Message

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**Sent:** 12/13/2013 5:24:46 PM
**To:** Pranav Patel [/o=theranos organization/ou=exchange administrative group (fydibohf23spdlt)/cn=recipients/cn=pranav patel268]; Adam Rosendorff [/o=theranos organization/ou=exchange administrative group (fydibohf23spdlt)/cn=recipients/cn=adam rosendorfd92]
**Subject:** naat validations

Pranav, Adam,

1. I believe that with regard to the idea of using a comparator method, only certain tests will require this. For many of the analytes, we can argue very well that there is no FDA approved molecular comparator method. An inspector could argue that we could have used culture as the "gold standard". However I believe that strong arguments could be made that what you did with PCR was a BETTER comparator for the test, since it is well established that PCR is more sensitive than culture for the vast majority of cases.

2. It might help if we had publications showing that the PCRs we have used as comparators have already been compared to a predicate tests, like culture or an FDA approved test. Because then we could validate to the comparator PCR and then argue that we have also validated TNAA against a "gold standard" method by way of the transitive axiom, so to speak. We could reference the publication in the documentation of the validation. It would look good too.

3. Tests where we should seek doing at minimum of 20 comparator tests (10 pos, 10 neg) would be: MTB, Chlamydia, N. gonorrhoeae, Influenza, HIV, Hep B and C, and maybe the respiratory viruses. These are the tests that will attract scrutiny, and are the tests for which we will have the highest patient test volumes. The other tests will be ordered very infrequently and have fewer, if any, predicate tests that are FDA approved.

4. Reference ranges are key portions of validations. But for qualitative tests with Boolean results, they are not relevant-- The ranges are "positive" or "negative". However I think we should at least state this somewhere in the validation, as some CLIA may seek a Reference Range section in the validations.

5. I believe that all validation documents for lab developed tests must be submitted to a governing body in New York before they can be used in New York, or on New York specimens. I believe it is called

"CLEP". We might need to submit these to them. Just a thought. Maybe they would be a good vetting agency prior to using these tests in CA or elsewhere.

6. In section 4 of each existing validation document, I would change the word "about" to "approximately". Nitpick, but "about" is more colloquial in my opinion and is replaced in scientific literature by "approximately". In general, I adhere to this.

7. In section 3, I of each existing validation document, I would change the word "run" to "performed" for reasons above.

8. In two occasions, at least, where I have been inspected by CLIA and validations were reviewed, the inspectors asked us to have a concluding statement that indicated that the Laboratory has determined that based upon the data, that the test is safe and effective for use with human beings / patients. These validations are excellent, but they are missing this element: The intro should state that the goal was to determine if the test is safe for use on people, and the conclusion should state that the test is safe for people.

9. There is no mention of extraction procedures in these validations. The TNAA was validated but for use with specimens that were extracted by some method. The extraction method is part of the analytical processs and therefore will need to be indicated in the validation. If we change extraction methods, we will have to do a mini-validation to show that it doesn't change the results.

10. It might benefit us if we indicate that the primers were constructed at Theranos.

Ok, hope this helps. I will work with Adam to start looking for comparators.