To: Elizabeth Holmes[eholmes@theranos.com]
From: Sunny Balwani
Sent: Tue 10/28/2014 1:24:18 AM
Importance: Normal
Subject: FW: Critical ISEs
Received: Tue 10/28/2014 1:24:17 AM

we need to prioritize this asap. as this is causing us a lot of issues. we need CTN issue solved.

From: Nishit Doshi
Sent: Monday, October 27, 2014 6:17 PM
To: Sunny Balwani; Tina Lin; Daniel Young
Subject: RE: Critical ISEs

Hi,

Moving to XPTs is an option we should definitely explore but I think our biggest pain point in Normandy is amount of plasma recovered. Currently we are only able to use ~ 50% of plasma volume (with automated liquid transfer with Tecans).

An increase in plasma volume recovered will help with the following:

- Possibility to reduce our dilution factor resulting in higher analyte sensitivity. This should greatly help ISEs and some of the other GC assays.

- Tecan dilution errors. Currently we are only going 0.1 mm inside the surface of liquid for aspiration and we still see the nozzle hit the gel in some cases. This will also reduce short sampling issues on Advia.

- Ability to rerun in some cases.

One option that we have discussed previously is to move to a single capillary + thin nanotainer CTN which according to my calculations can reduce the overage by upto 70%. This will significantly change the way we process samples in Normandy. Please let me know if this is a feasible option. We can still keep the nominal design with dual capillary but use this for single anticoagulant.

Thanks,

Nishit

From: Nishit Doshi
Sent: Monday, October 27, 2014 4:59 PM
To: Sunny Balwani; Tina Lin; Daniel Young
Subject: RE: Critical ISEs

We will start a proof-of-concept study later this week to evaluate if there will be any significant challenges in transferring the P-protocols to XPTs.

Thanks,

Nishit

From: Sunny Balwani
Sent: Monday, October 27, 2014 4:39 PM
To: Tina Lin; Nishit Doshi; Daniel Young
Subject: RE: Critical ISEs

seems like they will help. don't know if they will completely solve the problems. we can bring in 1 XPT asap and ask Sam to bring up our protocols there and start running assays and bring it live – keep it for 30 days. and if everything looks good, swap out 1800s and send thm to PHX.

From: Tina Lin
Sent: Monday, October 27, 2014 4:38 PM
To: Nishit Doshi; Sunny Balwani; Daniel Young
Subject: RE: Critical ISEs

We should also consider whether XPT will solve the problems we're currently seeing...

Thanks,

Tina

From: Nishit Doshi
Sent: Monday, October 27, 2014 4:37 PM
To: Sunny Balwani; Daniel Young; Tina Lin
Subject: RE: Critical ISEs

Hi Sunny,

Can you please let us know the timeline for this.

Thanks,

Nishit

From: Sunny Balwani
Sent: Monday, October 27, 2014 4:36 PM
To: Nishit Doshi; Daniel Young; Tina Lin
Subject: RE: Critical ISEs

the reason we need XPT is so we can send the 1800s to AZ as all the AZ employees are trained on 1800s and they can easily go on the aptio.

From: Nishit Doshi
Sent: Monday, October 27, 2014 4:34 PM
To: Sunny Balwani; Daniel Young; Tina Lin
Cc: Elizabeth Holmes
Subject: RE: Critical ISEs

That is because ISEs are run separately from other CMP assays.

So if it's a dilution error or short sample on ISE T-cup, all ISEs should be voided.

If it's a dilution error or short sample on Non ISE T-cup, all non ISE assays in CMP should be voided.

If it's a sample integrity concern, it depends on which side was sampled for ISE or non-ISE assays (it could be just one side or sampled from both sides).

I agree with expediting the bring up XPT. Once we settle down here, that will be the highest priority.

Thanks

Nishit

From: Sunny Balwani
Sent: Monday, October 27, 2014 4:29 PM
To: Nishit Doshi; Daniel Young; Tina Lin
Cc: Elizabeth Holmes
Subject: RE: Critical ISEs

but why specific to certain ranges for certain assays. I agree with the following 3 cases.

moreover, in the light of this, I think we need to expedite bring up of XPT in Normandy and swap the 1800s to Arizona. we have trained them on 1800s anyway.

From: Nishit Doshi
Sent: Monday, October 27, 2014 3:48 PM
To: Sunny Balwani; Daniel Young; Tina Lin
Cc: Elizabeth Holmes
Subject: RE: Critical ISEs

Hi Sunny,

For ISEs, sometime results need to be voided if it is a process issue or sample integrity issue.

We have asked CLIA to void the results in the following cases:

1) Sample integrity issues. This could involve inteference, clots, bridge features etc

2) Short sampling on Advia

3) Dilution error in Tecan

ISEs are run after other assays ordered in CMP. So if there was enough sample to run other assays and if there was a dilution error or short sampling on Advia, then other assays will be released but not ISEs.

Thanks

Nishit

From: Sunny Balwani
Sent: Monday, October 27, 2014 3:40 PM
To: Daniel Young; Nishit Doshi; Tina Lin
Cc: Elizabeth Holmes
Subject: RE: Critical ISEs

I have not heard any issues on Advias or ISEs but I know there are issues that are now causing us a lot of pain.

Nishit/Tina. can I get an update on this? none of us are aware of these policy changes around so critical.

From: Daniel Young

Sent: Monday, October 27, 2014 3:37 PM
To: Sunny Balwani; Nishit Doshi
Cc: Elizabeth Holmes
Subject: RE: Critical ISEs

I have not heard about high frequency of critical ISEs. There have been some bring-up challenges of the Advia's and Nishit and team have been recalibrating to bring them in line. This was not specific to ISE's, however.

From: Sunny Balwani
Sent: Monday, October 27, 2014 3:26 PM
To: Daniel Young; Nishit Doshi
Cc: Elizabeth Holmes
Subject: FW: Critical ISEs
Importance: High

can I get an update on this? we are beginning to see all these issues and I am not getting this information from either of you or Tina. When I hear ISE issues from CLIA and not from anyone else, it makes us look bad. there is growing suspicion in CLIA that the non-CLIA team involved with CLIA lab tries to hide information from Elizabeth and myself and I know that's not the case but we need to know about problems in real time so we can push on all fronts to solve the problem.

when did the following problem surface. I assume this is only on T Protocol and not on the predicate protocol.

From: Adam Rosendorff
Sent: Monday, October 27, 2014 3:20 PM
To: Sunny Balwani
Cc: Elizabeth Holmes
Subject: FW: Critical ISEs

Hi

I wanted to bring this important issue to your attention. Right now, after much cooperative discussion between CLIA and R&D and thought, if the CTN sodium is below 120mM or above 160mM we end up voiding the result, because we have no way of knowing for sure whether the result is truly abnormal or artifactual to the assay, or related to a specimen integrity issue.

Unfortunately, there are 2 conditions: Diabetes Insipidus and SIADH, where patients can live quite happily with a "Critical" sodium of <120mM or >160mM.

The patient below has diabetes insipidus which normally results in high sodium, but is probably being treated with DDAVP, which lowers the sodium. Therefore accurate measurement of sodium is important for this patient. I am not sure of the clinical value of a sodium assay, in which the only time we can report it is when it is *not critical*, and the very situations that require accurate measurement and reporting of abnormal of sodium results are voided. All of us in CLIA share the same concerns. How is the 4S Sodium doing? Maybe we can use the 4S for ISEs?

Thanks,

Adam

From: Anam Khan
Sent: Monday, October 27, 2014 3:08 PM
To: Adam Rosendorff
Subject: Critical ISEs

Hi Adam,

Griselda Gutierrez's physician called today asking why ISEs weren't included on her final report. Only Comp was ordered, but ISEs were voided, so I explained that the patient would need to come back in to be redrawn. The lady I spoke to mentioned that they really needed the Sodium result because the patient had low Sodium levels and that's what they were checking. I noticed the Sodium results were critical low so I assume that's why we voided it. Is it possible that that was the true value? If she comes in again and the value is still critical low, will it just be voided again?

Thanks,

Anam