URGENT

Ortho Clinical Diagnostics

July 2018

URGENT PRODUCT CORRECTION NOTIFICATION

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

Dear Customer,

Cc: Chairman Medical Board and relevant Head of Department

The purpose of this notification is to inform you that Ortho Clinical Diagnostics has determined that 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 [redacted]	1513266	These changes are applicable to all expired, in-date and future lots released.
VITROS® Immunodiagnostic Products Free PSA Reagent Pack [redacted]	6842845	
VITROS® Immunodiagnostic Products FSH Reagent Pack [redacted]	1931922	
VITROS® Immunodiagnostic Products Prolactin Reagent Pack [redacted]	1849793	
VITROS® Immunodiagnostic Products TSH Reagent Pack [redacted]	1912997	

Description of Issue

We previously issued a notification (Ref. CL2018-056) regarding the trend in some countries 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 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 not be practical. 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 fromg 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 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	14.9 nmol/L	+ 1.86 nmol/L
		15 ng/mL	33.3 nmol/L	+ 5.43 nmol/L
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 27, 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. We have anticipated some questions in the following Question and Answer section. If you have additional questions, please contact your local Ortho representative or our Ortho Care™ Technical Solutions Centre 1800-5646-766.

Sincerely,

[redacted]

Jon Wong,
QA Manager

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).

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