Message

From: Pranav Patel [/O=THERANOS ORGANIZATION/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=PRANAV PATEL268]
Sent: 12/14/2013 7:38:41 PM
To: Mark Pandori [/o=theranos organization/ou=exchange administrative group (fydibohf23spdlt)/cn=recipients/cn=mark pandori16d]
CC: Daniel Young [/o=theranos organization/ou=first administrative group/cn=recipients/cn=dyoung]
Subject: RE: b. parapertussi valid. sugg.

That will help a LOT!

Thanks

From: Mark Pandori
Sent: Saturday, December 14, 2013 11:38 AM
To: Pranav Patel
Cc: Daniel Young
Subject: RE: b. parapertussi valid. sugg.

Sure. And I can become involved in the incorporation / writing, if that would help.

Mark

From: Pranav Patel
Sent: Saturday, December 14, 2013 11:37 AM
To: Mark Pandori
Cc: Daniel Young
Subject: RE: b. parapertussi valid. sugg.

Hi,

These are great suggestions, can we touch base on these on Monday?

Thanks

Pranav

From: Mark Pandori
Sent: Saturday, December 14, 2013 11:29 AM
To: Pranav Patel
Cc: Daniel Young
Subject: b. parapertussi valid. sugg.

Pranav,

I've gone through what you sent me back. I will go through every validation in detail, like this, if the company deems this to be of

use. I really think these are solid,

but with some tweaking, they would become well referenced documents, air-tight against inspection

Also, I'd love to learn the TNAA, and even run it at some point. -- I would like to help with these validations

at all levels.

My suggestions for B. parapertussis validation:

1. We have to indicate in the methods, intro and conclusion the specimen types that were included in the validation (nasal exudates and nasal swabs). This indicates what the assay is validated on, and going forward, what specimen types we can accept and reject from customers.

2. Section 5. We should indicate that this is the LOWEST amount of analyte detectable with the given frequency.

3. Section 6. I think referring to the lowest titer specimen as a "high negative" is probably not appropriate. Maybe refer to the three levels as "very low", "low" and "high"

4. Were all specimens that came up negative on the TNAA tested for integrity by some internal control, like amplification of a housekeeping gene or something? Ultimately,these assays will require internal controls to assess specimen integrity so that a negative result can be relied upon .. and not the result of bad specimen collection or faulty extraction.

5. The false positive of a small amount of e.coli and holmseii is tiny red flag. But I believe a statement indicating that e.coli would not be resident in respiratory specimens would be good. Also, for holmseii, here are two references that indicate that it is quite rare and not a significant concern: http://www.ncbi.nlm.nih.gov/pubmed/?term=mazengia+holmesii http://www.ncbi.nlm.nih.gov/p

ubmed/?term=yih+holmesii holmseii comes up as an issue when people talk about rtpcr and b.p. but no one ever takes this into account. In general, I am a big supporter of having validations well referenced, scientifically.

6. The LOD of 1802 cfu/ml is rather insensitive compared to many RTPCR methods. However it is apparently sufficient for detection in physiologically relevant specimens, based on studies, literature: http://iai.asm.org/content/81/5/1390.long, http://jmm.sgmjournals.org/content/50/5/436.long

7. In terms of specificity, while the testing of related organisms is excellent, we should include in that section, the fact that 100 human specimens were tested and came up negative. Those presumably have the best representation of what would challenge the assay as they are real. 100 negative exudates and swabs from people were a great specificity challenge.

Mark Pandori