URGENT

Ortho Clinical Diagnostics

November XX, 2022

URGENT FIELD SAFETY NOTICE

Potential for Negative Bias when using VITROS® Immunodiagnostic Products Intact PTH Reagent Pack

Dear Valued Customer,

This notification is to inform you that Ortho Clinical Diagnostics confirmed an issue involving the potential for negatively biased results when using specific lots of VITROS Intact PTH (iPTH) Reagent Pack.

Affected Product	Product Code (Unique Device Identifier)	Affected Lots	Expiry	Impacted Product
VITROS Immunodiagnostic Products Intact PTH Reagent Pack	6802892 (10758750006267)	1610	24-Apr-2023	VITROS Immunodiagnostic Products Intact PTH Calibrators
		1621	24-Apr-2023	
		1630	08-May-2023	
		1640	08-May-2023	
		1645	08-May-2023	
		1650	29-May-2023	
		1670	06-Jun-2023	
VITROS Immunodiagnostic Products Intact PTH Reagent Pack is used in the quantitative measurement of intact parathyroid hormone (iPTH) in human serum and plasma (EDTA or heparin) using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems. Intact PTH is indicated to aid in the differential diagnosis of hyperparathyroidism, hypoparathyroidism, or hypercalcemia of malignancy and can be used intraoperatively.				

Issue Description/Investigation

Ortho received 166 complaints for VITROS iPTH Reagent Pack related to observations of lower-than-expected iPTH patient and Quality Control (QC) results with the affected lots listed above. Customers reported the negatively biased iPTH results when comparing results produced from the affected reagent lots to results produced from unaffected lots for patient correlation testing as well as assessing QC results from BioRad and Thermo Fisher.

Ortho's investigation compared results produced from affected reagent lots to results produced from unaffected reagent lots and confirmed an average -12% shift in patient sample results. Ortho's investigation included 119 patient samples, with patient sample concentrations ranging from 10 pg/mL – 2391 pg/mL, with the highest bias observed on an individual sample at approximately -26.7% and an overall estimated average bias of approximately -12%.

A variable negative shift in performance was also confirmed using BioRad Liquicheck/Lyphocheck Specialty Immunoassay Controls and Thermo Scientific MAS Omni•IMMUNE Immunoassay Controls when compared to their published assigned values. VITROS Immunodiagnostic Products iPTH Controls do not detect this bias, therefore no performance shifts of the controls were observed.

Impact to Results

When using the affected lots listed above, customers may experience lower than expected results. When processing patient samples an average negative bias of approximately -12% may be observed. Ortho has assigned new mean and SD values for available BioRad and Thermo Fisher control lots for use specifically with the affected lots listed above. These values can be found in the table at the end of this communication.

A negative bias observed with this assay may influence its application for intraoperative monitoring of iPTH, which could potentially miss an unsuccessful parathyroidectomy, leaving the patient still with higher-than-normal PTH levels, which may require additional treatment. However, given the magnitude of the bias, the likelihood of the impact is considered low. Also, for evaluating the parathyroid function and the aid in the diagnosis of hyperparathyroidism or hypoparathyroidism, a negative bias of PTH results may trigger additional tests or may miss the detection of low or moderately elevated PTH level causing a delay of the diagnosis of hyperparathyroidism.

Because the bias is consistent within a lot, if using this product intraoperatively, Ortho recommends using the same lot of VITROS iPTH Reagent Pack and QC material to determine the baseline and throughout the procedure.

The results from any diagnostic test should be evaluated in conjunction with a patient's history, risk factors, clinical presentations, signs, and symptoms as well as the results of other tests.

Discuss any concerns you may have regarding previously reported results with your Laboratory Medical Director to determine the appropriate course of action. However, if a patient's PTH level was monitored across different lots or if the patient sample results were close to the upper limit of the reference range, Ortho recommends a review of previous results.

Resolution

Ortho's investigation has identified the root cause of this issue stems from a raw material used in the affected lots. Lots released after Lot 1670 will not be affected by this issue.

REQUIRED ACTIONS

- When using the affected lots of VITROS iPTH Reagent Pack intraoperatively, patient samples should be tested using the same reagent lot and QC material for baseline and throughout the procedure.
- When performing patient sample testing using the affected lots of VITROS iPTH Reagent Pack, adjust your laboratory's reference interval by -12%.
- Until a new lot of VITROS iPTH Reagent Pack is available, be aware that the potential exists to observe negatively biased results when using the affected lots of VITROS iPTH listed above.
- If you choose not to continue using the affected lots of VITROS iPTH, Ortho will credit your account. Indicate quantities to be credited via the Confirmation of Receipt form.

  Please note: Ortho is in the process of manufacturing new reagent lots with an expected ETA of December 19th.
- Complete the enclosed Confirmation of Receipt form no later than **November XX, 2022.**
- Please forward this notification if the affected product was distributed outside of your facility.

REQUIRED ACTIONS CONT'D

- Save this notification with your user documentation or post this notification by each VITROS ECi/ECiQ/3600/5600/XT 7600 System until your laboratory receives a lot of VITROS iPTH unaffected by this issue.
- If your laboratory has experienced the issue with this product and you have not already done so, please report the occurrence to your local Ortho Care™ Technical Solutions Center.

Contact Information

We apologize for the inconvenience this will cause your laboratory. If you have further questions, please contact Ortho Care™ Technical Solutions Center at *insert number.*

Insert signatory of required in your region.

Enclosure:
Confirmation of Receipt Form

Questions and Answers

1. **What is the impact to my results?**

   Patient samples were tested using sample concentrations ranging from 10 pg/mL – 2391 pg/mL of the affected and unaffected reagent lots, with the highest bias observed on an individual sample at approximately -26.7% and an overall estimated average bias of approximately -12%. The bias is expected to be consistent within the reagent lot.

   A variable negative bias has been observed across different lots of BioRad and Thermo Fisher controls used with the affected lots of iPTH reagent. Ortho has included new assigned mean and SD values for use with available BioRad and Thermo Fisher controls. Should other control lots be in use, Ortho recommends users establish their own acceptance range for such control lots used with the affected reagent lots.

2. **Was this issue observed when using VITROS Immunodiagnostic Products Intact PTH Controls?**

   No, Ortho is currently investigating why this issue was not observed when using VITROS iPTH Controls.

3. **Did these affected lots meet release criteria during the release process?**

   Yes, the affected lots of VITROS iPTH met and continue to meet the release criteria. Ortho is assessing the manufacture and release process (as part of corrective action) to optimize and prevent this issue from occurring in the future.

4. **Can I still use this product for intraoperative iPTH testing?**

   Yes, however, if used in intraoperative testing, Ortho recommends using the same reagent lot for patient sample testing to reduce the impact of negative bias. Since this negative bias is consistent throughout the reportable range, iPTH levels in both pre and post-parathyroidectomy would be affected.

5. **How do I verify assay performance of the affected reagent lots using control material?**

   VITROS iPTH Controls do not detect the negative bias confirmed for the affected lots of VITROS iPTH Reagent Pack listed above. Assay performance can be verified using controls from BioRad and Thermo Fisher. When using another manufacturer's control material with the affected reagent lots, your results may not match the assay range provided in the original package insert or peer data. Only use the values for the respective Bio-Rad and/or Thermo Fisher control material provided in this communication when using the affected VITROS iPTH Reagent lots listed in this communication.

New Control Values for Affected Lots of VITROS iPTH Reagent Pack

(All data values below are in units pg/mL)

Bio-Rad Liquichek Specialty Immunoassay Controls #64920 EXP: 31-Mar-2023

	Mean	SD	Lower 3SD Range	Upper 3SD Range
Level 1 (#64921)	19.6	2.82	11.1	28.1
Level 2 (#64922)	152.9	20.34	91.9	213.9
Level 3 (#64923)	485.4	64.56	291.7	679.1

Bio-Rad Liquichek Specialty Immunoassay Controls #64950 EXP: 30-Sep-2024

	Mean	SD	Lower 3SD Range	Upper 3SD Range
Level 1 (#64951)	23.3	3.36	13.2	33.4
Level 2 (#64952)	182.5	24.27	109.7	255.3
Level 3 (#64953)	468.0	62.24	281.3	654.7
Level LTA (#64951L)	23.0	3.31	13.1	32.9

Bio-Rad Liquichek Specialty Immunoassay Controls #64960 EXP: 28-Feb-2025

	Mean	SD	Lower 3SD Range	Upper 3SD Range
Level 1 (#64961)	26.2	3.77	14.9	37.5
Level 2 (#64962)	186.6	24.82	112.1	261.1
Level 3 (#64963)	564.0	75.01	339.0	789.0
Level LTA (#64961L)	27.3	3.93	15.5	39.1

Thermofisher MAS® Omni-Immune® #OIM2411 EXP: 30-Nov-2025

	Mean	SD	Lower 3SD Range	Upper 3SD Range
Level 1 (#OIM24111)	22.5	3.24	12.8	32.2
Level 2 (#OIM24112)	67.4	9.10	40.1	94.7
Level 3 (#OIM24113)	1186	154.2	723.4	1649

Bio-Rad Lyphochek Specialty Immunoassay Controls #88700 EXP: 31-Dec-2023

	Mean	SD	Lower 3SD Range	Upper 3SD Range
Level 1 (#88701)	40.4	5.45	24.1	56.8
Level 2 (#88702)	622.8	82.83	374.3	871.3
Level 3 (#88703)	1283	166.8	782.6	1783

Bio-Rad Lyphochek Specialty Immunoassay Controls #88710 EXP: 31-Jul-2024

	Mean	SD	Lower 3SD Range	Upper 3SD Range
Level 1 (#88711)	44.0	5.94	26.2	61.8
Level 2 (#88712)	587.4	78.12	353.0	821.8
Level 3 (#88713)	1247	162.1	760.7	1733

Bio-Rad Lyphochek Specialty Immunoassay Controls #88720 EXP: 31-Jan-2025

	Mean	SD	Lower 3SD Range	Upper 3SD Range
Level 1 (#88721)	47.6	6.43	28.3	66.9
Level 2 (#88722)	659.4	87.70	396.3	922.5
Level 3 (#88723)	1361	176.9	830.3	1892

Confirmation of Receipt – Response Required

Communication ID: CL2022-275a_EU Date of Issue: DD-MMM-2022

URGENT FIELD SAFETY NOTICE

Potential For Negative Bias When Using VITROS® Immunodiagnostic Products Intact PTH Reagent Pack

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

Send to: **Name** e-Mail Address: **Email** Fax: **Fax**

Verification Request

☐ ***I confirm this contact information and no changes are required***

Institution: _____ UCN: _____

Contact: _____

Address: _____

City: _____ State/Prov: _____

Zip/Postal Code: _____ Phone: _____

e-Mail: _____ Fax: _____

Please complete this section if any of this information has changed

Institution: _____

Contact: _____

Address: _____

City: _____ State/Prov: _____

Zip/Postal Code: _____ Phone: _____

e-Mail: _____ Fax: _____

Please Confirm

I received the Urgent Field Safety Notice regarding an issue involving VITROS Intact PTH (iPTH) Reagent Pack with specific lots having the potential to report results with a negative bias. The affected lots are: Lot 1610, 1621, 1630, 1640, 1645, 1650, 1670.

Please choose from the following:

☐ My laboratory has not received the affected lots VITROS® iPTH Reagent Pack and therefore is not affected by this issue.

☐ My laboratory uses VITROS® iPTH Reagent Pack but does not have any of the affected lots remaining in inventory.

☐ My laboratory will continue to use the affected lot(s) of VITROS® iPTH Reagent Pack following the instructions provided in the communication.

☐ My laboratory has the affected lot(s) of VITROS® iPTH Reagent Pack. I have discontinued using and discarded the quantity listed in the table below.

Please indicate your choice of credit or replacement:

☐ Credit my account (Credit only will be issued for discarded partial sales units, credit can also be issued for discarded full sales units.)

For reference: One Sales Unit of VITROS® iPTH Reagent Pack (Product Code 6802892) = 1 Pack containing 100 wells
One Sales Unit of VITROS® iPTH Calibrators (Product Code 6802893) = 1 box containing 3 sets of calibrators

Product Name / Product Code / LOT	Quantity of Full Sales Units Discarded (unopened)	Quantity of wells remaining in partially used (opened) Packs
VITROS iPTH Reagent Pack / 6802892 /		
VITROS iPTH Reagent Pack / 6802892 /		
VITROS iPTH Calibrators / 6802893 /		
VITROS iPTH Calibrators/ 6802893 /		

Print Name: _____

Phone Number: _____ Date: _____

Signature: Required
Your signature confirms that you have received and understand this communication.

Your Comments: _____

If you are responding for more than one location, please list below all locations and Customer Numbers (UCNs) that your signature represents:

Locations you Represent: _____

For Customers Who Order from a Distributor	Distributor Name
If you order from a Distributor, please provide the name of your distributor	

Content ID: _____