Ortho Clinical Diagnostics

PART OF THE Johnson & Johnson FAMILY OF COMPANIES

October xx, 2013

URGENT FIELD SAFETY NOTICE

VITROS® Chemistry Products Na^+ Slides (Product Code 8379034)
VITROS® Chemistry Products Calibrator Kit 2 (Product Code 1662659)

Dear Customer,

As part of a Field Safety Corrective Action, this is to inform you of an urgent field safety notice involving the following products:

Product Code	Name of Product	Affected Generations (GENs)/Lots	Expiry Dates (YYYY-MM-DD)
8379034	VITROS® Chemistry Products Na^+ Slides	**GENs 7 - 13**	2013-11-01 thru 2015-01-01
1662659	VITROS® Chemistry Products Calibrator Kit 2	**Lot 212**	2014-08-31
		Lot 292	2014-02-28

The VITROS Na^+ Slide method is performed using VITROS® Na^+ Slides and VITROS® Chemistry Products Calibrator Kit 2 on VITROS® 250/350/5,1 FS and 4600 Chemistry Systems and the VITROS® 5600 Integrated System.

Description of Issue

Ortho Clinical Diagnostics (OCD) has confirmed that positively biased serum or plasma sample results may occur when using VITROS® Na^+ Slides, GENs 7 - 13. Our data determined that the largest bias was observed when using slides from GENs 7 - 13 when calibrated with VITROS® Calibrator Kit 2, Lots 212 and 292.

This notification provides information regarding the effect of the bias on your patient samples, quality control results, and calculated or derived tests such as Osmolality Gap, Osmolality, and Anion Gap.

Impact to Results

The amount of bias in the VITROS® Na^+ method is dependent upon multiple sources of variability that include but are not limited to slide GEN, Calibrator Kit lot, calibration event and VITROS® System. It is important to note that not all combinations of VITROS® Na+ Slide GENs and Calibrator Kit lots resulted in biased Na^+ results.

The table shows the bias observed in our investigation across the measuring range*:

Observed Bias for Serum Samples using VITROS® Na^+ Slides, GENs 7-13	
Overall Average (Mean) Bias	Range of Bias
+1.5 mmol/L	(-0.8) up to (+4.3) mmol/L
*VITROS® Na^+ Slide Measuring Range for serum or plasma samples is 75.0 - 250.0 mmol/L VITROS® Na^+ Slide Reference Interval is 137 - 145 mmol/L	

Our testing confirmed that serum and plasma samples are similarly affected by this issue. If this issue occurs, Na^+ results for serum/plasma samples will be positively biased and quality control fluids may be outside of the expected Range of Means. The bias can cause an increase in your patient means as well as in the number of individual patient results outside of the reference interval for your laboratory.

NOTE: Urine results generated using VITROS® Na^+ Slides are not affected by this issue.

Impact to Results (Continued)

Depending upon the magnitude of the bias, the Osmolality, Osmolality Gap and Anion Gap calculations will also be affected as described below:

- A positively biased serum Na^+ result will cause a *positively* biased calculated Osmolality, resulting in a *negatively* biased Osmolality Gap.
- A positively biased serum Na^+ result will cause a *positively* biased Anion Gap.

The VITROS® System and the VITROS® Assay Summary information sheet contain the following calculations:

(Na^+ (mmol/L) x 1.86) + (GLU mmol/L) + (BUN mmol/L) = OSMO

or

(Na^+ (mmol/L) x 1.86) + (GLU (mg/dL) /18) + (BUN (mg/dL) /2.8) = OSMO

When using either of these formulas, a positively biased serum Na^+ result would be multiplied by 1.86 and included in the calculated Osmolality. Therefore, any bias would be magnified in the calculated Osmolality when compared to the measured Osmolality.

There are *many* different formulas used to calculate Osmolality, some may not include a Na^+ result. The effect of a positively biased Na^+ result would be dependent on the multiplier used in the specific calculation.

The Osmolality Gap is calculated by:

Measured Osmolality - Calculated Osmolality = Osmolality Gap

For detailed information regarding the potential impact of a positively biased result, refer to the Questions and Answers 1, 2 & 3 located on page four.

Summary Information & Actions

Calculated Serum Osmolality: Since positively biased results may affect your calculated serum Osmolality and Osmolality Gap, please inform your laboratory medical director and physicians/health care professionals of this issue to determine the appropriate course of action for your facility.

VITROS® Calibrator Kit 2 (Lots 212 & 292): Since the largest bias observed was using VITROS® Na^+ Slides calibrated with Lots 212 and 292, we will replace your remaining inventory for these calibrator lots. It is acceptable to use Lot 212 or 292 to calibrate VITROS® CHOL, Cl^-, ECO_2, and TRIG Slides until your replacement product arrives.

NOTE: *VITROS® K^+ Slides are used to blank VITROS® Na^+ Slide urine results and must be calibrated with the same lot of VITROS® Calibrator Kit 2. Although VITROS® K^+ Slides are not impacted by this issue, do not use Lots 212 or 292 for future calibration events of VITROS® Na^+ or K^+ Slides.*

VITROS® Na^+ Slides (GENs 7 - 13): Our investigation confirmed that VITROS® Na^+ Slides, GENs 7-13 meet our existing product performance specifications. It is acceptable to continue to use your remaining inventory of GENs 7 – 13 providing all of the following criteria are met:

1. Calibration is successful
2. Quality control results are within the established Range of Means/acceptable limits
3. Distribution of normal results for serum or plasma samples are centered within the established reference interval for your laboratory.

If present, the bias can cause an increase in your patient means as well as in the number of individual patient results outside of the reference interval for your laboratory. If any of the above criteria are not met, OCD will replace your remaining inventory of GENs 7 - 13.

Corrective Actions: Based on internal studies, we have taken actions to reduce variability in our release process. Our root cause analysis is ongoing and we will implement additional corrective and preventive actions upon completion of our investigation.

Required Actions

- Inform your laboratory medical director and physicians/health care professionals regarding the effect that positively biased results may have on your calculated Osmolality and Osmolality Gap for the appropriate course of action for your facility.
- Do **not** use VITROS® Calibrator Kit 2, Lots 212 or 292 for future calibration of VITROS® Na^+ or K^+ Slides. It is acceptable to use Lot 212 or 292 to calibrate VITROS® CHOL, Cl^-, ECO_2, and TRIG Slides until your replacement product arrives.
- Continue to use your remaining inventory of VITROS® Na^+ Slides, GENs 7 - 13, if it meets all three of the acceptable criteria listed on page two. Product replacement is available upon request.
- Complete the Confirmation of Receipt Form and return by October xx, 2013.
- Place this notification near each VITROS® System that processes VITROS® Na^+ Slides.
- Forward this information if you have distributed this product outside of your facility.

Contact Information

We have anticipated some questions you may have in the following Questions and Answers section. If you have any questions regarding this notification, please call Customer Technical Service at *insert appropriate number.*

Sincerely,

insert appropriate name
insert appropriate title

Questions and Answers

1. How would a positively biased VITROS® Na^+ Slide result affect an Osmolality?

A positively biased serum Na^+ result would generate a positively biased calculated Osmolality and lead to a negatively biased Osmolality Gap, which could potentially delay the diagnosis of alcohol intoxication (i.e., methanol, ethylene glycol, isopropanol, ethanol). However, other laboratory tests are typically ordered and together with patient's history, clinical signs and symptoms are used for the diagnosis.

2. Are previously reported results using VITROS® Na^+ Slides affected?

If the bias had occurred, it would have caused an increase in your patient means as well as in the number of individual patient results outside of the reference interval for your laboratory. VITROS® Na^+ Slides, GENs 7 - 13 have the potential to generate positively biased serum and plasma results, but they continue to meet our product performance specifications. Serum/plasma Na^+ results are typically used in conjunction with a patient's history, clinical signs and symptoms, physical examination and results from other electrolyte assays. Mild or moderate hyponatremia, especially in a chronic setting, may not be symptomatic and may not be diagnosed by other means. Please consult your Medical Director to determine the impact to your previously reported results.

3. How would a positively biased VITROS® Na^+ Slide result affect an Anion Gap?

A positively biased Na^+ result will generate a positively biased anion gap. An unusually high anion gap would prompt questioning and additional tests to determine the underlying cause of the elevated Anion Gap.

4. How is the Anion Gap calculated on VITROS® Systems?

The Anion Gap can be calculated <u>with</u> or <u>without</u> a K^+ result as follows:

$$(Na+ + K+) - (Cl^- + ECO_2)$$

or

$$(Na+) - (Cl^- + ECO_2)$$

5. How is Osmolality calculated?

The VITROS® System and VITROS® Assay Summary information sheet contain the following calculations:

(Na^+ (mmol/L) **x 1.86) + (GLU** mmol/L**) + (BUN** mmol/L**) = OSMO**

or

(Na^+ (mmol/L) **x 1.86) + (GLU** (mg/dL) **/18) + (BUN** (mg/dL) **/2.8) = OSMO**

When using either of these formulas, a positively biased serum Na^+ result would be multiplied by 1.86 and included in the calculated Osmolality. Therefore any bias would be magnified in the calculated Osmolatity when compared to the measured Osmolality.

There are *many* different formulas used to calculate osmolality, not all include a Na^+ result. The effect of a positively biased Na+ result would be dependent on the multiplier used in the specific calculation.

6. What is an Osmolality gap?

There are two types of Osmolality, <u>calculated</u> Osmolality (refer to Question 5) and <u>measured</u> Osmolality. The Osmolality Gap is the difference between the Osmolality (<u>measured</u> by an Osmometer) and the osmolality calculated from Na^+, GLU, and BUN results.

Measured Osmolality - Calculated Osmolality = Osmolality Gap

Questions and Answers (Continued)

7. Does this issue affect urine results using VITROS® Na^+ Slides?

No, this issue only affects the serum or plasma results.

8. Are VITROS® K^+ or Cl^- Slides affected by this issue?

The positive bias only affects VITROS® Na^+ Slide serum results.

9. If I also have a VITROS® DT60/DT60II Systems, are my Na^+ results affected by this issue?

No, we have confirmed that VITROS® Na^+ DT Slides processed on the VITROS® DT60/DT60II Systems are not affected by this issue.

10. Will service on my VITROS® System resolve/eliminate the bias in Na+ results?

It is unlikely that service to your VITROS® System will resolve this issue. Our data indicates this is assay-related depending upon the combination of *specific* VITROS® Na^+ Slide GENs and Calibrator Kit lots.

11. Can I continue to use VITROS® Calibrator Kit 2, Lots 212 & 292 to calibrate other assays?

Yes, it is acceptable to use Lot 212 or 292 to calibrate VITROS® CHOL, Cl^-, ECO_2, and TRIG Slides until your replacement calibrator kit arrives.

NOTE: *VITROS® K^+ Slides are used to blank VITROS® Na^+ Slide urine results and must be calibrated with the same lot of VITROS® Calibrator Kit 2. Although VITROS® K^+ Slides are not impacted by this issue, do not use Lots 212 or 292 for future calibration events of VITROS® Na^+ or K^+ Slides.*

We have an adequate inventory of calibrator kits and we will send your order upon receipt of your Confirmation of Receipt form.

12. If I am currently using VITROS® Na^+ Slides GENs 7 - 13, can I get replacement for my remaining inventory?

Our investigation confirmed that VITROS® Na^+ Slides, GENs 7- 13 meet our existing product performance specifications. It is acceptable to continue to use your remaining inventory of GENs 7 – 13 providing all of the following criteria are met:

1. Calibration is successful
2. Quality control results are within the established Range of Means/acceptable limits
3. Distribution of normal results for serum or plasma samples are centered within the established reference interval for your laboratory.

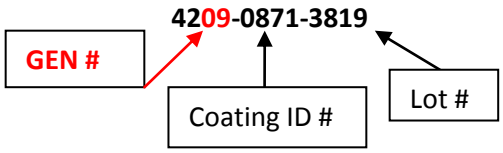
If any of the above criteria are not met, OCD will replace your remaining inventory of GENs 7 - 13. Please choose this option on the Confirmation of Receipt form.

We have added additional manufacturing events for VITROS® Na^+ Slides to our production schedule and we will continue to do so until all orders are fulfilled. In order to provide product for all customers, product allocation (i.e., partial shipments) may be necessary.

Questions and Answers (Continued)

13. How can I determine the GEN Number for the VITROS® Na+ Slides in my inventory?

Use the example below to determine the GEN on the product packaging:



14. When will this issue be resolved?

Based on internal studies, we have taken actions to reduce variability in our release process. Our root cause analysis is ongoing and we will implement additional corrective and preventive actions upon completion of our investigation.

Confirmation of Receipt - Important Response Required

URGENT FIELD SAFETY NOTICE

VITROS® Chemistry Products Na^+ Slides (Product Code 8379034)
VITROS® Chemistry Products Calibrator Kit 2 (Product Code 1662659)

So that we can complete our records, please return this form to us no later than October xx, 2013.

FAX TO: *insert appropriate name*
FAX: *insert appropriate number*

Section I – Confirmation

I received Urgent Field Safety Notice (Ref. CL13-299_EU) and understand the information this contained in this notification. ***Please choose all of the appropriate options:***

- ❑ My laboratory does not use VITROS® Na^+ Slides and is not affected by this issue.
- ❑ My laboratory uses VITROS® Na^+ Slides, I am currently using GEN 14 or above. I am not affected by this issue.
- ❑ My laboratory uses VITROS® Na^+ Slides. I am currently using GEN(s) 7 - 13, and my product performance is acceptable for use in my laboratory.
- ❑ My laboratory uses VITROS® Na^+ Slides; I am currently using GEN(s) 7 - 13, and I would like product replacement or credit for my remaining inventory. Please indicate the quantity below.
- ❑ I have remaining inventory of VITROS® Calibrator Kit 2, Lot 212 and/or 292 that will require replacement. Please indicate the quantity in the table below.

Product Name	Lot No.	Indicate # of Sales Units Discarded	Please circle your preference
VITROS® Na^+ Slides (GENs 7-13) *Sales unit = 5 pack of 50 slides each*			***credit*** *or* ***replacement***
			credit *or* ***replacement***
VITROS® Calibrator Kit 2 (Lots 212 & 292) *Sales unit – 1 box of 4 sets each*			***credit*** *or* ***replacement***

In order to provide product for all customers, allocation may be required for VITROS® Na^+ Slides.

Your signature provides confirmation that you have received and understood this notification.

Your Name: _____ Job Title (optional): _____

Signed*: _____ Date: _____

Fax Number: _____ Telephone Number: _____

J Number: _____ Institution: _____

Your comments are always welcome:

_____

_____

Section II – Your Name and Address

Verify your name and mailing address:

Please complete this section if your name or mailing address has changed:

Institution Name: _____

Contact Name: _____

Address: _____

City: _____ State/Province:_____ Zip/Postal Code:_____

Telephone: _____ FAX:_____