



URGENT

Ortho Clinical Diagnostics

June 2018

URGENT PRODUCT CORRECTION NOTIFICATION
Potential for Positively Biased Results using VITROS® Chemistry Products Na⁺ Slides

Dear Customer,

The purpose of this notification is to inform you that Ortho Clinical Diagnostics has determined that 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-Nov-2018 through 01-Nov-2019	04-May-2017 through current date
*GEN 15 is not affected as there are no lots in distribution that are within expiry.				

Description of Issues

This product correction notification is 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 the 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 <u>Urine</u> 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 Calculated Osmolality, Osmolality Gap and Anion Gap

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

VITROS Result	Effect on Calculation
Positively biased serum Na ⁺ result	<ul style="list-style-type: none">Positively biased calculated Osmolality result leading to negatively biased Osmolality GapPositively biased Anion Gap

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

$$(Na^+ \times 1.86) + GLU + UREA = OSMO$$

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:

$$\text{Measured Osmolality} - \text{Calculated Osmolality} = \text{Osmolality Gap}$$

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 the quantity discarded on the Confirmation of Receipt form. Credit will be issued for the quantity indicated.
- Place an order for new product.
- It is acceptable to continue using the GENs 8 & 13 until new product arrives if your quality control results are acceptable.

REQUIRED ACTIONS, continued

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 is centred within the established reference interval for your laboratory.
- If your remaining slides cannot be used, place an order for new product and indicate the quantity discarded on the Confirmation of Receipt form. Credit will be issued for the quantity indicated.

For VITROS Na⁺ Slides, All GENs:

- 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 13, 2018**. Ortho will credit your account.
- 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.

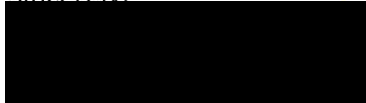
Resolution

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. We have anticipated some questions in the following Question and Answer section. If you have additional questions, please contact your local Ortho representative or our Ortho Care™ Technical Solutions Centre at 1800 5646 766.

Sincerely,



Jon Wong/ QA Manager

8 June 2018

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.

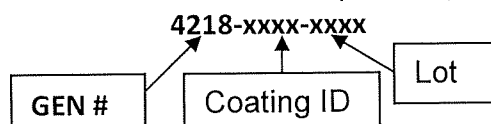
Discuss any concerns you may have regarding previously reported Na⁺ results with your Laboratory Medical Director or with the requesting physician.

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 the distribution of normal results for serum or plasma samples are centred 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 credit for my remaining inventory?

For GENs 8 & 13: If you have slides from GENs 8 or 13 remaining in your inventory, Ortho will credit your account.

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 is centred 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 Urine Na⁺ results that I may observe when transitioning to GENs 19 & above?

The maximum average bias observed at different concentration ranges for **GENs 8 & 13** is 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 shift in performance of -2.4 mmol/L within a concentration range of 40 – 210 mmol/L.

8. What is the change in Serum 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 minimise variability in Na⁺ results?

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