Ortho Clinical Diagnostics	**FOLLOW UP to URGENT FIELD SAFETY NOTICE** **Positively Biased Results using VITROS® Immunodiagnostic Products Intact PTH Reagent Packs**

Date Issued November xx, 2016

Affected Product

Product Name (Unique Device Identifier No)	**Product Codes**	**Affected Lot Number (Expiry Date)**	
VITROS Immunodiagnostic Products Intact PTH Reagent Pack (10758750006267)	6802892	0700 (Expired) 0710 (Expired) 0728 (12-Dec-16) 0738 (02-Jan-17) 0748 (06-Feb-17)	0758 (06-Mar-17) 0768 (10-Apr-17) 0778 (13-Jun-17) 0780 (11-Oct-17)
VITROS Immunodiagnostic Products Intact PTH Calibrators (10758750006250)	6802893		

This issue affects all in-date lots (listed above) and lots that have expired.

Issue Description

This is a follow up to a notification that Ortho Clinical Diagnostics (Ortho) issued in October 2016 (Ref. CL2016-196). At that time, we reported a positive bias of 40% for samples with iPTH concentrations <100pg/mL when testing with VITROS iPTH Reagent Packs in comparison to the Roche Elecsys PTH test. We also indicated that our investigation was still in progress.

Purpose

The purpose of this notification is to provide results of our additional testing and new actions.

Summary of Previous vs New Information

The following is a summary of the previous notification versus new information obtained from our recent testing.

	Previous Information (Ref. CL2016-196)	**New Information**
VITROS System vs Roche Elecsys	*Preliminary* data indicated a positive bias of **40%** with iPTH concentrations <100pg/mL.	Additional testing using fresh and frozen samples with iPTH concentrations of 12 to 137 pg/mL indicated a positive bias up to **20%** (not 40%).
Reference Interval	Current Reference Interval: 7.5-53.5pg/mL (0.8-5.7 pmol/L)	Additional testing suggests a Reference Interval of: **10.8-79.4 pg/mL** **(1.1 -8.4 pmol/L)**

NOTE: *In our preliminary assessment, we believe sample handling was a contributing factor that led to the initial bias estimate of 40%. Samples obtained from our external vendor may not have been properly handled prior to or concurrent with shipping to Ortho. Additional testing was performed on alternate samples which had been tested or frozen within 8 hours of being drawn prior to testing with one freeze-thaw cycle.*

New Investigation Summary

Since our initial assessment in October, Ortho performed additional testing. In summary, it appears the performance of the assay has not changed since product launch. Recently generated data suggests an update to the reference interval listed in the Instructions for Use may be required, in line with the data provided above. Proper sample handling is essential for accurate results.

New Investigation Information	
Calibration Traceability	Reference Calibrators used at product launch continue to generate expected values using recent reagent kit lots. **Conclusion:** There is no evidence of calibration drift for the VITROS iPTH assay.
Assay Linearity	Linearity has been verified and confirmed throughout the VITROS iPTH Measuring (Reportable) Range using Clinical and Laboratory Standards Institute's (CLSI) guidelines. **Conclusion:** Linearity, essential for intraoperative use, has been verified.
Lot to Lot Variability	Data confirmed that lot to lot bias is within ± 10% using multiple reagent lots. **Conclusion:** Lot to lot variability confirmed to be within ± 10%.
Impact of Proper Sample Handling	Samples improperly stored and/or mishandled, may generate different results compared to samples which were handled according to acceptable practice for iPTH sample handling. Ortho's testing was performed using fresh samples or frozen within 8 hours of being drawn. Your results may vary if samples are handled differently. The VITROS iPTH IFU includes sample handling and storage guidance, additional information about iPTH sample stability can be found in Hanon et al. Clin Chem Lab Med 2013; 51(10): 1925–1941. **Conclusion:** Proper storage and handling of patient samples is important to ensure accurate results.
VITROS System vs Siemens Centaur	During development, Ortho evaluated several comparative methods, including Siemens Centaur. To verify that current assay performance is consistent with the performance established at product launch, Ortho performed a correlation study of iPTH results generated on the VITROS System versus Siemens Centaur System. Data showed that the results on the VITROS System remain within 10% and are comparable to the performance at product launch in 2010. **Conclusion:** VITROS Assay performance does not appear to have changed since 2010.

Required Actions

- Consider verifying or re-establishing the reference interval. It is recommended that each laboratory establish its own expected values for the population it serves.
- As stated in VITROS iPTH IFU: Serum and plasma samples may be stored for up to 2 days at 2–8 °C (36–46 °F) or 4 weeks at -20 °C (-4 °F).
- Retain this notification by your VITROS System or with your user documentation.
- Complete the Confirmation of Receipt form and return by **November xx, 2016.**

Product Consistency

Ortho is working to ensure that future lots of VITROS iPTH Reagent Packs give a performance consistent with current (in-date) lots.

NOTE: *If your laboratory chooses not to use VITROS iPTH Reagent Packs, credit is available for any inventory that you discard. Ortho will credit your account as indicated on your Confirmation of Receipt form.*

Contact Information

We have anticipated some questions you may have in the following Question and Answer section. If you have any questions, please contact the Ortho Care™ Technical Solutions Center at insert number.

Insert signature if required

Enclosure: Confirmation of Receipt Form

Questions and Answers

1. **What caused the initial bias to be reported as 40%?**

   iPTH is a labile analyte, and sample handling is a critical factor. Ortho's preliminary investigation used externally sourced frozen samples whose handling history was unknown and may have been inappropriately stored or handled. This may have introduced additional artificial biases leading to the preliminary conclusion of a 40% positive bias. The use of fresh samples handled in accordance with the IFU determined the 20% bias.

2. **Do I need to review previously reported results?**

   No, Ortho is not requiring a review of previously reported results. Our investigation has concluded that the performance of the VITROS iPTH assay has not changed over time.

3. **Does this issue affect my quality control or proficiency data?**

   Our investigation concluded that the performance of the assay has not changed over time, quality control and proficiency/QAS testing are valid.

4. **How will I know if inappropriate sample handling affects my results?**

   Ortho has clarified the sample handling guidance in this notification to minimize sample handling errors that could adversely affect results:

   > As stated in VITROS iPTH IFU: Serum and plasma samples may be stored for up to 2 days at 2–8 °C (36–46 °F) or 4 weeks at -20 °C (-4 °F).

   Ortho's testing was performed using fresh samples or frozen within 8 hours of being drawn. Your results may vary if samples are handled differently. The VITROS iPTH IFU includes sample handling and storage guidance, additional information about iPTH sample stability can be found in Hanon et al. Clin Chem Lab Med 2013; 51(10): 1925–1941. As always, you should investigate discrepant results according to your own established procedures.

Confirmation of Receipt – Response Required

Follow up to URGENT FIELD SAFETY NOTICE

Ortho Clinical Diagnostics

Positively Biased Results using VITROS® Immunodiagnostic Products Intact PTH Reagent Packs

*Please return completed form by **fax** or **scan to PDF** and email so that we can complete our records no later than*: **DD-MM-YYYY**

Send to: Name e-Mail Address: email address Fax: Fax Number

Please Confirm

I received the follow up to the previous Field Safety Notice (Ref. CL2016-196_EU) regarding results obtained from VITROS iPTH Reagent Packs that were positively biased compared to an alternative commercially available method.

I understand that the performance of the assay has not changed, I should consider verifying or re-establishing the reference interval and proper sample handling is essential for accurate results. I am aware of the potential for up to 20% positively biased results compared to the Roche Elecsys PTH test using VITROS iPTH Reagent Packs for samples with iPTH concentrations of up to 137 pg/mL.

Please choose from the following:

- ☐ My laboratory does not currently use VITROS iPTH Reagent Packs and is not affected by this issue.
- ☐ My laboratory uses VITROS iPTH Reagent Packs; I am aware of this issue and will continue to use this product.
- ☐ My laboratory has VITROS iPTH Reagent Packs. I am aware that I may continue to use the product, but have decided to discontinue using and discard the quantity listed in the table below. Credit my account (Credit can be issued for full or partial sales units.)

Product Name/Product Code/LOT	Quantity Discarded
VITROS iPTH Reagent Packs / 6802892	
VITROS iPTH Calibrators / 6802893	

One Sales Unit for VITROS iPTH Reagent Packs = 1 Pack containing 100 wells
One Sales Unit for VITROS iPTH Calibrators = 1 box containing 3 sets of calibrators

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

Your Name: _____

Phone Number: _____ Date: _____

Signature: Required if sent by fax or a scanned PDF

Your Comments: _____

Your Name and Address

Verify your name and mailing address:

Please complete this section if any of this information has changed

Institution/
Contact Name: _____
Address: _____
City: _____ State/Prov: _____ Zip/Postal Code: _____
Phone: _____ Fax: _____
e-Mail: _____