URGENT

Ortho Clinical Diagnostics

November xx, 2018

UPDATED: URGENT FIELD SAFETY NOTICE

Potential for Biased Results due to Biotin Interference for the VITROS Immunodiagnostic Products NT-proBNP Assay

Dear Customer,

This is an **update** to an Urgent Field Safety Notice that was issued in July 2018 (Ref. CL2018-149_EU). The purpose of this notification is to inform you that Ortho Clinical Diagnostics determined that biased results may also occur for an additional VITROS Immunodiagnostic Products (MicroWell Assay) at biotin concentrations which are lower than indicated in the current Instructions for Use (IFU).

The following VITROS MicroWell assay that uses streptavidin-biotin in its design is also affected.

Product Name (Unique Identifier No.)	Product Code	Affected Lots
VITROS® Immunodiagnostic Products NT-proBNP Reagent Pack (10758750002061)	**6802156**	These changes are applicable to all expired, in-date and future lots released

Background Information

In February 2018: Ortho issued a notification (Ref. CL2018-056a) regarding the trend toward the use of higher-dose biotin supplements.

As a follow up, we conducted further studies to assess the impact of biotin on all susceptible VITROS MicroWell Assays.

In July 2018: Ortho issued a notification (Ref. CL2018-149_EU) that indicated that patients who are taking biotin supplements could potentially have biased sample results at biotin concentrations lower than indicated in the current IFU for specific assays (i.e., Folate, Free PSA, FSH, Prolactin & TSH).

October 2018: Recent testing determined that the VITROS NT-proBNP assay is also affected by biotin interference at concentrations which are lower than indicated in the current IFU.

Impact

Samples affected by biotin interference are not easily identifiable without knowledge of biotin administration for each patient; thus, a review of previous results may be impractical. Follow your normal laboratory procedures as you would for troubleshooting of samples containing other known assay interferences.

Discuss any concerns you may have regarding previously reported results using the affected assays with your Laboratory Medical Director to determine the appropriate course of action. The results from this or any other diagnostic test should be used and interpreted only within the context of the overall clinical picture.

Revisions to Instruction for Use (IFU)

Historically, these assays were evaluated for interference consistent with CLSI document EP7. Biotin was tested and was not found to cause a bias sufficient to interfere with the assay.

To assess the potential interference of biotin supplements on VITROS MicroWell Assays, Ortho performed testing using the new CLSI guidelines EP7 and EP37 and determined that the information in the current IFUs is no longer supported for the following additional assays.

The concentration of biotin that causes ≥ 10% bias is listed in the table below:

Assay	Concentration at which Current IFU Indicates No Biotin Interference (< 10% Bias)	NEW Information: Concentration at which Biotin Interference is Observed (≥ 10% Bias)		
		Biotin Concentration	Analyte Concentration	Bias Observed
NT-proBNP	20 ng/mL (2 µg/dL)	20 ng/mL	116.1 pg/mL	-19.32 pg/mL
		20 ng/mL	406.5 pg/mL	-70.76 pg/mL

Resolution

VITROS Instructions for Use (IFUs) will be revised to include the updated interferent information in the *Limitations of the Procedure* section for all affected assays.

REQUIRED ACTIONS

- Prior to the availability of the revised IFU, be aware that biased results may occur for patient samples containing high doses of biotin. Follow your normal laboratory procedures as you would for troubleshooting of samples containing other assay interferences.
  Note: It is acceptable to continue using the VITROS NT-proBNP assay.
- Post this notification by your VITROS System or with your user documentation.
- In accordance with regulatory requirements, complete the Confirmation of Receipt form and return by **November xx, 2018.**
- Forward this notification if the product was distributed outside of your facility.

Contact Information

We apologize for any inconvenience this may cause in your laboratory. If you have questions, please contact Ortho Care™ Technical Solutions Center at insert number.

Insert signatory if appropriate in your region

Questions and Answers

1. **Can I continue to use the affected assays?**

   It is acceptable to continue using the VITROS NT-proBNP assay with an awareness that biased results may occur for patients who are taking biotin supplements.

2. **What is the clinical utility of over-the-counter biotin supplements?**

   Vitamin supplement manufacturers have introduced over-the-counter biotin supplements with claims of health and beauty benefits. This has resulted in a trend in certain populations toward daily consumption of high doses of biotin. Supplements with very high doses of biotin (i.e., 1,000, 5,000 and 10,000 mcg/tablet) have more recently become available.

   For healthy patients, over-the-counter supplements with these high doses of biotin are 20 to >300 times greater than the adequate daily intake for adults of 30 mcg/day established by the Institute of Medicine[i].

3. **Is there anything I need to do?**

   Because the trend is prevalent in the US, available references tend to be from US sources. However, they can be useful to laboratories in all countries to help manage biotin interference in your facility, as well as communications with your clinicians:

   FDA Safety Communication: https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm586505.htm

   Ortho supports the FDA Safety Communication recommendation for laboratory, clinician and patient education about reporting all prescription medication and supplements prior to blood draws.

4. **What is Ortho doing?**

   Ortho takes interference due to biotin very seriously. In addition to updating all IFUs to reflect current consumer trends, we have developed new MicroWell technology to eliminate biotin interference in future assays. We are currently updating several of our assays with this new technology including TSH and Free PSA. All new assays launched since 2015 are developed with this new design and are not affected by biotin.

   In the interim, we will issue a Technical Bulletin that will contain this updated biotin interference information. We will notify you upon availability.

[i] https://ods.od.nih.gov/factsheets/Biotin-HealthProfessional/

Confirmation of Receipt – Response Required

Communication ID: CL2018-250_EU Date of Issue: 2018-xx-xx

UPDATE: URGENT FIELD SAFETY NOTICE

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*Please return this completed form by **fax** or **scan to PDF** and email so that we can complete our records no later than:* **DD-NOV-2018**

Send to: Name e-Mail Address: email address Fax: Fax Number

Your Name and Address

Verify your name and mailing address:

Please complete this section if any of this information has changed

Institution/
Contact Name: _____
Address: _____
City: _____ State/Prov: _____ Zip/Postal Code: _____
Phone: _____ Fax: _____
e-Mail: _____

Please Confirm

I received the updated Urgent Field Safety Notice regarding biased results that may occur for the VITROS NT-proBNP assay at biotin concentrations which are lower than indicated in the current Instructions for Use (IFU).

I understand the information provided in the customer letter and will follow my normal laboratory procedures for samples containing assay interferences.

Your Name: _____

Phone Number: _____ Date: _____

Signature:
Required if sent by fax or a scanned PDF

Your Comments: _____