Ortho Clinical Diagnostics
a Johnson & Johnson company

May xx, 2011

URGENT FIELD SAFETY NOTICE

Biased Results using VITROS® Chemistry Products VALP Reagent (Product Code 6801710)

Dear Customer,

As part of a Field Safety Corrective Action, the purpose of this notification is to inform you that Ortho Clinical Diagnostics (OCD) was notified by a proficiency testing agency that results using VITROS® Chemistry Products VALP Reagent were negatively biased compared to other manufacturers. OCD performed an internal investigation and confirmed that patient results are also affected by this issue. As a result, we will be adjusting the calibrator values for VITROS® VALP Reagent. Refer to the table on page two that contains the magnitude of observed bias.

The adjusted calibrator values for VITROS® VALP Reagent will be sent to you via Assay Data Disk (ADD) Data Release Version (DRV) 5632. We anticipate that ADD DRV 5632 will be mailed to your laboratory during the week of May 16, 2011. ***In the interim, immediately discontinue using all lots of VITROS® VALP Reagent in your inventory.****

VITROS® Chemistry Products VALP Reagent is used on the VITROS® 5,1 FS Chemistry System and the VITROS® 5600 Integrated System to quantitatively measure valproic acid (VALP) concentration in human serum and plasma. The affected lots are listed below.

Name of Product Affected	Product Code	Lot Numbers Affected
VITROS® VALP Reagent Generation (GEN) 14	**6801710**	1511-14-1230 1511-14-9776 1511-14-9894 1511-14-1094 1511-14-9637

If your laboratory does not have an alternative valproic acid method available, we recommend that you consider sending patient samples to a commercial laboratory. Refer to the Question and Answer section on page three for additional information.

Please do the following:

1. Immediately discontinue using all lots of VITROS® VALP Reagent in your inventory.*
2. Post this notification by each VITROS® 5,1 FS and/or 5600 System in your facility that utilizes the VITROS® VALP Reagent or with your user documentation.
3. Complete and return the enclosed Confirmation of Receipt form upon receipt of this notification. Please return this form no later than **May xx, 2011**.
4. Forward the information in this notification, if you have distributed this product outside of your facility.

****Upon the loading of ADD DRV 5632 and a successful re-calibration of these VITROS® VALP Reagent lots, it will be acceptable to resume using your current inventory.***

Due to this issue, we have determined that results using VITROS® VALP Reagent are negatively biased as shown below.

Observed Bias Results for VITROS® VALP Reagent			
Conventional Units		**SI Units**	
Concentration Range (µg/mL)	**Average Bias in Results (µg/mL)**	Concentration Range (µmol/L)	Average Bias in Results (µmol/L)
10-50	-8.8	69.3-346.5	-61.0
50-100	-11.4	346.5-693.0	-79.0
100-150	-6.7	693.0-1039.5	-46.4

The VITROS® Chemistry Products Instruction For Use for VALP Reagent states that the following guidelines represent a combination of the recommendations of the National Academy of Clinical Biochemistry and Jacobs, et al.[1, 2] Each laboratory should verify the validity of these recommendations for the population it serves.

Classification	Conventional Units (µg/mL)	SI Units (µmol/L)	Alternate Units (mg/L)
Minimal	50.0	346.5	50.0
Therapeutic	50.0–120.0	346.5–831.6	50.0–120.0
Possible Toxic	> 100.0	693.0	> 100.0
Serious Toxic	> 200.0	1386.0	> 200.0

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

1. National Academy of Clinical Biochemistry Symposium. Standards of laboratory practice: antiepileptic drug monitoring. Ann Warner, Michael Privitera, and David Bates. Clinical Chemistry 44:5 1085
2. Jacobs, DS, DeMott WR, Grady HJ, Horvat RT, Kasten BL, Jr. Laboratory Test Handbook. 4th ed. Hudson, Ohio: Lex –Comp Inc; 1996: 577

Questions and Answers

1. **Should I take any action on previously reported patient results using VITROS® VALP 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.

2. **How much bias has been observed when using VITROS® VALP Reagent?**

   Our internal testing included several lots of GEN 14, dating back to Feb 2010. The table below shows the bias that you may observe prior to the re-calibration of your VITROS® VALP Reagent with ADD DRV 5632.

Expected Shift in Results for VITROS® VALP Reagent			
Conventional Units		**SI Units**	
Concentration Range (µg/mL)	**Average Change in Results (µg/mL)**	**Concentration Range (µmol/L)**	**Average Change in Results (µmol/L)**
10-50	-8.8	69.3-346.5	-61.0
50-100	-11.4	346.5-693.0	-79.0
100-150	-6.7	693.0-1039.5	-46.4

3. **What type of samples can be affected by this issue?**

   Any sample type (i.e., patient, quality control fluid, and proficiency fluids) could be affected.

4. **Is the Reference Interval impacted as a result of the change in performance?**

   The current reference interval and method correlation data, as defined in the Instructions For Use documents, are not impacted by this change. If your laboratory has established a reference interval for valproic acid, you may need to reevaluate this reference interval for the population you serve *after* re-calibration using ADD DRV 5632.

5. **Will this issue be detected by routine quality control fluid testing?**

   No, quality control fluids will not detect this issue as the range established for the control fluids in your laboratory are similarly affected.

6. **If I cannot use my inventory of VITROS® VALP Reagent until ADD DRV 5632 arrives, what action shall I take for obtaining valproic acid test results?**

   If your laboratory does not have an alternative valproic acid method available, we recommend that you consider sending patient samples to a commercial laboratory.

   Ortho Clinical Diagnostics understands the inconvenience of this issue. We are internally investigating how we may assist laboratories in a compliant manner during the interim time period when valproic acid testing is not available on VITROS systems.

Questions and Answers (Continued)

7. When will this issue be resolved?

The adjusted calibrator values for VITROS® VALP Reagent will be sent to you via ADD DRV 5632. We anticipate that the ADD will available during the week of May 16, 2011.

NOTE: Loading ADD DRV 5632 will automatically un-calibrate all lots of VITROS® VALP Reagent. For systems that are e-connected, the ADD will not be auto downloaded. ADD DRV 5632 will only be issued via mail with a communication that will contain instructions and revised VITROS® Chemistry Products TDM Performance Verifier ranges.

In preparation for the re-calibration of your VITROS® VALP Reagent, please ensure that you have an adequate supply of VITROS® Chemistry Products Calibrator Kit 12 in your inventory. To place an order for VITROS® Calibrator Kit 12 (**Product Code 680 1697**), please contact our customer service representatives at *insert appropriate number.*

8. How can I determine if I have an affected lot of VITROS® VALP Reagent in my inventory?

The affected lots are listed on page one. Use the example below to determine the Generation (GEN) and lot number on the product packaging: