggests a "tiered" system of regulation as follows:

1. All LDTs above a certain test or dollar volume must undergo formal FDA review as medical devices.

2. LDTs below the test/dollar volume threshold in #1 above will continue to be regulated under CLIA, but CLIA inspectors will be required to review the validation data, not just the validation process, for these LDTs. Although CLIA regulations already require this, it is our understanding that many CLIA inspectors do not review the validation data due to time constraints.

   Reviewing the validation data is critical, and CLIA's compliance programs must review the validation data. For a possible alternative to reviewing the laboratory's validation data, see point #3 below.

   This tier of regulation would be broader than FDA's Humanitarian Device Exemption (HDE) rule.

3. Utilize a "modified" proficiency testing (PT) program for the "low volume" LDTs described in point #2 above. The modified PT program would operate as follows:

   LDTs performed by a minimum of three laboratories would enroll in a "specimen exchange" program. Specimens utilized for LDTs would be "split," with one portion being used by the laboratory for LDT testing and another portion being forwarded to a CLIA-approved proficiency testing program. The approved PT program would repackage the specimen to mask its origin and forward the specimen to one (or more) laboratories offering a similar LDT. These laboratories would test the specimen(s) using their LDTs and report the results to the PT program. Test results from all participating laboratories would then be compared by the PT program, and the results reported to the participating laboratories and the CLIA compliance program.

   If the results are comparable, this could be substituted for the required review of validation data, thereby saving CLIA surveyors the time it takes to review the validation data. [Although AAB operates a CLIA-approved Proficiency Testing program and is willing to offer a "specimen exchange" service, we expect it will be a

break-even enterprise, at best, due to the projected low volume of participating laboratories. Nevertheless, AAB believes having some form of external quality control for LDTs will provide patients and physicians with a practical way of judging the accuracy, reliability, and reproducibility of low volume LDTs.]

4. Include an "Emergency Health Event" exception whereby FDA's formal medical device review process can be temporarily suspended for infectious disease outbreaks, epidemics, pandemics, or other public health emergencies.

AAB understands the difficulties facing the FDA in effectively overseeing LDTs. More importantly, AAB understands how important it is to patients and their health care providers that test results from LDTs be accurate and reliable.

AAB offers these ideas as a way to improve the assessment of the quality of LDT results without depriving patients of the possible benefits of the cutting edge technology found in many LDTs, and we are very willing to provide the FDA with more information or feedback on these suggestions and ideas.

Sincerely yours,

Mark S. Birenbaum, Ph.D.
Administrator

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