URGENT

Ortho Clinical Diagnostics

June x, 2018

URGENT FIELD SAFETY NOTICE

Potential for Positively Biased Results using VITROS® Chemistry Products Na^+ Slides

Dear Customer,

As part of a Field Safety Corrective Action, Ortho Clinical Diagnostics initiated this Urgent Field Safety Notice due to positively biased results may occur when using the following VITROS Chemistry Products Na^+ Slides.

Name (Unique Identifier No.)	Product Code	Affected Generation (GENs)	Expiry Dates	Dates of Distribution
VITROS® Chemistry Products Na^+ Slides (10758750004812)	**8379034**	**GENs: 8, 13, 14, 16, 17, 18***	**01-Oct-2018 through 01-Nov-2019**	**04-May-2017 through current date**
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 VITROS 5600 Integrated Systems. *GEN 15 is not affected as there are no lots in distribution that are within expiry.				

Description of Issues

This product correction notification has been initiated due to the potential for positively biased sample results to occur when using the affected VITROS Na^+ Slides listed above. Results for serum/plasma and urine samples obtained using VITROS Na^+ Slides listed above may be positively biased and quality control fluids may be outside of the expected ranges. The amount of bias in the VITROS Na^+ method is dependent upon multiple sources of variability.

Two separate issues have been identified:

- **VITROS Na^+ Slides, GENs 8 & 13:** Positively biased **urine** sample results
- **VITROS Na^+ Slides, GENs 13, 14, 16, 17 & 18:** Positively biased **serum or plasma** sample results

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.

Ortho obtained results using representative slide lots from the GENs listed above; you may observe different magnitudes of bias on your VITROS Systems.

Impact to URINE Sample Results using GENs 8 & 13

The table below shows the bias that was observed in our investigation of samples tested between 25 – 175 mmol/L.

Observed Bias vs. Reference Method for Urine Samples using VITROS Na^+ Slides, GENs 8 & 13		
Affected GENs	**Maximum Average Bias Observed at 25 - 50 mmol/L**	**Maximum Average Bias Observed at 51 – 175 mmol/L**
GEN 8	+ 6.7 mmol/L	+13.8 mmol/L
GEN 13	+ 6.1 mmol/L	+12.0 mmol/L

Impact to SERUM/PLASMA Sample Results using GENs 13, 14, 16, 17 & 18

The overall average bias observed in our investigation for samples tested between 125 – 155 mmol/L is shown below:

Observed Bias vs. Reference Method for Serum Samples using VITROS Na^+ Slides, GENs 13, 14, 16, 17 & 18	
Concentration Range	**Average Bias Observed**
125 - 135	1.6 mmol/L
136 - 145	2.9 mmol/L
146 - 155	4.6 mmol/L
Our testing confirmed that serum and plasma samples are similarly affected.	

If present, the bias can cause an increase in your patient mean as well as in the number of individual patient results outside of the reference interval for your laboratory.

Impact to Osmolality, Osmolality Gap and Anion Gap Calculations

If a positive bias occurs, the Osmolality, Osmolality Gap and Anion Gap calculations will also be affected.

VITROS Result	Effect on Calculation
Positively biased serum Na^+ result	• Positively biased calculated Osmolality result leading to negatively biased Osmolality Gap • Positively biased Anion Gap

The VITROS Systems calculate the Osmolality per the following equation shown in conventional units for BUN and GLU (mg/dL) as indicated on the VITROS MicroSlide Assay Summary:

(Na+ x 1.86) + (GLU/18) + (BUN /2.8) = OSMO

When using this formula, 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 calculation. The Osmolality Gap is calculated by:

Measured Osmolality - Calculated Osmolality = Osmolality Gap

REQUIRED ACTIONS

For VITROS Na^+ Slides, GENs 8 & 13:

- Discontinue using and discard all remaining inventory of VITROS Na^+ Slides, GENs 8 & 13, regardless of sample type used for testing. Please indicate requested replacement on the Confirmation of Receipt form.
- It is acceptable to continue using the GENs 8 & 13 until your replacement order arrives providing that your quality control results are acceptable.

For VITROS Na^+ Slides, GENs 14, 16, 17 & 18:

- It is acceptable to continue to use remaining slides provided both of the following criteria are met:
  1. Calibration is successful and Quality Control results are within acceptable limits.
  2. Distribution of normal results for serum or plasma samples are centered within the established reference interval for your laboratory.
- Product replacement is available upon request. Indicate requested replacement on the Confirmation of Receipt form.

REQUIRED ACTIONS, continued

IMPORTANT TO NOTE: *Until GEN 19 is available from your distributor, you may be shipped an affected GEN. Continue to assess the use of GENs 14, 16, 17 & 18 as described on page two. Your distributor will notify you when GEN 19 is available for order.*

For VITROS Na^+ Slides, <u>All GENs</u>:

- Discuss any concerns you may have regarding previously reported Na+ results with your Laboratory Medical Director or with the requesting physician.
- Complete the Confirmation of Receipt form no later than **June xx, 2018**. Ortho will replace your remaining inventory of the affected GENs or credit your account. Partial sales units can only be credited and not replaced.
- Post this notification by each VITROS System in your facility or with the user documentation.
- Forward this notification if the product was distributed outside of your facility.

Resolution

As an outcome of our investigation, the Na^+ target value was set to match results obtained on our comparative reference method starting with the release of VITROS Na^+ Slides GEN 19. Our root cause investigation is ongoing; we will implement additional corrective actions as appropriate.

Contact Information

We apologize for any inconvenience this may cause in your laboratory. If you have questions, please contact Ortho Care™ Technical Solutions Center at insert number.

Insert signatory if appropriate in your region

Questions and Answers

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

   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. Laboratory tests, together with the patient's history, clinical signs and symptoms, are all used to aid in the diagnosis.

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

   If the bias is present, it would cause an increase in your patient mean for serum/plasma as well as an increase in the number of individual patient results outside of the reference interval for your laboratory. The affected GENs of VITROS Na^+ Slides have the potential to generate positively biased Na^+ results that 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.

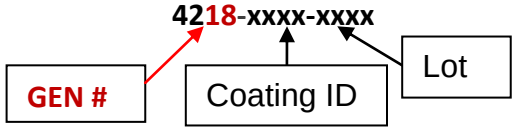
   Discuss any concerns you may have regarding previously reported Na^+ results with your Laboratory Medical Director or with the requesting physician.

3. **Will this issue be detected by Quality Control testing?**

   This issue may not be readily detectable by processing quality control fluids. It is possible for Na^+ quality control results to appear acceptable even though patient results are higher than expected. Product performance is acceptable if distribution of normal results for serum or plasma samples are centered within the established reference interval for your laboratory.

4. **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:



5. **If I am currently using an affected GEN of VITROS Na^+ Slides, can I get replacement for my remaining inventory?**

   For GENs 8 & 13: If you have slides from GENs 8 or 13 remaining in your inventory, Ortho will replace or credit your account. Partial sales units can only be credited not replaced.

   For GENs 14, 16, 17 & 18: It is acceptable to continue to use your remaining inventory of these GENs providing the following criteria are met:

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

   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)

6. Why have I received this letter if I do not have any of the affected GENs?

All lots within expiration dating were investigated. These issues may be observed with VITROS Na^+ Slides, GENs 8, 13, 14, 16, 17 and 18. VITROS Na^+ Slides, GENs 5 -12 performed acceptably during our investigation. All customers are expected to observe a shift in Na^+ performance when transitioning to GENs 19 and above. Customers with unaffected GENs may observe a smaller shift in performance.

7. What is the change in <u>Urine</u> Na^+ results that I may observe when transitioning to GENs 19 & above?

The maximum average positive bias observed at different concentration ranges in our investigation for **GENs 8 & 13** are shown below. When transitioning to GENs 19 & above from these GENs, you may observe negative shifts in performance of similar magnitudes.

Maximum Average Bias Observed in Ortho Investigation for GENs 8 & 13		
Affected GENs	**Maximum Average Bias Observed at 25 - 50 mmol/L**	**Maximum Average Bias Observed at 51 – 175 mmol/L**
GEN 8	+ 6.7 mmol/L	+13.8 mmol/L
GEN 13	+ 6.1 mmol/L	+12.0 mmol/L

For GENs 5 -7, 10-12, 14, 16 – 18: When transitioning to GENs 19 & above, you may observe an average negative shift in performance of -2.4 mmol/L within a concentration range of 40 – 210 mmol/L.

8. What is the change in <u>Serum</u> Na^+ results that I may observe when transitioning to GENs 19 & above?

When transitioning to GENs 19 & Above from **GENs 13, 14, 16, 17, 18**, you may observe a negative shift in performance for serum samples. The average shift in performance is shown below:

Average shift in performance for <u>Serum</u> samples when transitioning to GENs 19 & Above from GENs 13, 14, 16, 17, 18	
Concentration Range	**Average Shift in Performance**
125 - 135	-1.6 mmol/L
136 - 145	-2.9 mmol/L
146 - 155	-4.6 mmol/L

For GENs 5 – 12: The average bias observed in our investigation at a concentration range of 140 – 150 mmol/L is + 1.5 mmol/L. When transitioning to GENs 19 & above, you may observe a negative shift in performance of a similar magnitude.

9. What is Ortho doing to help mitigate variability in Na^+ results?

Ortho is actively developing solutions to enable more consistent Na^+ performance over time.