URGENT

Ortho Clinical Diagnostics

July XX, 2018

URGENT FIELD SAFETY NOTICE

Potential for Biased Results due to Biotin Interference for Specific VITROS MicroWell Assays

Dear Customer,

As part of a Field Safety Corrective Action, Ortho Clinical Diagnostics initiated this Urgent Field Safety Notice due to biased results may occur for specific VITROS Immunodiagnostic Products (MicroWell Assays) at biotin concentrations which are lower than indicated in the current Instructions for Use (IFU).

The following VITROS MicroWell assays that use streptavidin-biotin in their design are affected.

Product Name (Unique Identifier No.)	**Product Code**	**Affected Lots**
VITROS® Immunodiagnostic Products Folate Reagent Pack (10758750009237)	**1513266**	These changes are applicable to all expired, in-date and future lots released.
VITROS® Immunodiagnostic Products Free PSA Reagent Pack (10758750013517)	**6842845**	
VITROS® Immunodiagnostic Products FSH Reagent Pack (10758750000302)	**1931922**	
VITROS® Immunodiagnostic Products Prolactin Reagent Pack (10758750000111)	**1849793**	
VITROS® Immunodiagnostic Products TSH Reagent Pack (10758750000227)	**1912997**	

Description of Issue

In February 2018, we issued a notification (Ref. CL2018-003) regarding the trend toward the use of higher-dose biotin supplements. As a follow up, Ortho conducted further studies to assess the impact of biotin on all susceptible VITROS MicroWell Assays. Our data indicates that patients who are taking biotin supplements could potentially have biased sample results for the assays listed above at biotin concentrations 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 of ≥10%.

To assess the potential interference of biotin supplements on VITROS MicroWell Assays, Ortho performed more robust testing using the new CLSI guidelines EP7 and EP37 and determined that the information in the current IFUs is no longer supported for these five 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
Folate	10 ng/mL (1 µg/dL)	10 ng/mL	6.59 ng/mL	+ 0.82 ng/mL
		15 ng/mL	14.7 ng/mL	+ 2.4 ng/mL
Free PSA	10 ng/mL (1 µg/dL)	8 ng/mL	1.01 ng/mL	- 0.12 ng/mL
		13 ng/mL	11.0 ng/mL	- 1.3 ng/mL
FSH	10 ng/mL (1 µg/dL)	8 ng/mL	4.24 mIU/mL	- 0.51 mIU/mL
		8 ng/mL	37.7 mIU/mL	- 4.2 mIU/mL
Prolactin	10 ng/mL (1 µg/dL)	8 ng/mL	403.9 mIU/mL	- 56.0 mIU/mL
		8 ng/mL	4202 mIU/mL	- 721 mIU/mL
TSH	5 ng/mL (0.5 µg/dL)	5 ng/mL	0.350 mIU/L	- 0.060 mIU/L
		8 ng/mL	7.74 mIU/L	- 1.77 mIU/L

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 IFUs, 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 five affected VITROS MicroWell Assays.
- 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 **July 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 five affected VITROS MicroWell assays 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?**

   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 (estimated to be in September 2018).

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

Confirmation of Receipt – Response Required

Communication ID: CL2018-149_EU Date of Issue: 2018-xx-xx

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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-JULY-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 Urgent Field Safety Notice regarding biased results that may occur for these specific VITROS Immunodiagnostic Products (MicroWell Assays) 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: _____