URGENT

Ortho Clinical Diagnostics

Month DD, YYYY

URGENT FIELD SAFETY NOTICE

VITROS® Immunodiagnostic Products FSH, LH and Prol Reagents Low End Imprecision

Dear Customer,

As part of a Field Safety Corrective Action, this notification provides important information regarding low end imprecision of VITROS® Immunodiagnostic Products FSH, LH and Prol Reagents.

Affected Product Name	Product Code (Unique Device Identifier)	Affected Lots
VITROS® Immunodiagnostic Products FSH Reagent Pack	1931922 (10758750000302)	See enclosure for all affected lots. Until further notice, future lots will also be affected.
VITROS® Immunodiagnostic Products LH Reagent Pack	1350198 (10758750008902)	
VITROS® Immunodiagnostic Products Prolactin Reagent Pack	1849793 (10758750000111)	

Issue Description

Ortho Clinical Diagnostics has observed an increase in complaints, and confirmed the imprecision observed, for low-level quality control (QC) and patient samples at the low end of the Measuring (Reportable) Range when using VITROS FSH, LH and Prol Reagent. Complaints have also been received regarding calibration failures, driven by imprecision observed with Calibrator Level 1.

The investigation indicates the imprecision is caused by additional signal generated during processing, resulting in falsely elevated results. This additional signal is caused by an interaction between reagent lots and some VITROS Systems.

While all reagent lots have the potential for imprecision, **the majority of customers are not affected**.

Impact

1) **Patient Results**: If your reagent lot/VITROS System combination is resulting in low end imprecision, it is possible that some truly low samples may incorrectly fall within the reference interval and some truly normal samples may incorrectly fall outside of the upper end of the reference interval. A falsely high result could potentially suggest normal or abnormally high FSH/LH/Prol levels and may cause confusion in determining the cause of infertility or dysfunction and may trigger additional testing.

   Because multiple assays are typically evaluated along with patient history, a misdiagnosis or harm to patients due to this failure mode is unlikely. Therefore, review of previous reported results is not recommended. Discuss any concerns you may have regarding previously reported results with your Laboratory Medical Director to determine the appropriate course of action.

2) **QC Results**: QC results may fail current published recommendations (within-lab SD, ranges). This could lead to QC troubleshooting and a delay in result reporting.

3) **Calibration Failures**: Calibration failures could lead to troubleshooting and a delay in result reporting.

Resolution

Ortho recommends processing daily low-level QC material in duplicate in addition to the other levels in singleton. Low-level QC failures with high results indicate low end imprecision.

If your laboratory is not experiencing calibration failures or low-level control imprecision, you should continue to test patient samples as usual.

If your laboratory is experiencing this low end imprecision (such as calibration failures or imprecision of your low-level control) with VITROS FSH, LH or Prol Reagent, Ortho recommends you test all samples that are over the upper end of the lowest reference interval in duplicate. This can be done either by testing all samples in duplicate (Algorithm A) or by re-testing samples with an initial result over the high end of the lowest reference interval (Algorithm B).

Refer to the enclosed procedure (Ref. CL2022-069_Protocols) for details. A Technical Bulletin with this information will be issued in the future.

Note: As recommended in the Instructions for Use (IFU), ensure your laboratory is running a daily low-level control such as VITROS® Immunodiagnostic Products RE Controls Level 1.

(eg. RE Control 1 is targeted as follows: FSH 3.8 – 10.5 mIU/mL, LH 1.9 – 6.3 mIU/mL, Prol 142.0 – 315.0 mIU/L)

The investigation is ongoing. Ortho will send a follow-up communication when the issue is resolved, and the additional testing protocol is no longer necessary.

REQUIRED ACTION

- Run daily low-level QC in duplicate to confirm acceptable performance.
- If your laboratory is experiencing low end imprecision with VITROS FSH, LH or Prol Reagent, follow one of the suggested testing algorithms as described in the enclosure.

  Note: If your laboratory is not experiencing low end imprecision, continue testing patient samples as usual (single replicate).
- On the enclosed Credit Form, track the additional quantities of VITROS FSH, LH and/or Prol tests used due to the testing protocol. Periodically submit the form to Ortho. Ortho will credit your account.
- Complete the enclosed Confirmation of Receipt form no later than **Month ##, YYYY**.
- Please forward this notification if the affected product was distributed outside of your facility.
- Save this notification with your user documentation.
- 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 phone number.

Insert signatory if appropriate in your region.

Enclosures:
1) Confirmation of Receipt Form
2) Affected Lots
3) Duplicate Testing Protocols
4) Request for Credit

Frequently Asked Questions

1) What should I do if I cannot obtain a successful calibration?

Repeat the calibration. If repeat calibrations are not successful after 2-3 attempts, contact the Ortho Care Technical Solutions Center. Not all calibrations failures are caused by low end imprecision.

2) What is the difference between Testing Algorithm A and Testing Algorithm B?

Testing Algorithm A recommends processing all samples for FSH, LH or Prol in duplicate. This option allows you to configure your System to automatically process each sample in duplicate regardless of the concentration. In addition, the System will automatically compare the results and determine whether they are outside the acceptable 25% limit from the mean for replicate results. If the replicate results exceed the limit, an SC code (Spread Check) will be reported. The mean and the individual replicates will be printed on the Laboratory Report. All samples for the configured assay will be processed in duplicate if you choose this algorithm.

Testing Algorithm B recommends confirming only samples with concentrations within the retesting threshold range (refer to question 2). The difference between the maximum and the minimum results must be manually calculated and within 25% of the mean of the two results. Each result will be printed on the Laboratory Report.

3) Why does testing Algorithm B recommend re-testing of samples only within the ranges listed below?

	Lower retesting Threshold (**X**)	Upper retesting Threshold (**Y**)
FSH	9.58 mIU/mL	25 mIU/mL
LH	12.1 mIU/mL	26 mIU/mL
Prolactin	380 mIU/L or 17.9 ng/mL	640 mIU/L or 30.8 ng/mL

The re-test recommendation lower testing thresholds are based on the URL for the lowest of each assay's reference intervals. Since the imprecision is occurring only at the low end, the upper testing thresholds are set at a concentration above where imprecision has been observed.

4) How will the replicate results be transmitted to my Laboratory Information System (LIS)?

The VITROS System uploads each of the individual results, not the mean. Check with your LIS vendor to determine how your LIS processes multiple results for the same Sample ID.

5) If I choose to use Algorithm B and repeat samples above the URL, how do I calculate the percent difference between results?

a) Calculate the mean of R_1 & R_2:

$$\frac{R_1 + R_2}{2} = \text{Mean}$$

b) Calculate the % difference between results:

$$\frac{R_{Max} - R_{Min}}{R_{Mean}} * 100 = \%$$

6) What can I do to minimize the occurrence of falsely elevated results?

Perform all daily and weekly maintenance procedures following your VITROS System Maintenance & Diagnostics Guide or V-Docs, paying close attention to the processing center/microwell incubator cleaning.

7) **How can I configure my System to automatically process samples in duplicate?**
Note: The configuration should be performed for all body fluids that are processed for the assay (serum/plasma).

VITROS ECi/ECiQ Systems

- Touch **Options & Configuration** on the Main Menu screen.
- Type the access code, then press **Enter** or touch **OK.**
- Touch **Configure Analytes** on the Options & Configuration screen to display the Configure Analytes screen.
- Select the body fluid then choose the assay**.**
- Touch **Review/Edit Analyte Data**.
- Press the **Tab** key twice to advance the cursor to the Wells per Assay field.
- Type 2 and press **Enter**.
- Touch **Return/Save.**
- Touch **Return** twice to return to the Main Menu.

VITROS 3600/5600/XT 7600 Systems

- Touch **Options on the System Status** screen.
- Touch **Configure Assays**.
- Select the body fluid then choose the assay.
- Touch **Review/Edit Configuration**.
- Press the **Tab** key five times to advance the cursor to the Per Assay field.
- Type 2 and press **Enter**.
- Touch **Save** and select **Yes** at the pop-up message to **'Save New Assay Configuration'.**
- Touch **Return** three times to return to the System Status Screen.

8) **Can my VITROS System be configured to automatically reflex samples with results within the retest threshold range listed for each assay in enclosure (Ref CL2022-069_Protocol)?**

Yes, if using Algorithm B refer to the Operators Manual or V-Docs for instruction to set up reflex testing to the same assay.