Ortho Clinical Diagnostics

part of the Johnson & Johnson family of companies

May xx, 2012

URGENT FIELD SAFETY NOTICE

Software Anomaly Using VITROS® 5,1 FS System Software Version 2.6.1 & Below VITROS® 4600 Chemistry System Software Version 2.0 & Below VITROS® 5600 Integrated System Software Version 2.0 & Below

Dear Customer,

As part of a Field Safety Corrective Action, the purpose of this communication is to inform you that Ortho Clinical Diagnostics (OCD) has identified an anomaly using the VITROS® System Software listed above. We received complaints of an unexpected product lot switch that occurred following the successful calibration of a new generation (GEN) for the products listed below. Our records indicate that you were shipped some of the products to which the lot switch can occur.

Product Code	Name of Product	GENs No Longer Supported	Comments
6801709	VITROS® Chemistry Products VANC Reagent	GENs 19 or 20	GENs 19 & 20 have expired
6801710	VITROS® Chemistry Products VALP Reagent	GENs 14 or 15	GENs 14 & 15 will be replaced

Summary of Anomaly

VITROS® Systems allow multiple lots of the same reagent to be on board the system at the same time. The system will automatically switch to the next (or alternate) lot when the "in use" lot is depleted or when the operator manually changes the lot that is in use.

Our investigation determined that following the successful calibration of the *new* GENs of VITROS® VANC Reagent (*GEN 21 & above*) or VITROS® VALP Reagent (*GEN 16 & above*) the system unexpectedly switched and used the *previous* lot on board the system to process post calibration quality control samples. If the operator does not notice the lot switch condition code (i.e., PV2-097) that was posted, the new calibration may not be verified by the proper quality control assessment. Refer to Question and Answer #1 for additional information.

If the anomaly occurs and is undetected by the operator, biased results could potentially occur from a calibration that is suboptimal. While the VITROS® VALP and VANC Reagents are performing to specifications, to prevent this issue from occurring, OCD will discontinue supporting VITROS® VALP GENs 14 & 15 and VITROS® VANC GENs 19 & 20 on a future Assay Data Diskette (ADD). OCD will therefore replace your remaining inventory of non-expired GENs 14 or 15 for VITROS® VALP Reagent only. (Note: VITROS® VANC Reagent, GENs 19 & 20 are now expired.) In the interim, it is acceptable to continue to use your VITROS® VALP Reagent, GENs 14 or 15 only until your replacement order arrives providing that your quality control is within acceptable criteria. This anomaly will be resolved in a future version of software.

Required Actions

1. All customers are required to complete and return the enclosed Confirmation of Receipt form no later than **May xx, 2012**.
2. Review your quality control results beginning on the date that you calibrated VITROS® VANC Reagent (GEN 21 & above) or VITROS® VALP Reagent (GEN 16 & above) to verify that the QC results were within acceptable ranges. Refer to Question and Answer # 4.

Required Actions (Continued)

3. ***For customers using VITROS® VALP Reagent, GENs 14 or 15***
   - Indicate the quantity of non-expired GENs 14 and 15 remaining in your inventory on the Confirmation of Receipt form so that we can process your replacement order.
   - Continue to use your remaining inventory of GENs 14 or 15 until your replacement order arrives providing that it is within expiry dating and quality control results are acceptable.
   - Load and use only one GEN of VITROS® VALP Reagent at a time on your system until your replacement order arrives.
   - Discard all remaining inventory of GENs 14 or 15 upon receipt of your replacement order.
4. Post this notification by each VITROS® System in your facility that utilizes the VITROS® VALP Reagent or VITROS® VANC Reagent or with your user documentation.
5. Forward the information in this notification, if you have distributed these products outside of your facility.

Although we have had no reported occurrences of biased results, the enclosure contains results from our simulated experiment on the effects of a suboptimal calibration.

We recommend that you discuss any concerns you may have regarding previously reported patient results with your Laboratory Medical Director to determine the appropriate course of action.

We apologize for any inconvenience this may cause your laboratory. We have anticipated some questions you may have in the following Question and Answers section. If you have any additional questions, please call Customer Technical Services at *insert appropriate number*.

Sincerely,

insert appropriate name
insert appropriate title

Enclosure:
Effects of Suboptimal Calibration on Sample Results

Questions and Answers

1. How does this issue occur on a VITROS® System?

Our investigation determined that following the successful calibration of the *new* GENs of VITROS® VANC Reagent (*GEN 21 & above*) or VITROS® VALP Reagent (*GEN 16 & above*) the system can perform an unexpected lot switch and use the *previous* lot on board the system to perform the quality control testing.

As an example, for VITROS® VALP Reagent the following can occur:

- GEN 15 is the current in use lot.
- New Gen 16 is loaded and successfully calibrated.
- The operator programs the quality control samples to verify the calibration of GEN 16. An unexpected lot switch occurs but the operator does not notice the 'PV2-097' condition code.
- Quality control samples are processed using GEN 15 reagent instead of GEN 16.
- GEN 16 is on board the system when GEN 15 is depleted, the system automatically switches to GEN 16. Therefore, it is possible to release VALP results without processing quality control samples to verify the calibration for GEN 16.

2. What is the impact if the unexpected lot switch occurs on my VITROS® System?

If the operator notices the 'PV2-097' condition code indicating that an unexpected lot switch occurred, they would need to unload the previous GEN, then process quality control samples using the new GEN.

If the operator does not notice the 'PV2-097' condition code, results could be generated on a calibration that has not been verified by the appropriate quality control. If this occurs, it may not be detected until the next time quality control is processed on your system using the new GEN (i.e., next shift or the following day).

3. If a calibration is suboptimal, what is the impact to my VITROS® VALP Reagent or VITROS® VANC Reagent results?

The system performs multiple checks for irregularities that can cause a calibration to be unsuccessful. If this occurs, the message "Calibration Failed" is reported in place of the calibrator parameters. However, a successful, yet suboptimal calibration is possible and if undetected, biased results can occur.

Although we have had no reported occurrences of biased results, the enclosure contains results from our simulated experiment on the effects of a suboptimal calibration.

4. How can I determine if my system had a suboptimal calibration on my VITROS® System?

We recommend that you review your quality control results beginning on the date you first calibrated GEN 16 or above for VITROS® VALP Reagent and/or GEN 21 or above for VITROS® VANC Reagent to verify that the results are within the expected range for each affected GEN used during this time. If your quality control results were within acceptable limits, there is no impact to your results due to the unexpected lot switch on your system.

If your quality control results were outside of the expected range, you should follow your normal laboratory procedures for the appropriate course of action.

Questions and Answers (Continued)

5. **Can this anomaly occur if *ONLY* GENs 16 or higher for VITROS® VALP Reagent or GENs 21 or higher for VITROS® VANC Reagent are in use?**

   No. The anomaly only occurs while performing a calibration and the following GENs are on board at the same time:

   ✓ VITROS® VALP Reagent GENs 14 or 15 ***and*** GEN 16 or above

   OR

   ✓ VITROS® VANC Reagent GENs 19 or 20 or ***and*** GEN 21 or above

6. **Should I take any action on previously reported patient results using VITROS® VALP Reagent or VITROS® VANC Reagent?**

   We recommend that you discuss any concerns you may have regarding previously reported patient results with your Laboratory Medical Director to determine the appropriate course of action. Results should be reviewed and interpreted in the context of the overall clinical picture.

7. **When did this anomaly occur and what products are affected?**

   The anomaly exists in the software listed below:

   - VITROS® 5,1 FS System Software Version 2.6.1 & Below
   - VITROS® 4600 Chemistry System Software Version 2.0 & Below
   - VITROS® 5600 Integrated System Software Version 2.0 & Below

   However, the anomaly was detected after OCD implemented a manufacturing revision to an *internal* assay identifier for products that were released beginning in November 2011.

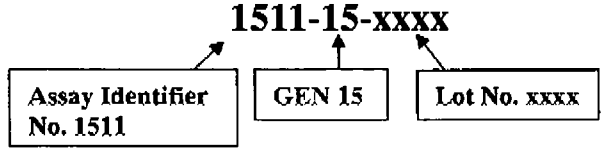
Name of Product	GENs Affected	Comments
VITROS® VANC Reagent	GEN 21 & above	All previous GENs are expired.
VITROS® VALP Reagent	GEN 16 & above	Product replacement is only required for GENs 14 & 15. All other previous GENs are now expired.

8. **Can I continue to use VITROS® VALP GEN 15 Reagent until my replacement order arrives?**

   It is acceptable to continue to use non-expired GENs 14 or 15 Reagent only until your replacement order arrives providing that your quality control is within acceptable criteria.

9. **How can I determine if I have a GEN of VITROS® VALP Reagent in my inventory that will require product replacement?**

   OCD will replace your remaining inventory of non-expired VITROS® VALP Reagent, GENs 14 or 15 only. All other affected GENs are expired. Use the example below to determine the GEN on the product packaging:



10. **When will this issue be resolved?**

    This anomaly will be resolved in a future version of software.

Confirmation of Receipt - Important Response Required

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VITROS® 5,1 FS System Software Version 2.6.1 & Below
VITROS® 4600 Chemistry System Software Version 2.0 & Below
VITROS® 5600 Integrated System Software Version 2.0 & Below

So that we can complete our records, please return this form to us no later than May xx, 2012.

FAX TO: *Insert appropriate name*
FAX: *Insert appropriate number*

Section I: Confirmation

I received and understand the Urgent Field Safety Notice (Ref. CL12-154_EU) and have implemented the instructions provided in this notification. *Please choose from the following options:*

☐ I do NOT have any inventory of non-expired VITROS® VALP Reagent, GENs 14 or 15. Product replacement is not required.

☐ I no longer use VITROS® VALP or VANC Reagent. My facility is not affected by this issue.

☐ I have inventory of non-expired VITROS® VALP Reagent, GENs 14 or 15. In order to process your replacement order, please complete the table below:

Product	GEN No.*	No. of Kits to be replaced
VITROS® VALP Reagent (6801710)	GEN 14	
	GEN 15	

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

Your Name: _____ Job Title (optional): _____

Signed*: _____ Date: _____

Fax Number: _____ Telephone Number: _____

J Number: _____ Institution: _____

Your comments are always welcome:

Section II – Verification of your Name and Address

Verify your name and mailing address:

Please complete this section if your name and/or mailing address have changed:

Institution / Contact Name: _____

Address: _____

City: _____ State/Province: _____ Zip/Postal Code: _____

Telephone: _____ FAX: _____

Effects of a Suboptimal Calibration on Sample Results

Although we have had no reported occurrences of biased results, this enclosure contains results from our *simulated* experiment on the effects of a suboptimal calibration in which the following was performed:

1. A calibration curve (optimized) was created and results were predicted.
2. Calibration responses from the calibration curve (optimized) were then biased by the theoretical (percentage) amounts and the results were re-predicted.

The difference between the two predicted values are presented in the table below.

Difference Between Optimized Calibration Curve (Correct) Versus Suboptimal Calibration Curve						
Theoretical Impact to VITROS® VALP Results						
Concentration Range µg/mL	**-1%**	**1%**	**-2.5%**	**2.5%**	**-5%**	**5%**
15.2	2.3	-2.2	6.1	-4.9	13.5	-8.8
34.4	3.5	-4.2	9.2	-7.8	19.8	-14.4
60.2	4.7	-5	12.3	-10.8	26.4	-20.2
92.1	6.1	-2.4	15.7	-14	33.5	-26.3
110.2	6.8	1.2	17.6	-15.6	37.3	-29.4
129.9	7.5	6.6	19.3	-17.3	41	-32.8
150.9	8.3	14.8	21.2	-19	45	-36.1
Theoretical Impact to VITROS® VANC Results						
Concentration Range µg/mL	**-1%**	**1%**	**-2.5%**	**2.5%**	**-5%**	**5%**
5.9	0.47	-0.44	1.16	-1.06	2.44	-2.07
8.86	0.56	-0.54	1.41	-1.26	2.98	-2.44
12.24	0.69	-0.66	1.76	-1.53	3.76	-2.94
16.23	0.87	-0.82	2.26	-1.91	4.86	-3.65
21.09	1.11	-1.07	2.97	-2.48	6.48	-4.65
27.19	1.49	-1.41	4.07	-3.3	9.02	-6.11
35.21	2.09	-1.94	5.86	-4.59	13.27	-8.35
46.35	3.14	0.17	9.1	-6.76	21.26	-12.04

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