Ortho Clinical Diagnostics

PART OF THE Johnson & Johnson FAMILY OF COMPANIES

November 5, 2015

IMPORTANT PRODUCT CORRECTION NOTIFICATION

Temperature Monitoring Anomaly on VITROS® Systems Using Software Version 3.2 and Below

(Immediate Action Required)

Please distribute this information to the appropriate personnel at your facility

Dear Valued Customer,

Ortho Clinical Diagnostics (Ortho) initiated this Urgent Product Correction notification due to software anomaly in which the temperature in the well Wash module may be out of range without notification to the operator.

Temperature monitoring is performed by the VITROS® System for each subsystem (i.e. MicroSlide, MicroTip and MicroWell). Our investigation confirmed that under very specific conditions (described on page 2), the temperature for the Well Wash module may be out of range without alerting the operator. Refer to the Question and Answer section for detailed information.

Affected Products

Product Name	Product Code	Unique Device Identifier No.
VITROS® 3600 Systems Software version 3.2 & Below	6802413	10758750009930
VITROS® 5600 System Software version 3.2 & Below	6802783	10758750009916

Impact to Results

If the anomaly occurs, it is possible for the VITROS® System to process sample outside of the proper temperature range, potentially leading to a biased patient result. The results will not be flagged with a "WT" (Wash Temperature) result code. Refer to the enclosure for the potential bias that may occur. Events that occurred prior to this communication are not easily identifiable; thus, a review of previous result is impractical. Therefore, discuss any concerns regarding previously reported results with your Laboratory.

Medical Director to determine the appropriate course of action.

Resolution

The resolution related to the temperature monitoring software anomaly will be contained in the next version of software currently under development. Until the new software is installed, follow the enclosed instructions.

In addition, there will be a modification to the temperature monitoring device for the Microwell subsystem. An Ortho-trained service representative will contact you to schedule the installation upon availability.

Actions Required from You

1. Verify that the temperature for the MicroWell subsystem within proper temperature range prior to sample processing by following the instructions provided.

2. If a temperature is out of range and the status bar indicates that the system is “Ready” or the temperature icon is NOT present, contact our Technical Solutions Center.

3. Post this notification by the affected VITROS® System(s) or with your user documentation.

4. Complete and return the **Customer Acknowledgement Form** within **(2) two business days** to acknowledge your reading and understanding of this notice.

If you have any questions, please contact Customer Technical Services at **1800 5646 766** at any time.

Yours sincerely,

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Lee, Ching Hwee
Senior Regulatory Affairs Specialist

Attachment A

Questions and Answers

1. **How is the VITROS® System designed to monitor temperature?**

   Incubator and fluid temperatures are monitored by the VITROS® System for each subsystem (i.e., MicroSlide, MicroTip and MicroWell). If a temperature is out of range, the system will post a condition code to alert the operator, and a temperature icon will appear on the Status bar. The results will be flagged with "IT" (incubator temperature) or "WT" (well wash temperature) for results produced from that module. Sample metering for the affected subsystem will be discontinued.

2. **What subsystems are affected by this issue?**

   Our investigation determined that this issue predominantly affects the MicroWell subsystem. The temperature monitoring device (i.e., Thermistor) is located within the MicroWell Wash Assembly that mounts on the movable Well Wash arm. The MicroWell Wash Assembly is the only module in which the wires are continually moving and flexing during normal processing. Over time, the Thermistor wires may degrade resulting in an electrical short/open circuit, causing the intermittent issue that may not be detected due to the software anomaly.

   The MicroSlide and MicroTip subsystems utilize a solid mounting of the Thermistor. If there is an issue with the Thermistor, it would not be intermittent, and therefore, it would be detected by the software.

3. **What causes the anomaly to occur?**

   The anomaly is associated with an intermittent failure due to an electrical short/open circuit in the MicroWell Wash Assembly.

   The resolution will be contained in the next version of software currently under development. In addition, there will be a modification to the MicroWell Wash Assembly that will help to decrease the potential for the electrical short or open circuit to occur.

4. **How often does this issue occur?**

   Analysis of e-Connectivity® data estimates the probability of affected results, to be approximately 1 out of 200,000 results using the MicroWell subsystem (approximately 0.0005%). The probability for the other sub-systems is less than 1 in 14 million.

5. **What is the impact to MicroWell Assay results if my VITROS® System was out of temperature range?**

   If the issue occurs, samples will not be properly flagged with a 'WT' result code (Wash Temperature) and the results may be biased.

   Ortho conducted testing for selected temperature-sensitive assays that use the MicroWell module. Samples were tested at nominal temperature (37°C) and at ambient room temperature (~25°C). A summary of the data is provided in the enclosure.

Questions and Answers (continued)

6. Are other VITROS® Systems affected by this issue?

This issue predominantly affects VITROS® 3600 and 5600 Systems which contain a MicroWell subsystem.

VITROS® System	Type of Affect
VITROS® 4600 or 5,1 FS Systems	• Software contains the anomaly • No MicroWell subsystem • Frequency of occurrence for MicroSlide and MicroTip subsystems is significantly reduced (i.e., **1 in 14 million**) • No further action is required.
VITROS® 250/350 Systems	• Software does not contain the anomaly • No MicroWell subsystem • Systems are not affected
VITROS® ECi/ECiQ Immunodiagnostic Systems	• Software does not contain the anomaly • Systems are not affected
VITROS® 3600/5600 Systems connected to enGen™ Laboratory Automation (or other automation track)	• Anomaly is associated with VITROS® Software. • Follow the instructions in the enclosed procedure

7. What assays utilize the MicroWell subsystem?

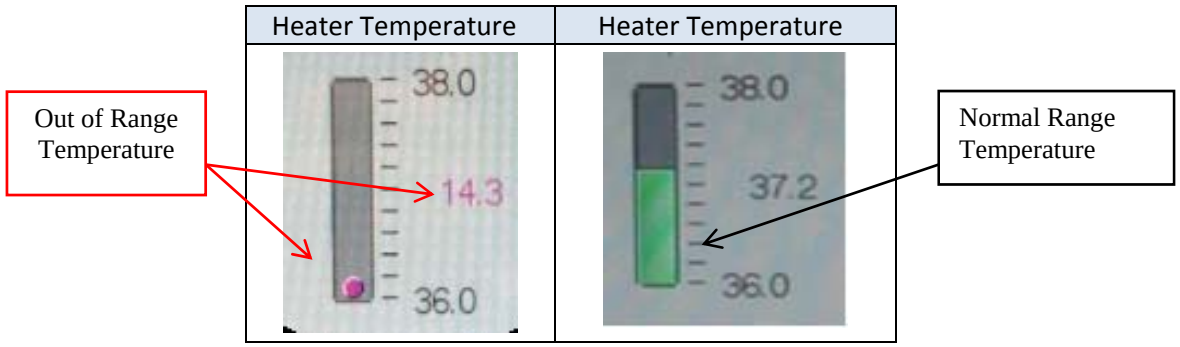
The following VITROS Immunodiagnostics assays utilize the MicroWell subsystem:

AFP	CA 15-3	Free T3	NTBNP	Total PSA II
Anti-HAV IgM	CA 19-9	Free T4	Progesterone	Total T3
Anti-HAV Total	CEA	FSH	Prolactin	Total T4
Anti-HBc	CK-MB	HBeAg	PSA	Toxoplasma IgG
Anti-HBc IgM	CMV	HBsAg	Rubella IgG	Toxoplasma IgM
Anti-HBe	Cortisol	HBsAg ES	Rubella IgM	TroponinI ES
Anti-HBs	Estradiol	Intact PTH	Syphillis TPA	TSH
Anti-HCV	Ferritin	LH	T3 Uptake	Vitamin B12
Anti-HIV 1+ 2	Folate	Myoglobin	Testosterone	Vitamin D Total
CA 125 II	Free PSA	N-Telopeptide	Total B-hCG II	

8. Will Quality Control testing identify if the issue occurred on my VITROS System?

Quality Control samples are expected to exhibit the same magnitude of bias as patient samples and would be detected if the results exceeded the QC limits. If an assay is calibrated at ambient temperature, quality control results may not detect the anomaly.

Attachment B
Instructions to Verify Temperature using VITROS® 3600/5600 Systems

Instructions to Verify Temperature using VITROS® 3600/5600 Systems
Verify that the MicroWell subsystem is within temperature range *prior to* sample processing. We recommend that you observe the '*Environmental Monitoring*' screen while processing samples. **From the Main Menu:** → Select '*Diagnostics'* → Select '*System Information*' → Select '*Environmental Monitoring*'. Enable *'Start Monitoring*' by touching the icon at the bottom of the screen. → Verify that all temperatures are within range (i.e., thermometer indicator is green for both the Preliminary and Final Well Wash) → It is acceptable to start sample metering if all of the temperature icons are green. → It is recommended that you keep *Environmental Monitoring*' screen open while processing samples **Note:** VITROS® Systems connected to an enGen™ Laboratory Automation System must follow this procedure to verify the temperature of the MicroWell subsystem on all VITROS® 3600 or 5600 Systems.
Out of range temperatures will be flagged/highlighted as shown in the example below 
If Out of Range Temperature is Identified: • *If a temperature is out of range*, and the status bar indicates that the system is "*Ready*" or the Temperature icon is not present: o Contact our Technical Solutions Center to report the occurrence o Follow the instructions on page two of this document to resume normal operation • Review all results generated since the last time you verified the temperature following your normal lab procedures. **NOTE**: Analysis of e-Connectivity® data estimates the probability of affected results, to be **approximately 1 out to 200,000 results using the MicroWell subsystem** (approximately 0.0005%) and less than 1 in 14,000,000 using the MicroSlide and MicroTip subsystems.

To Resume Normal Operation if an Out of Range Temperature is identified:

→Select '*Diagnostics*'

→Power **off** Circuit Breaker (CB) 14

→Power **on** Circuit Breaker (CB) 14, wait 20 seconds after the last PER-328 condition code occurs

→ Exit '*Diagnostics*' to initialize the system

→Contact your Ortho-trained field service representative to resolve the Thermistor issue.

NOTE: It is normal for an MJR condition code to occur as the system initializes and re-establishes its communication.

Attachment C
Impact To Results on VITROS® 3600/5600 Systems

Impact to Results on VITROS® 3600/5600 Systems
Testing was conducted for assays that are sensitive to well wash fluid temperature utilizing the MicroWell Wash module. Samples were tested at nominal temperature (37°C) and at ambient room temperature (~25°C). The data provided below summarizes our assessment. **NOTE:** Seventeen assays were tested across multiple concentrations; the values deemed to affect a clinical decision are shown below. Data for other assays will be available upon request.

For assays that have cutoff values, only those samples with results close to the cutoff values may potentially lead to a misclassification.

Potential Bias if Assays Calibrated at Nominal Temperature (37°C), Samples Processed at Ambient Temperature (~25°C)		
Assay Name	**Concentration Range**	**Bias Observed**
NT proBNP	Cutoff value: 300 pg/mL	19.5%
TSH	Lower Reference Range: 0.465 mIU/L	6%
Intact PTH	Lower Reference Range: 7.5pg/mL	18%
Rubella IgG	Cutoff value for Negative: 9.99 IU/mL	-2.8%
Anti-HBs	Cutoff value for Positive: 10 mIU/mL	26%
Potential Bias if Assays Calibrated at Ambient Temperature (~25°C), Samples Processed at Nominal Temperature (37°C)		
Assay Name	**Concentration Range**	**Bias Observed**
NT proBNP	Cutoff value: 450 pg/mL	-16%
TSH	Upper Reference Range: 4.68 mIU/L	-1.6%
Intact PTH	Upper Reference Range: 53.5 pg/mL	-13%
Troponin	0.034 ng/mL	-8.8%
Anti-HBc	Cutoff value for Negative: 0.9	-10%
HBsAg	Cutoff value for Negative: 0.9	-2.9%
Rubella IgM	Cutoff value for Negative: 0.8	-2.8%
Syphilis	Cutoff value for Negative: 0.8	-6.6%
Toxoplasma IgG	Cutoff value for Negative: 3.99	-4.8%
Toxoplasma IgM	Cutoff value for Negative: 0.8	-5.5%
HAV Total	Cutoff for Positive: 0.8	-6.3%

NOTE: Testing is ongoing for other MicroWell assays and will be available upon request by contacting our Technical Solutions Center representatives.