Ortho Clinical Diagnostics	**URGENT PRODUCT CORRECTION NOTIFICATION** **Positively Biased Results using VITROS® Immunodiagnostic Products Estradiol Reagent Packs**

Date Issued July 2016

Affected Product

Product Name (Unique Device Identifier No)	Product Code	In-Date Lot No. (Expiry Date)	
VITROS Immunodiagnostic Products Estradiol Reagent Pack (10758750005017)	8552630	1470 (02-Aug-16)	1528 (01-Nov-16)
		1480 (05-Aug-16)	1538 (14-Mar-17)
		1490 (10-Oct-16)	1548 (09-Mar-17)
		1500 (10-Oct-16)	1558 (09-Mar-17)
		1510 (01-Nov-16)	1568 (29-Mar-17)

Issue Description

Ortho Clinical Diagnostics (Ortho) has been alerted to the potential for medications that are derivatives of oestrogen (e.g. Fulvestrant, brand name: FASLODEX®) to interfere with oestradiol immunoassays and cause positively biased sample results. Due to this issue, we are initiating this Urgent Product Correction.

Fulvestrant is an oestrogen receptor antagonist medication. The drug is used in the treatment of patients with metastatic, postmenopausal, hormone receptor-positive breast cancer.

Impact to Results

Our investigation confirmed positively biased oestradiol results on samples obtained from postmenopausal females containing 30 ng/mL of Fulvestrant (peak serum concentration of this therapeutic drug). The results using VITROS Estradiol Reagent Packs are on page two.

Consider the need to notify your clinicians/physicians regarding previously reported oestradiol results for women who were administered Fulvestrant. Discuss any concerns you may have regarding previously reported oestradiol results 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.

Resolution

The VITROS Immunodiagnostic Products Estradiol Instructions for Use (IFU) will be revised to include this new information in the *Limitations of the Procedure* section. We will notify you when the revised IFU is available on our website.

Required Actions

- Prior to the availability of the revised IFU, be aware that positively biased results may occur for patients taking Fulvestrant. Follow your normal laboratory procedures as you would for other known sample interferences.
  Note: It is acceptable to continue using VITROS Estradiol Reagent Packs.
- Discuss any concerns regarding previously reported results with your Laboratory Medical Director to determine the appropriate course of action.

Required Actions (continued)

- Post this notification by your VITROS System or with your user documentation.
- In accordance with regulatory requirements, complete the Confirmation of Receipt form. Please return your form by **July 27, 2016.**

Contact Information

We have anticipated some questions you may have in the following Question and Answer section. If you have additional questions, contact your local Ortho representative or our Technical Solutions Centre at **1800 5646 766.**

Sincerely,

Lee, Ching Hwee
Associate Manager Regulatory Affairs

Enclosure: Confirmation of Receipt Form

Questions and Answers

1. **How does Fulvestrant medication affect VITROS Estradiol test results?**

   Certain drugs and clinical conditions are known to alter oestradiol concentrations in vivo. Ortho recently became aware that Fulvestrant medication is known to interfere with oestradiol immunoassays.

   Fulvestrant (brand name: FASLODEX®) is a prescription medication which blocks oestrogen for tumours that require oestrogen for growth. It used in the treatment of patients with metastatic, postmenopausal, hormone receptor-positive breast cancer. Fulvestrant is a synthetic derivative of oestradiol and is a receptor antagonist. It has a higher affinity for the receptor than oestrogen and irreversibly binds, altering the structure of the receptor. Since the structure of Fulvestrant is similar to oestrogen, it can cross-react in oestradiol assays causing positively biased test results.

2. **What is the impact to my results?**

   Ortho's investigation confirmed positively biased oestradiol results on samples obtained from postmenopausal females containing 30 ng/mL of Fulvestrant. The following biases were observed using VITROS Estradiol Reagent Packs:

Sample ID	Results for Samples with 0 ng/mL Fulvestrant	Results for Samples Containing 30* ng/mL Fulvestrant
Sample 1	35 pmol/L (9.534 pg/mL)	1295 pmol/L (352.8 pg/mL)
Sample 2	43 pmol/L (11.71 pg/mL)	1366 pmol/L (372.1 pg/mL)
Sample 3	128 pmol/L (34.87 pg/mL)	1687 pmol/L (459.5 pg/mL)
Sample 4	138 pmol/L (37.59 pg/mL)	1758 pmol/L (478.9 pg/mL)
*30 ng/mL of Fulvestrant is the peak serum concentration of this therapeutic drug (Cmax concentration)		
Measuring (Reportable) Range for Estradiol: 23.347–14,000 pmol/L (6.360–3813.6 pg/mL)		

3. **Should I take any action on previously reported results generated using VITROS Estradiol Reagent Packs?**

   If the oestradiol result is inconsistent with the other tests, clinical impressions and symptoms, the result should be confirmed using an alternate method (non-immunoassay) that is not affected by Fulvestrant.

   Discuss any concerns you may have regarding previously reported oestradiol results 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 in the context of the overall clinical picture.

4. **Can I continue to use VITROS Estradiol Reagent Packs?**

   It is acceptable to continue using VITROS Estradiol Reagent Packs but be aware that positively biased results may occur for patient's taking Fulvestrant medication.