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Urgent Field Safety Notice:

**ADVIA Centaur® Systems
 Dimension Vista® Systems
 IMMULITE® Systems**

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

Dear Sirs,

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

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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.

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.

Sincerely yours,

Siemens Healthcare Diagnostics GmbH



i.V. Dipl. Ing. Franz Schwarz
Head of RAQS Austria & SEE



i.A. Martina Sattler, MSc., MSc.
Product Manager Austria & SEE

Appendix 1: Additional Information
Appendix 2 Frequently Asked Questions

Appendix 1: 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:

$$\%Change = (\text{spiked sample result} - \text{neat sample result}) / \text{neat sample result} \times 100$$

$$\%Cross\ Reactivity = (\text{spiked sample result in ng/mL} - \text{neat sample result in ng/mL}) / \text{concentration of DHEA-S in ng/mL} \times 100$$

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

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

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

Appendix 2 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.