

**IMMULITE®  
IMMULITE® 1000**

### Androstenedione Over-Recovery

Our records indicate that your facility may have received the following product:

**Table 1. IMMULITE Systems Affected Product**

Assay	Test Code	Catalog Number	Siemens Material Number (SMN)	Lot Number
IMMULITE/IMMULITE 1000 Androstenedione	AND	LKA01	10381158	409 – 418

### Reason for Recall

In December 2013, Siemens Healthcare Diagnostics issued Urgent Field Safety Notice (UFSN) #4008 for IMMULITE®/IMMULITE® 1000 Androstenedione. The UFSN advised customers to verify Androstenedione samples with values >5.5 ng/mL (>19.2 nmol/L) using an alternate method due to an observed over-recovery.

During efforts to restore performance of the Androstenedione assay, Siemens observed over-recovery in the IMMULITE/IMMULITE 1000 Androstenedione for samples across the assays' reportable range of 0.3 – 10 ng/mL (1.1 – 35 nmol/L). Siemens confirmed the issue noted in December 2013 is not limited to samples >5.5 ng/mL (>19.2 nmol/L). Please refer to Figures 1 and 2 for more information.

Siemens has identified that the root cause of the over-recovery is related to the variability of a critical raw material. This issue has been resolved beginning with IMMULITE/IMMULITE 1000 Androstenedione, kit lot 431. Please refer to the Additional Information section for more information.

### Risk to Health

The risk to health when using the affected reagent lots listed in Table 1 is negligible and limited to further investigations for a source of excessive androstenedione production. Siemens is recommending a laboratory look back for any existing androstenedione sample(s) with values generated using the reagent lots listed in Table 1 during the period of time within sample stability labeling, and retesting using an alternate method.

### Actions to be Taken by the Customer

- Please review this letter with your Medical Director.
- Discontinue use of and discard the kit lots listed in Table 1.

- Review your inventory of these products to determine your laboratory's replacement needs and to provide information to Siemens for reporting to the authorities.
- Complete and return the Field Correction Effectiveness Check attached to this letter within 30 days.

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.

### **Additional Information**

#### **Comparison of Restored versus Current Kit Lots**

IMMULITE/IMMULITE 1000 Androstenedione, kit lot 431 will begin shipping to customers the week of December 1, 2014.

#### **Restoration of Linearity**

Beginning with IMMULITE/IMMULITE 1000 Androstenedione, kit lot 431, Siemens has corrected the over-recovery of samples, restoring the linearity of the assay to 10 ng/mL (35 nmol/L). Refer to Table 2 for data demonstrating linearity up to 10 ng/mL (35 nmol/L) on different sample types. The overall average percent recovery is 96% for Sample 1, 100% for Sample 2, 106% for Sample 3, 102% for Sample 4, and 112% for Sample 5.

Conversion Factor:  $\text{ng/mL} \times 3.4916 = \text{nmol/L}$

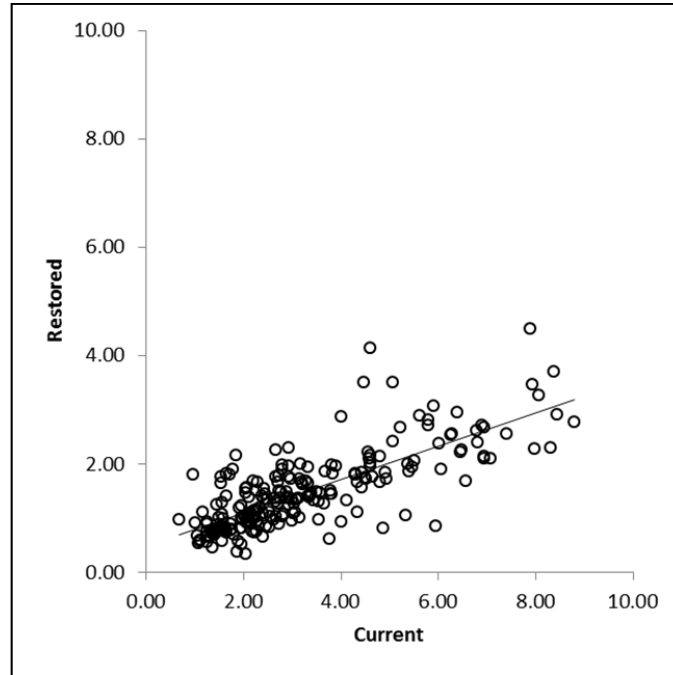
**Table 2. Restoration of the Linearity of the Assay up to 10 ng/mL (35 nmol/L)**

Dilution	Observed Dose (ng/mL)	Expected Dose (ng/mL)	% O/E
<b>Sample 1 (Bio-Rad Quality Control)</b>			
8 in 8	10.14	--	--
7 in 8	8.75	8.99	97%
6 in 8	7.38	7.84	94%
5 in 8	6.68	6.70	100%
4 in 8	5.40	5.55	97%
3 in 8	3.89	4.40	88%
2 in 8	3.01	3.26	92%
1 in 8	2.20	2.11	104%
<b>Sample 2 (Calibrator F)</b>			
8 in 8	6.35	--	--
7 in 8	5.81	5.56	105%
6 in 8	4.61	4.76	97%
5 in 8	3.60	3.97	91%
4 in 8	3.19	3.18	100%
3 in 8	2.39	2.38	100%
2 in 8	1.74	1.59	109%
1 in 8	0.78	0.79	98%
<b>Sample 3 (Patient Sample)</b>			
8 in 8	9.64	--	--
7 in 8	8.90	8.44	106%
6 in 8	7.84	7.23	108%
5 in 8	6.45	6.03	107%
4 in 8	4.82	4.82	100%
3 in 8	4.07	3.62	113%
2 in 8	2.60	2.41	108%
1 in 8	1.23	1.21	102%
<b>Sample 4 (Patient Sample)</b>			
8 in 8	8.16	--	--
7 in 8	6.89	7.14	96%
6 in 8	6.57	6.12	107%
5 in 8	4.94	5.10	97%
4 in 8	4.09	4.08	100%
3 in 8	3.25	3.06	106%
2 in 8	1.96	2.04	96%
1 in 8	1.13	1.02	111%
<b>Sample 5 (Patient Sample)</b>			
8 in 8	7.49	--	--
7 in 8	6.68	6.57	102%
6 in 8	6.33	5.65	112%
5 in 8	4.96	4.73	105%
4 in 8	4.13	3.82	108%
3 in 8	3.34	2.90	115%
2 in 8	2.45	1.98	124%
1 in 8	1.29	1.07	121%

### Comparison of Current vs. Restored IMMULITE 1000 Androstenedione Kit Lots

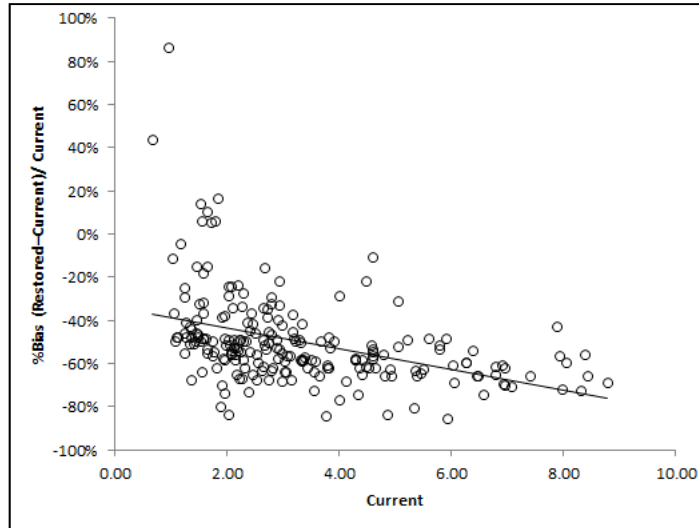
Refer to Figures 1 and 2 for method comparison and bias plots for the current lot of IMMULITE 1000 Androstenedione versus the restored kits of IMMULITE/IMMULITE 1000 Androstenedione.

**Figure 1. Method Comparison of IMMULITE/IMMULITE 1000 Current (Kit Lots 414 and 416) vs. Restored Kits Androstenedione (ng/mL)**



$$\text{Restored} = 0.307 \times \text{Current} + 0.487 \text{ ng/mL}$$
$$R = 0.769, n = 218$$

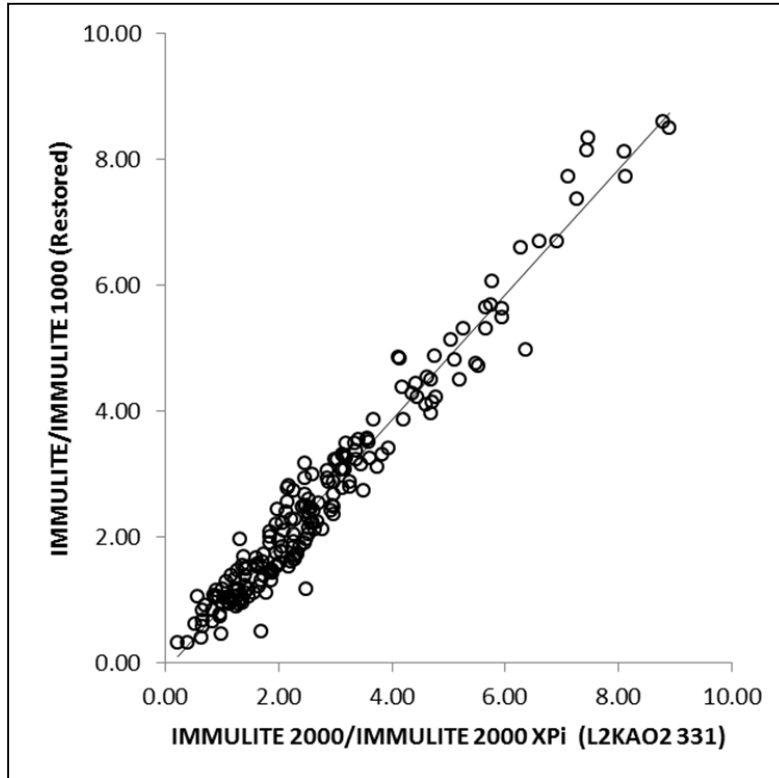
**Figure 2. Bias Plot of IMMULITE/IMMULITE 1000 Current (Kit Lots 414 and 416) vs. Restored Kits Androstenedione (ng/mL)**



**Comparison of IMMULITE 2000/IMMULITE 2000 XPi vs. IMMULITE/IMMULITE 1000 for Restored Androstenedione Kit Lots**

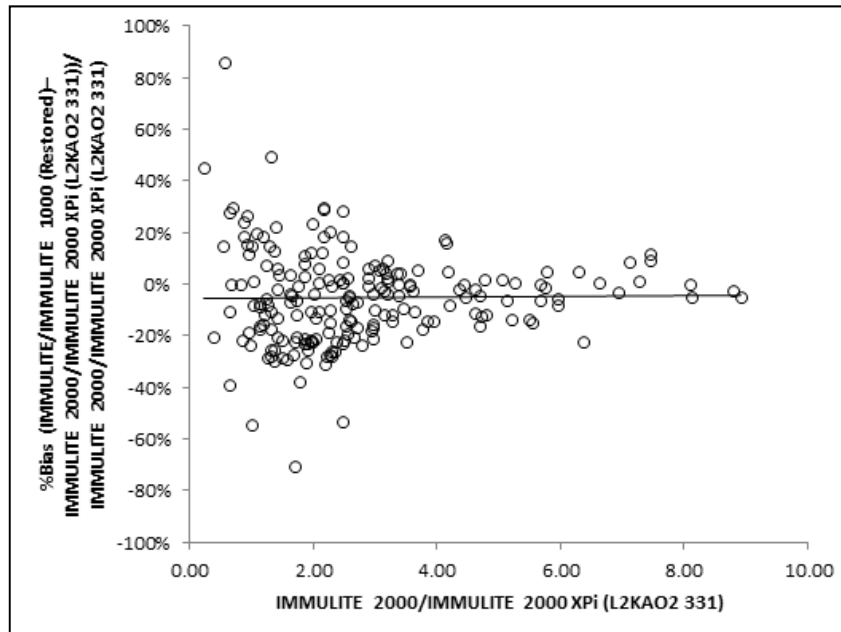
Refer to Figures 3 and 4 for method comparison and bias plots for the restored IMMULITE 2000/IMMULITE 2000 XPi Androstenedione versus the restored IMMULITE/IMMULITE 1000 Androstenedione.

**Figure 3. Method Comparison of Restored IMMULITE 2000/IMMULITE 2000 XPi (L2KAO2 Kit Lot 331) vs. Restored IMMULITE/IMMULITE 1000 Androstenedione (ng/mL)**



$$\begin{aligned} \text{Restored IMMULITE/IMMULITE 1000} &= 0.991 \times \\ \text{IMMULITE 2000/IMMULITE 2000 XPi} &- 0.114 \text{ ng/mL} \\ R &= 0.978, n = 199 \end{aligned}$$

**Figure 4. Bias Plot of Restored IMMULITE 2000/IMMULITE 2000 XPi (L2KAO2 Kit Lot 331) vs. Restored IMMULITE/IMMULITE 1000 Androstenedione (ng/mL)**



### Expected Values

Siemens has performed a verification of the reference ranges published in the Instructions For Use (IFU) Expected Values section. The verification study was performed on 135 donor subjects.

Equivalence to published reference ranges in the IFU was determined by a non-parametric statistical analysis (Kolmogorov-Smirnov Two-Sample Test).

Reference range data is population-dependent; for this reason, the reference ranges provided should be considered as guidelines only. Each laboratory should establish its own reference ranges.

**Table 3. Expected Values**

IMMULITE/IMMULITE 1000	Current IFU Reference Range		Reference Range from Restored Assay	
	Males (n=48)	Females (n=58)	Males (n=58)	Females (n=77)
<b>Median</b>	1.8 ng/mL (6.3 nmol/L)	1.9 ng/mL (6.6 nmol/L)	1.5 ng/mL (5.2 nmol/L)	1.4 ng/mL (4.9 nmol/L)
<b>Central 95% Range</b>	0.7 – 3.6 ng/mL (2.4 – 12.6 nmol/L)	0.3 – 3.5 ng/mL (1.0 – 12.2 nmol/L)	0.7 – 3.5 ng/mL (2.4 – 12.2 nmol/L)	0.2 – 3.7 ng/mL (0.7 – 12.9 nmol/L)

**Precision**

Precision performance using the restored assay verifies the information published in the current version of the IMMULITE/IMMULITE 1000 Androstenedione IFU.

**Table 4. Precision Comparison Between IFU and Restored**

Current IFU Precision					Restored Assay Precision				
Mean Dose (ng/mL)	Within-Run*		Total**		Mean Dose (ng/mL)	Within-Run*		Total**	
	SD	CV	SD	CV		SD	CV	SD	CV
0.66	0.06	9.1%	0.10	15.2%	0.70	0.06	8.4%	0.08	11.5%
1.57	0.08	5.1%	0.13	8.3%	1.04	0.07	6.5%	0.09	8.7%
3.69	0.23	6.2%	0.27	7.3%	3.53	0.12	3.4%	0.13	3.8%
4.35	0.23	5.3%	0.28	6.4%	4.51	0.24	5.2%	0.31	6.9%
9.11	0.58	6.4%	0.87	9.5%	9.50	0.37	3.9%	0.43	4.6%

\*Within-Run is synonymous with repeatability.



\*\*Total is synonymous with within lab.

**Revised Control Targets and Ranges**

Refer to Tables 5 – 14 for Bio-Rad Liquichek™ and Lyphochek™ Immunoassay Plus Control lots 40820, 40830, 40840, 40850, 40860, 40870, 40270, 40280, 40290, and 40300 value assignments and ranges to be used with kit lots 431 and above.

Bio-Rad control updates will be posted on the Bio-Rad QCNet website.

**Table 5. Bio-Rad Liquichek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40820 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKA01 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	0.904	0.791	0.074	0.4303 – 1.152
2	3.31	2.37	0.12	1.59 – 3.15
3	10.0	5.20	0.27	4.20 – 6.20

**Table 6. Bio-Rad Liquichek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40830 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKA01 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	1.27	0.987	0.078	0.537 – 1.437
2	4.32	2.78	0.14	1.86 – 3.70
3	>10.0	5.29	0.32	4.28 – 6.31

**Table 7. Bio-Rad Liquichek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40840 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKA01 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	n/a	1.66	0.08	0.90 – 2.41
2	n/a	2.43	0.15	1.63 – 3.23
3	n/a	5.35	0.35	4.32 – 6.38

**Table 8. Bio-Rad Liquichek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40850 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKAO1 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	1.21	0.717	0.073	0.390 – 1.04
2	4.83	2.17	0.11	1.46 – 2.89
3	>10.0	5.42	0.36	4.38 – 6.46

**Table 9. Bio-Rad Liquichek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40860 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKAO1 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	n/a	1.01	0.07	0.551 – 1.47
2	n/a	2.35	0.12	1.58 – 3.13
3	n/a	4.88	0.37	3.94 – 5.82

**Table 10. Bio-Rad Liquichek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40870 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKAO1 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	n/a	1.09	0.09	0.591 – 1.58
2	n/a	2.84	0.14	1.90 – 3.77
3	n/a	5.87	0.43	4.74 – 6.99

**Table 11. Bio-Rad Lyphocheck Immunoassay Plus Revised Control Targets (ng/mL) Lot 40270 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKAO1 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	1.45	1.02	0.10	0.555 – 1.48
2	6.92	3.73	0.19	2.50 – 4.96
3	>10.0	8.84	0.36	7.15 – >10.0

**Table 12. Bio-Rad Lyphocek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40280 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKA01 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	1.37	0.967	0.095	0.526 – 1.41
2	7.37	3.96	0.18	2.65 – 5.26
3	>10.0	9.15	0.46	7.39 – >10.0

**Table 13. Bio-Rad Lyphocek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40290 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKA01 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	n/a	0.352	0.040	<0.300 – 0.513
2	n/a	1.69	0.10	1.13 – 2.24
3	n/a	4.60	0.19	3.72 – 5.48

**Table 14. Bio-Rad Lyphocek Immunoassay Plus Revised Control Targets (ng/mL) Lot 40300 Applicable to IMMULITE/IMMULITE 1000 Androstenedione LKA01 Kit Lots 431 and Above**

Previous		Revised		
Level	Mean	Mean	SD	3SD Range (ng/mL)
1	0.780	0.629	0.064	0.342 – 0.915
2	5.63	2.24	0.11	1.50 – 2.99
3	>10.0	4.91	0.28	3.97 – 5.86

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Liquichek and Lyphocek are trademarks of Bio-Rad Laboratories, Inc.

**FIELD CORRECTION EFFECTIVENESS CHECK**

Androstenedione Over-Recovery

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice # 1113 dated November 2014 regarding Androstenedione Over-Recovery. Please read each question and indicate the appropriate answer. Fax this completed form to Siemens Healthcare Diagnostics at the fax number provided at the bottom of this page.

1. I have read and understood the Urgent Field Safety Notice instructions provided in this letter. Yes  No
2. Do you now have any of the noted product on hand? Please check inventories before answering. Yes  No

If the answer to the question above is yes, please complete the table below to indicate the quantity of affected product in your laboratory and replacement product required.

Product Description Product Catalog #/SMN #	Lot #	Quantity of Affected Product in inventory that has been discarded	Replacement Quantity Required
LKAO1 / 10381158			

Name of person completing questionnaire: \_\_\_\_\_

Title: \_\_\_\_\_

Institution: \_\_\_\_\_ Instrument Serial Number: \_\_\_\_\_

Street: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_

Phone: \_\_\_\_\_ Country: \_\_\_\_\_

Customer Sold To #: \_\_\_\_\_ Customer Ship To #: \_\_\_\_\_

Please fax this completed form to the Customer Care Center at (###) ###-####. If you have any questions, contact your local Siemens technical support representative.