Message

From: Elizabeth Holmes [/O=THERANOS ORGANIZATION/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS/CN=EHOLMES]
Sent: 2/23/2012 10:29:06 PM
To: Daniel Young [dyoung@theranos.com]; Daniel Edlin [dedlin@theranos.com]
CC: Surekha Gangakhedkar [surekhag@theranos.com]
Subject: RE: Celgene assays

I am on board with this.

OK to send out with Daniel's comments below.

Elizabeth.

From: Daniel Young
Sent: Thursday, February 23, 2012 10:10 AM
To: Daniel Edlin; Elizabeth Holmes
Cc: Surekha Gangakhedkar
Subject: RE: Celgene assays

This new draft is fine. One suggestion:

- Change "Note that some sample processing will be required consistent with serum separation procedures." To "Note that the sample collection procedures at the clinical sites before shipping samples to Theranos will be consistent with typical serum separation procedures."

We will need Will Smith, Nalini Singh and Lisa Serme on the call to further discuss the sample collection process – so we can have this discussion t that time.

-Daniel

From: Daniel Edlin
Sent: Thursday, February 23, 2012 8:37 AM
To: Daniel Young; Elizabeth Holmes
Cc: Surekha Gangakhedkar
Subject: RE: Celgene assays

Thanks for the feedback, Daniel. Please see the revised email below.

I can also propose a call with Vicki tomorrow afternoon or next Friday regarding the sample collection process if you see fit.

Hi Vicki,

Please see below for our list of assays which we aim to deploy in your trial. We will be able to complete this list using 1mL of whole blood, as you previously suggested. Note that some sample processing will be required consistent with serum separation procedures.

1) ACE-011
2) BSAP
3) EPO*
4) Estradiol
5) FGF-23*
6) FSH
7) Hepcidin*
8) HGB
9) IGF-1
10) LH
11) Osteocalcin*
12) PTH*
13) Testosterone (free)
14) Testosterone (total)
15) TRAP5b*
16) Vit.D 25*

** Indicates which assays will be run in the Theranos CLIA Lab. Others may be transitioned into the CLIA lab over time.*

We are also preparing validation reports which we plan to send you over the coming weeks.

With regards to a call with Ron and Nianhang, we will be available on the following dates. Please let us know what works for you, as well as when you would be available to have a call with Steve, Will Smith, Nalini Singh and Lisa Serme.

- Friday, 3/2: 8AM-12PM PST, 3PM-4PM PST
- Monday, 3/5: 8AM-12PM PST, 3PM-4PM PST
- Tuesday, 3/6: 8AM-12PM PST, 3PM-4:30PM PST

If you would, please send us a copy of the final project protocol for our reference, and do let us know if you have any questions with the assay list proposal. Thank you, and we look forward to your feedback.

Best regards,

Dan

From: Daniel Young
Sent: Thursday, February 23, 2012 10:21 AM
To: Daniel Edlin; Elizabeth Holmes
Cc: Surekha Gangakhedkar
Subject: RE: Celgene assays

Comments on the draft:

- We should not distinguish if we are using Theranos devices/chemistry or kits. We can just star "*" some assays as ones that will be run in the Theranos CLIA lab (and possibly note that the others will be transitioned into the CLIA lab over time)
- "Please see below for our list of assays that we plan to develop by March." We should not mention this here, but just say that we aim to deploy in their trial. We do not yet have a firm timeline for validating all these tests.
- We should just mention that some sample processing will be required consistent with serum separation procedures, not detail the three vessels etc at this time.
- "We are preparing validation reports and will be able to send you reports for HGB, Testosterone (total and free), and BSAP this week, with more following next week." We should not make this so specific, as the Hgb report is "pre-validation" as it has not been tested on the Theranos platform (more on this below); free Testosterone requires ARUP testing, and the BSAP requires a few additions that are being evaluated.
- "If needed, we can aliquot the samples to you for retroactive assaying." Not clear what is meant by this. The idea is that we may be able to archive a portion of the sample for testing later by us after our assay is fully validated. I would not get into this option with them now either.

Additional thoughts:

- HGB: there are three options that I think we should discuss internally:

1. the current CLIA method requires 200 uL to run this test. The sample should be refrigerated, and is stable for 24 hours. (We can also offer to run their CBC assay to make greater use of the 200uL, but they will not be measuring CBC as often as Hgb)
2. To validate that Theranos assay, we would have to perform a large validation of the Theranos assay on the Theranos system (in CLIA or out).
3. Alternatively, we explore using a Hgb kit that is FDA approved that can be run on the plate reader (that Surekha is looking into)

- I wanted to also note that that I do not have a copy of Celgene's final protocol (we should get a copy from them ASAP.) However, typically they will not measure each of these analytes every time they collect a patient sample – rather some analytes will be measured more frequently than others. So there are some alternative options for us to consider regarding the sample collection process:

1. We collect the same total amount of sample each time and split into 3 vessels in the same manner each time a sample is drawn for Theranos to keep things simple for the clinics. When all tests are not requested by Celgene for a particular sample draw, this would provide additional sample for Theranos if we should need it for retesting or to run duplicates.

2. We always draw 1mL for Theranos testing purposes, but how the sample is split into three will depend on which tests are to be performed by us for that particular sample.

3. We will need to have a more detailed protocol that spells a specific sample collection process depending on the set of tests to be performed for each particular draw. This option would never draw more blood than is required, but becomes more complex operationally.

I favor option 1, but at some point we need to discuss this with Celgene.

-Daniel

From: Daniel Edlin
Sent: Thursday, February 23, 2012 5:44 AM
To: Elizabeth Holmes; Daniel Young
Cc: Surekha Gangakhedkar
Subject: RE: Celgene assays

Good morning,

Please see below a draft for Vicki, for your review. This considers that we will not need more than 1mL of whole blood.

Hi Vicki,

Please see below for our list of assays that we plan to develop by March. We will be able to complete this list using 1mL of whole blood, as you previously suggested. Note that we will be testing these assays using Theranos devices as well as third party kits in our CLIA lab. As such, we request that the sample be spun before shipment into three tubes:

- Whole blood (for Theranos developed assays)
- Serum (separated from clot and frozen immediately) for kit assays
- Serum (separated from clot and frozen immediately) with protease inhibitor for Osteocalcin kit assay

Assays developed on Theranos Devices:

1) ACE-011
2) FSH
3) LH
4) Estradiol
5) IGF-1
6) BSAP
7) Testosterone (total)
8) Testosterone (free)
9) HGB

Assays using Third Party Kits through Theranos' CLIA lab:

10) EPO
11) PTH
12) Vid D 25
13) TRAP5b
14) Osteocalcin
15) Hepcidin
16) FGF-23

We are preparing validation reports and will be able to send you reports for HGB, Testosterone (total and free), and BSAP this week, with more following next week. If needed, we can aliquot the samples to you for retroactive assaying.

With regards to a call with Ron and Nianhang, we will be available on the following dates. Please let us know what works for you, as well as when you would be available to have a call with Steve, Will Smith, Nalini Singh and Lisa Serme.

- Friday, 3/2: 8AM-12PM PST, 3PM-4PM PST
- Monday, 3/5: 8AM-12PM PST, 3PM-4PM PST
- Tuesday, 3/6: 8AM-12PM PST, 3PM-4:30PM PST

Please let us know if you have any questions with the assay list proposal, and we look forward to your feedback.

Best regards,

Dan

From: Elizabeth Holmes
Sent: Thursday, February 23, 2012 1:40 AM
To: Daniel Young
Cc: Surekha Gangakhedkar; Daniel Edlin
Subject: RE: Celgene assays

OK – Dan, in parallel with this follow up with Surekha, please prepare a draft to Vicki to send out as early as possible tomorrow morning after we've reviewed and signed off on it. The draft should confirm the sample volume and list of assays that will be available, incduing the breakdown of which ones will be done through the CLIA lab. You can mention validation reports are coming (starting this week with the ones discussed) and will be following next week and the week after; if needed we can aliquot the samples for retroactive assaying but we don't think we'll need to assuming the below plan gets implemented asap.

From: Daniel Young
Sent: Wednesday, February 22, 2012 10:33 PM

To: Elizabeth Holmes
Cc: Surekha Gangakhedkar; Daniel Edlin
Subject: RE: Celgene assays

Yes, the sample would need to be split (spun) pre-shipment. The clinical sites typically do this sort of sample prep for the lab send-outs (though of course it is not preferred from our standpoint).

-Daniel

From: Elizabeth Holmes
Sent: Wednesday, February 22, 2012 10:19 PM
To: Daniel Young
Cc: Surekha Gangakhedkar; Daniel Edlin
Subject: Re: Celgene assays

Are you assuming sample is split pre-shipment

On Feb 22, 2012, at 10:17 PM, "Daniel Young" <dyoung@theranos.com> wrote:

Hi all,

In summary, to run 16 assays for Celgene, we need to collect:

- Maximum sample requirement is 900 uL of whole blood; so we are ok with 1 mL total whole blood draw as mentioned by Celgene as being available to us
- The total sample will be split into three tubes:
  - Whole blood (for Theranos developed assays)
  - Serum (separated from clot and frozen immediately) for kit assays
  - Serum (separated from clot and frozen immediately) with protease inhibitor for osteocalcin kit assay

Additional details for internal communication only and outstanding questions to finalize our plans:

Assays to be run on Theranos devices:

- Cartridge #1: ACE-011; whole blood: 25 uL
- Cartridge #2: FSH + LH; whole blood: 25 uL (or 50 uL WB if running serum)
- Cartridge #3: Estradiol; whole blood: 25 uL (or 50 uL WB if running serum)
- Cartridge #4 : IGF-1 + BSAP: whole blood: 25 uL (or 50 uL WB if running serum)
- Cartridge #5: Testosterone (total and free): whole blood; 25 uL (or 50 uL WB if running serum)
- **Questions: Surekha, please confirm preferred anticoagulant and storage requirements for whole blood and serum for these assays**

Third Party Kits (we only need abbreviated validation reports in Theranos CLIA lab if these kits are already FDA approved, including precision and limited clinical samples; we can run these kits on any plate reader and the device qualification will be part of the kit validation process in the CLIA lab;):

- EPO: R&D or ALPCO kit, serum, frozen, (200uL WB)
- PTH: ALPCO kit, serum, frozen, (100uL WB)
- Vit D 25: IDS kit, serum, frozen, (50uL WB)
- TRAP5b: MicroVue Quidel kit; serum, says 2-8 deg, **but assume frozen is ok**; (100uL WB)
- Osteocalcin: Diasource or IBL kit; serum, **need additional protease inhib added**; says 2-8 deg, but assume frozen is ok; (50uL WB)
- Hepcidin: DRG kit, serum, frozen (50uL WB)
- FGF-23; Millipore kit; serum, frozen (100uL WB); **EDTA required?**
- **Questions:**

  - **Surekha please confirm for the above kits the preferred anticoagulant; I only saw it mentioned for FGF-23, and most plasma separator tubes are Li Heparin.**
  - **Surekha, what is your preferred plate reader for the CLIA lab to run these kits (also, please consider potential use by Paul's team and the CLIA lab at large)? We need to order this device ASAP.**
  - **Surekha, please confirm if each of these kits are already FDA approved.**

Other:

- HGB: Theranos color assay not fully validated yet on a Theranos device (only pre-validation); We need whole blood for this assay; 25uL or less on Theranos system (TBD depending on cartridge configuration which is not yet determined); or we can use the CLIA validated HGB assay on the predicate hematology analyzer, but the sample requirement will be more; I am collecting this remaining data now

Thanks,

Daniel

From: Surekha Gangakhedkar
Sent: Tuesday, February 21, 2012 9:39 AM
To: Daniel Young; Elizabeth Holmes
Cc: Daniel Edlin
Subject: RE: Celgene assays

My responses below:

From: Elizabeth Holmes
Sent: Monday, February 20, 2012 9:54 PM
To: Daniel Young
Cc: Daniel Edlin; Surekha Gangakhedkar
Subject: Re: Celgene assays

Also, how fast is current thinking on time to validation report from our CLIA lab?

On Feb 18, 2012, at 5:30 PM, "Daniel Young" <dyoung@theranos.com> wrote:

Based on the latest info, I think we may be able to perform the following tests at Theranos with 1ml of whole blood, but some questions still remain.

Assays on Theranos devices:

- ACE-011
- FSH
- LH
- Estradiol
- IGF-1
- BSAP: **Surekha, can IGF-1 and BSAP be run on the same cartridge with 20uL of whole blood?** Confirming on this, can be possible.
- Testosterone (total and free): **Surekha, can you confirm who much sample and type is required?** There is a multiplex protocol for TTest and free Test on the 3.0 cartridge and it will take 20 uL of W.B/Serum/Plasma. All three sample types were tested during development
- HGB: color assay

Kits:

- EPO
- PTH
- Vit D 25
- TRAP5b
- Osteocalcin
- FGF23
- Hepcidin: **Surekha, I checked DRG's kit, and they require serum only. Is there another kit, or can we use Intrinsic Lifesciences?** Mybiosource has a kit for serum & plasma, It is not as sensitive as the DRG kit. They are distributors only so difficult to find out who the MFG is. For Instrinsic lifesciences we may have to ship samples to their site.

Also, Surekha is exploring the storage requirements in whole blood (temp, time, etc before separation of plasma). Note that the prior assays developed for the Theranos system for Celgene were for whole blood samples. Surekha, did you validate for plasma at the same time? Assays were validated for Serum & plasma too since that was the available matrix for clinicals.

Thanks,

Daniel Young, PhD
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