Message

From: Adam Rosendorff [/O=THERANOS ORGANIZATION/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=ADAM ROSENDORFD92]
Sent: 4/1/2014 8:36:17 PM
To: Daniel Young [/o=theranos organization/ou=first administrative group/cn=recipients/cn=dyoung]
CC: Sunny Balwani [/o=theranos organization/ou=first administrative group/cn=recipients/cn=sbalwani]; Mark Pandori [/o=theranos organization/ou=exchange administrative group (fydibohf23spdlt)/cn=recipients/cn=mark pandori16d]
Subject: RE: CO2 (Bicarbonate) issue

Daniel

Please let us know when the bicarbonate correction is live in LIS.

Thanks,

Adam

From: Adam Rosendorff
Sent: Monday, March 31, 2014 8:52 PM
To: Daniel Young
Cc: Sunny Balwani; Mark Pandori
Subject: RE: CO2 (Bicarbonate) issue

Ok thanks- so I guess the 90% recovery is after bias correction- if this is the case then 20 normals most likely would all be within the predicate RR for HCO3?

We can discuss further tomorrow.

Best,

Adam

From: Daniel Young
Sent: Monday, March 31, 2014 8:47 PM
To: Adam Rosendorff
Cc: Sunny Balwani; Mark Pandori
Subject: RE: CO2 (Bicarbonate) issue

Thanks – I have been looking at the CO2 data you sent me today.

We are also evaluating the processing times in the lab (timing the processing steps), as this can have a big impact on CO2. The data from our in-house AAP dry runs (now 7 days of testing) looks ok overall – with an average of about 90% recovery. With a few more days of testing, I think we will have a good data set from which to make a decision.

Finally, moving forwards, we will apply a bias correction for CO2 fingerstick samples such that we report the results in the venous "equivalent" concentration. In this case, the reference range would not need to be changed.

Please let me know if you have any questions.

-Daniel

From: Adam Rosendorff
Sent: Monday, March 31, 2014 8:37 PM
To: Daniel Young
Cc: Sunny Balwani; Mark Pandori
Subject: RE: CO2 (Bicarbonate) issue

Pardon me I meant "bias observed between predicate and theranos methods."

From: Adam Rosendorff
Sent: Monday, March 31, 2014 8:36 PM
To: Daniel Young
Cc: Sunny Balwani; Mark Pandori
Subject: FW: CO2 (Bicarbonate) issue

Daniel

For March 2014 our central 95% for C02 was: 13.5-22.9mM (n=135)., compared to our reference range of 19-33mM as stated in the validation report. On the 135 data points, Zero (0) values were greater than 33mM and 81 values were less than 19. Using a parametric method, taking +/-2SD as the cutoff, the reference range would be 13.5-23.5mM. December only has 22 data points, and I am still waiting on January and February.

Based on this information, I suggest a new Bicarbonate reference range for our method of 13.5-22.9mM. The RR in the validation report was a transferred range based on the bias observed between V and FS methods. Is there any further transformation that is applied to the data before we see it in LIS?

Thanks,

Adam

From: Adam Rosendorff
Sent: Monday, March 31, 2014 12:51 PM
To: Sunny Balwani
Cc: Mark Pandori
Subject: RE: CO2 (Bicarbonate) issue

Thanks- I will review with Langley what our Levey-Jennings data looks like for both ADVIAs.

Adam

From: Sunny Balwani
Sent: Monday, March 31, 2014 12:49 PM
To: Adam Rosendorff
Cc: Mark Pandori
Subject: RE: CO2 (Bicarbonate) issue

We had generated tremendous amount of data on this and addresses this very point. I am meeting with the team to address this email and evaluate why we are seeing the 30% lower number and why if we have been seeing this for 6 days by R&D this didn't get flagged.

In the meantime, have we run this on both advias to make sure this is not an Advia issue?

Thanks.

From: Adam Rosendorff
Sent: Monday, March 31, 2014 12:38 PM
To: Sunny Balwani
Cc: Mark Pandori
Subject: CO2 (Bicarbonate) issue
Importance: High

Hi Sunny

At least 2/3 of our patients are reading below the normal range for bicarbonate (19-33 mM for CTNs). I do not expect outpatients to have abnormal bicarb values. Curtis's study with 6 days of data (24 data points) also shows that Bicarb is reading ~30% lower than matched venous, even after correction of the value for bias. The current best explanation is that there is rapid loss of CO2 from the CTNs during transport/processing. It is known that there is a loss of 6mM of bicarbonate for every hour a vacutainer is left open. Because of the small volumes we are dealing with, the rate of loss in our case is probably greater. ARUP specimen stability is 24hrs refrigerated. Our current validation report states that:

- Plasma samples for Bicarbonate analysis are stable sealed for 2 weeks at 2-8 °C.

However the ADVIA package insert says:

- Serum or lithium heparin plasma may be stored at 2-8°C for 7 days or at room temperature for up to 24 hours.

I wonder if Paul has any data on outgassing that we can use to decide on what our best course of action is.

CLSes have been asking me what we should do about Bicarb reporting. On the one hand, physicians are aware that if they want an accurate bicarb reading, they need to get the sample to the lab stat.

So far we have not had any phone calls regarding bicarb values- I think docs know that it's a highly context-dependant assay.

Your comments would be welcome.

Adam

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