Message

From: Adam Rosendorff [/O=THERANOS ORGANIZATION/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=ADAM ROSENDORFD92]
Sent: 11/27/2013 1:31:15 AM
To: Daniel Young [dyoung@theranos.com]
CC: Elizabeth Holmes [eholmes@theranos.com]; Sunny Balwani [sbalwani@theranos.com]
Subject: RE: proficiency testing for LDTs

Daniel

Thanks-

I'll write up the SOP and incorporate what we have discussed.

Adam

From: Daniel Young
Sent: Tuesday, November 26, 2013 5:03 PM
To: Adam Rosendorff
Cc: Elizabeth Holmes; Sunny Balwani
Subject: proficiency testing for LDTs

Here are my suggestions that I discussed with Adam. I'm providing some extra background info for reference.

Background:
There are 91 tests that are CLIA regulated and require proficiency testing (PT). For all other 'non-regulated' analytes, CLIA requires that labs have a quality assurance plan that establishes the accuracy and reliability of the testing at least twice per year. For example, the CAP Surveys and EXCEL proficiency testing programs offer products to assist labs in fulfilling this requirement. States and other accrediting agencies may also mandate additional requirements.

For our LDTs, all of which are CLIA regulated at the moment, we need SOPs for PT. However, there are several factors that prevent us from enrolling in the traditional PT programs. Most significantly is that performance in PT surveys is based on an evaluation against a peer group. A peer group is composed of different labs all running the same method/device. The goals of such PT is to compare the performance of an individual laboratory to their peer group and sometimes to target values established by reference methods or reference laboratories. The goals of PT differ from regular QC procedures which each lab also performs each day/shift that tests are performed. Namely, QC procedures ensure that performance within a given lab does not change over time and essentially assesses test precision. In contrast, PT assesses system accuracy.

Proposal:
Where traditional PT options are not available, we must initiate Alternative Assessment Procedures (AAP). Namely, for non-CMS-regulated tests, for those tests which lack FDA clearance or for tests that lack a suitable peer group, commercial or external PT programs are not available and AAP are used to help assess the quality/accuracy of laboratory test system performance. In essence, AAP are laboratory procedures by which Theranos defines an internal procedure to ensure quality/accuracy of our devices/methods. There are several methods that one can implemented for AAP, such as:

A. split sample analysis with reference or other laboratories;
B. split samples with an established in-house methods;
C. assayed material;
D. regional pools;
E. clinical validation by chart review; or

F. other suitable and documented means.

It is the responsibility of our CLIA lab to define such alternative assessment procedures, as applicable, in accordance with good clinical, scientific laboratory practice, and our business objectives.

I've recommended that we pursue options B, namely splitting samples where we take a venous sample and run it on the predicate and our LDT. The advantage of this approach is that we can use the predicate method for which PT is available to establish comparability for the Theranos LDT. It keeps the entire AAP process in-house for our LDTs.

Details to include in the SOP for AAP for each LDT:

- Frequency of AAP (2x per year; suggest scheduling it 1 month after predicate PT occurs)
- Predicate method for each LDT
- Sample type (suggest venous samples are used by default)
- Sample source (suggest in-house draws)
- Sample number: 10 different samples per AAP event per LDT (sample can be shared across multiple LDTs)
- Analytic range per LDT: if random samples do not cover the desired range based on an annual review, spike in or other specially collected samples may be used to supplement the data
- Acceptance criteria:
  - Each sample will be tested 3 times on the predicate method and the mean value considered the "truth"
  - Out of 10 samples tested, at least 8 LDT results must fall within the CLIA total error allowance compared to the predicate mean result
  - If <8 samples fall within the range, corrective actions need to be taken (follow typical SOP for PT)
- If a predicate method is not available, samples should be split with a reference lab

Please let me know if you have any questions.

-Daniel

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