SIEMENS

Urgent Field Safety Notice

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Our Reference FSN CC 17-06
Date 04/01/2017
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URGENT FIELD SAFETY NOTICE

Please find attached an Urgent Field Safety Notice (UFSN). This is an important communication about medical safety issued by Siemens Healthcare Diagnostics.

It is important that your organisation takes the actions detailed in the UFSN and replies immediately using the FIELD CORRECTION EFFECTIVENESS CHECK attached to the UFSN.

Your organisations reply is evidence which Siemens Healthcare, and subsequently the MHRA, needs to monitor the progress of the UFSN. Without your reply Siemens Healthcare Diagnostics cannot properly verify the completeness of the UFSN and the MHRA may need to issue a Medical Device Alert

Attachment:

FSN CC 17-06

If you have any questions or enquiries regarding this UFSN, please do not hesitate to contact the Siemens Healthcare Diagnostics Helpdesk:

Phone: 0845 600 1955

Email: Immunoassay.healthcare@siemens.com

Yours faithfully
Robert Davies
Regulatory Affairs Manager

Unrestricted

SIEMENS

Urgent Field Safety Notice

CC 17-06.A.OUS

January, 2017

ADVIA Centaur® Systems
Dimension Vista® Systems
IMMULITE® Systems

Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays

Our records indicate that your facility may have received one of the following products:

Table 1. Progesterone Assays Manufactured by Siemens Healthcare Diagnostics

Assay	Test Code	Catalog Number	Siemens Material Number (SMN)	Lot Number
ADVIA Centaur Progesterone[1]	PRGE	10310305 10315522 10333111	10310305 10315522 10333111	All Lots
Dimension Vista LOCI Progesterone[2]	PROG	K6464	10461743	All Lots
IMMULITE/ IMMULITE 1000 Progesterone	PRG	LKPW1	10381128	All Lots
IMMULITE 2000 Progesterone[3]	PRG	L2KPW2 L2KPW6	10381181 10381170	All Lots

1 The same reagents are used on the ADVIA Centaur XP, ADVIA Centaur XPT and ADVIA Centaur CP systems.

2 The same reagents are used on the Dimension Vista 500, 1000T, 1500 and 3000T systems.

3 The same reagents are used on the IMMULITE 2000 and IMMULITE 2000 XPi systems.

Reason for Correction

Siemens has confirmed that the presence of DHEA-S (a metabolite of DHEA, a steroid hormone that may be used as part of *in vitro* fertilization (IVF) protocols to improve ovarian response and IVF treatment outcomes) causes falsely elevated progesterone results on the platforms listed in Table 1 around the clinically important decision level of approximately 1 ng/mL (3.18 nmol/L) of progesterone. This threshold is used by some IVF protocols to determine whether to proceed with fresh embryo transfer in the current cycle.

Refer to Additional Information section for a summary of data.

511 Benedict Avenue
Tarrytown, NY 10591

Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays

Risk to Health

Progesterone may be used in the evaluation of ovarian and placental function. The risk to health is limited to patients taking DHEA supplements as part of their IVF treatment plan and who are also being considered for fresh embryo transfer. DHEA-S cross reactivity resulting in falsely elevated progesterone results around the clinical decision threshold of approximately 1.0 ng/mL (3.18 nmol/L) may lead to misinterpretation of progesterone levels and consideration of fresh embryo transfer cancellation and subsequent cryopreservation of the embryo(s). Siemens is not recommending a look back as a result of this issue.

Actions to be Taken by the Customer

- Please review this letter with your Medical Director.
- Siemens has confirmed interference of DHEA-S with the Progesterone products listed in Table 1 and therefore, these assays should not be used to report results for patients who are taking DHEA supplements. For patients taking DHEA supplements, an alternate method such as Liquid Chromatography-Mass Spectroscopy (LCMS) which is not expected to show cross reactivity to DHEA-S should be used to measure progesterone concentrations.
- Siemens' Progesterone assays may continue to be used to report results for patients who are not taking DHEA supplements.
- Complete and return the Field Correction Effectiveness Check Form attached to this letter within 30 days
- If you have received any complaints of illness or adverse events associated with the products listed in Table 1, immediately contact your local Siemens Customer Care Center or your local Siemens technical support representative.

Please retain this letter with your laboratory records, and forward this letter to those who may have received this product.

We apologize for the inconvenience this situation may cause. If you have any questions, please contact your Siemens Customer Care Center or your local Siemens technical support representative.

Product availability may vary from country to country and is subject to varying regulatory requirements. Due to local regulations, the ADVIA Centaur XPT is not available in all countries.

Additional Information

Two concentrations of DHEA-S were spiked into three serum sample pools. Samples were measured neat and spiked with DHEA-S.

The following equations were used to calculate %Change and %Cross Reactivity:

%Change = (spiked sample result-neat sample result)/neat sample result X 100

%Cross Reactivity = (spiked sample result in ng/mL- neat sample result in ng/mL)/concentration of DHEA-S in ng/mL) X 100

A summary of the investigation results is shown in Tables 2, 3, 4 and 5.

Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays

Table 2. ADVIA Centaur Progesterone

Neat Progesterone Concentration ng/mL (nmol/L)	DHEA-S Spiked Concentration ng/mL (umol/L)	Progesterone Results of Spiked Sample ng/mL (nmol/L)	%Change	%Cross Reactivity
0.21 (0.67)	5000 (13.57)	0.54 (1.72)	157	0.01
	20000 (54.28)	1.80 (5.72)	757	0.01
0.70 (2.23)	5000 (13.57)	0.92 (2.93)	31.4	0.00
	20000 (54.28)	2.18 (6.93)	211	0.01
16.9 (53.7)	5000 (13.57)	14.6 (46.4)	-13.6	-0.05
	20000 (54.28)	13.1 (41.7)	-22.5	-0.02

Table 3. Dimension Vista Progesterone

Neat Progesterone Concentration ng/mL (nmol/L)	DHEA-S Spiked Concentration ng/mL (umol/L)	Progesterone Results of Spiked Sample ng/mL (nmol/L)	%Change	%Cross Reactivity
0.24 (0.76)	5000 (13.57)	1.13 (3.59)	371	0.02
	20000 (54.28)	3.47 (11.0)	1346	0.02
1.06 (3.37)	5000 (13.57)	1.95 (6.20)	84.0	0.02
	20000 (54.28)	4.33 (13.8)	308	0.02
16.4 (52.2)	5000 (13.57)	17.5 (55.7)	6.71	0.02
	20000 (54.28)	19.4 (61.7)	18.3	0.02

Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays

Table 4. IMMULITE/IMMULITE 1000 Progesterone

Neat Progesterone Concentration ng/mL (nmol/L)	DHEA-S Spiked Concentration ng/mL (umol/L)	Progesterone Results of Spiked Sample ng/mL (nmol/L)	%Change	%Cross Reactivity
0.27 (0.86)	5000 (13.57)	0.37 (1.18)	37.0	0.00
	20000 (54.28)	0.87 (2.77)	222	0.00
1.20 (3.82)	5000 (13.57)	1.64 (5.22)	36.7	0.01
	20000 (54.28)	2.30 (7.31)	91.7	0.01
13.3 (42.3)	5000 (13.57)	13.3 (42.3)	0.00	0.00
	20000 (54.28)	14.7 (46.8)	10.5	0.01

Table 5. IMMULITE 2000 Progesterone

Neat Progesterone Concentration ng/mL (nmol/L)	DHEA-S Spiked Concentration ng/mL (umol/L)	Progesterone Results of Spiked Sample ng/mL (nmol/L)	%Change	%Cross Reactivity
0.23 (0.73)	5000 (13.57)	0.33 (1.05)	43.5	0.00
	20000 (54.28)	0.71 (2.26)	208	0.00
1.16 (3.69)	5000 (13.57)	1.47 (4.67)	26.7	0.01
	20000 (54.28)	2.09 (6.65)	80.2	0.00
11.7 (37.2)	5000 (13.57)	11.5 (36.6)	-1.7	0.00
	20000 (54.28)	12.6 (40.1)	7.7	0.00

Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays

Frequently Asked Questions

What should I communicate to IVF physicians who order or have ordered a Progesterone test?

Notify your IVF physicians that DHEA supplementation will increase the apparent concentration of progesterone in patients being treated with this drug. Physicians using progesterone levels as a criterion for fresh embryo transfer in patients supplemented with DHEA should assess progesterone levels using an assay that is not impacted by DHEA-S cross reactivity. It is possible that LC-MS chromatographic assays for progesterone may not be impacted by DHEA-S.

Are there other drugs that could cross react in these assays?

With the advent of new steroid based medications with similar chemical structures to progesterone, there is the possibility of cross-reactivity and falsely elevated results. For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings. If the progesterone results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.

Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays

FIELD CORRECTION EFFECTIVENESS CHECK

Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice CC 17-06.A.OUS dated January, 2017 regarding Elevated Results in Patient Samples Due to Cross Reactivity of DHEA-S with Progesterone Assays. Please read each question and indicate the appropriate answer.

CC 17-06 [C/3800]

1. I have read and understood the Urgent Field Safety Notice instructions provided in this letter.	Yes ☐	No ☐

Name of person completing questionnaire:	
Title:	
Institution:	Instrument Serial Number:
Street:	
City:	Email:
Phone:	Post Code:

Please complete and return to:
robert.davies@siemens.com or fax to 0845 605 6800

It is important that your organisation takes the actions detailed in the UFSN and replies immediately using the FIELD CORRECTION EFFECTIVENESS CHECK attached to this UFSN. Your organisations reply is evidence which, Siemens Healthcare needs to monitor the progress of the UFSN. Without your reply Siemens Healthcare cannot verify the completeness of the UFSN with the MHRA.