

cc Chairman Medical Board
and
Relevant Head of
Departments

Urgent Field Safety Notice
CC 17-15.A.OUS
June 2017

ADVIA Centaur®
ADVIA Centaur XP®
ADVIA Centaur XPT®

Enhanced Estradiol (eE2): Negative Bias Observed with Calibrator 30 Kit Lots Ending in 21

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

Table 1. ADVIA Centaur Systems Affected Product(s)

Product	Siemens Material Number (SMN)	Lot Number	Expiration Date	Date of 1st Distribution
Calibrator 30 (2 pack)	10379810	00387A21 16673A21 36243A21	2018-03-08	2017-01-11 2017-03-01 2017-04-19
Calibrator 30 (6 pack)	10379811	00388A21 15448A21 51211A21	2018-03-08	2017-01-09 2017-04-07 2017-05-26
Calibrator 30 (Ref 2 pack)	10697756	20640A21 51024A21	2018-03-08	2017-03-02 2017-05-26

Reason for Recall

Siemens Healthcare Diagnostics has confirmed a negative bias for ADVIA Centaur Enhanced Estradiol (eE2) on the ADVIA Centaur, ADVIA Centaur XP and ADVIA Centaur XPT systems when calibrating with Calibrator 30 kit lots ending in 21 (C3021) as compared to Calibrator 30 kit lots ending in 20 (C3020).

This issue is limited to the lots identified in Table 1 and does not affect the ADVIA Centaur CP system.

Siemens' internal investigation has determined that samples with estradiol concentrations of approximately 35 pg/mL (128 pmol/L) and lower exhibit a % bias greater than the expected historical performance of the product when comparing C3021 to C3020. Results observed indicate that as estradiol concentrations increase, the % biases observed become less pronounced.

A summary of bias results is provided in Table 2 below, and bias plots of individual samples are shown in the "Additional Information" section.

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Table 2: ADVIA Centaur XP eE2 Serum Sample % Bias (C3021 vs. C3020)

eE2 Dose	Average Bias	Range of Bias
≤ 35 pg/mL (≤128 pmol/L)	-33%	- 43% at a concentration of 22.3 pg/mL (81.9 pmol/L) to - 25% at a concentration of 30.8 pg/mL (113 pmol/L)
36 pg/mL to 100 pg/mL (132 pmol/L to 367 pmol/L)	-17%	- 26% at a concentration of 39.4 pg/mL (145 pmol/L) to - 10% at a concentration of 95.2 pg/mL (349 pmol/L)
>100 pg/mL (>367 pmol/L)	- 8%	- 12% at a concentration of 109 pg/mL (399 pmol/L) to - 5% at a concentration of 470 pg/mL (1723 pmol/L)

Quality Control (QC) material and Master Curve Material (MCM) will result low to assigned targets when calibrating with C3021. Depending on the target used, QC and MCM results may fall outside of acceptable ranges.

The root cause is under investigation. Preliminary investigation suggests the data set used in the value assignment of C3021 for the ADVIA Centaur/XP/XPT systems may be a contributing factor. A separate data set was used for the value assignment on the ADVIA Centaur CP system.

Calibrator 30 kit lots ending in 20 and 23 are not impacted by the issue and are available for use on all ADVIA Centaur systems. Please refer to the “Additional Information” section of this letter for representative method correlations.

Risk to Health

The negative bias observed for patient samples at clinically relevant concentrations of estradiol when using calibrator lot C3021 would not impact the clinical utility of the assay. Estradiol is not used in isolation but is correlated with clinical history and presentation, as well as additional diagnostic laboratory testing. Siemens is not recommending a review of previously generated results.

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Actions to be Taken by the Customer

Customers using ADVIA Centaur, ADVIA Centaur XP & ADVIA Centaur XPT Systems:

- Please review this letter with your Medical Director.
- Discontinue use of the Calibrator 30 kit lots ending in 21 listed in Table 1. Calibrator 30 kit lots ending in 20 and 23 are not impacted and can be used by customers.
- Review your inventory of Calibrator 30 kit lots ending in 21 listed in Table 1 to determine your laboratory's replacement needs and to provide information to Siemens for reporting to the authorities.
- Complete the Field Correction Effectiveness Check Form 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.

Customers using ADVIA Centaur CP Systems:

- All available Calibrator 30 kit lots are acceptable for use on the ADVIA Centaur CP systems.
- Even if you are solely using the ADVIA Centaur CP system, please complete the Field Correction Effectiveness Check Form 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.

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.

ADVIA Centaur is a trademark of Siemens Healthcare Diagnostics.

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Additional Information

Figures 1a and 1b demonstrate the patient bias between C3021 to C3020 and between C3023 to C3020 observed during Siemens' internal investigation.

Figure 1a: Representative Bland-Altman Difference Plot in **pg/mL (Common Units)**:
ADVIA Centaur XP eE2 Calibrator Lot C3021 and C3023 versus C3020

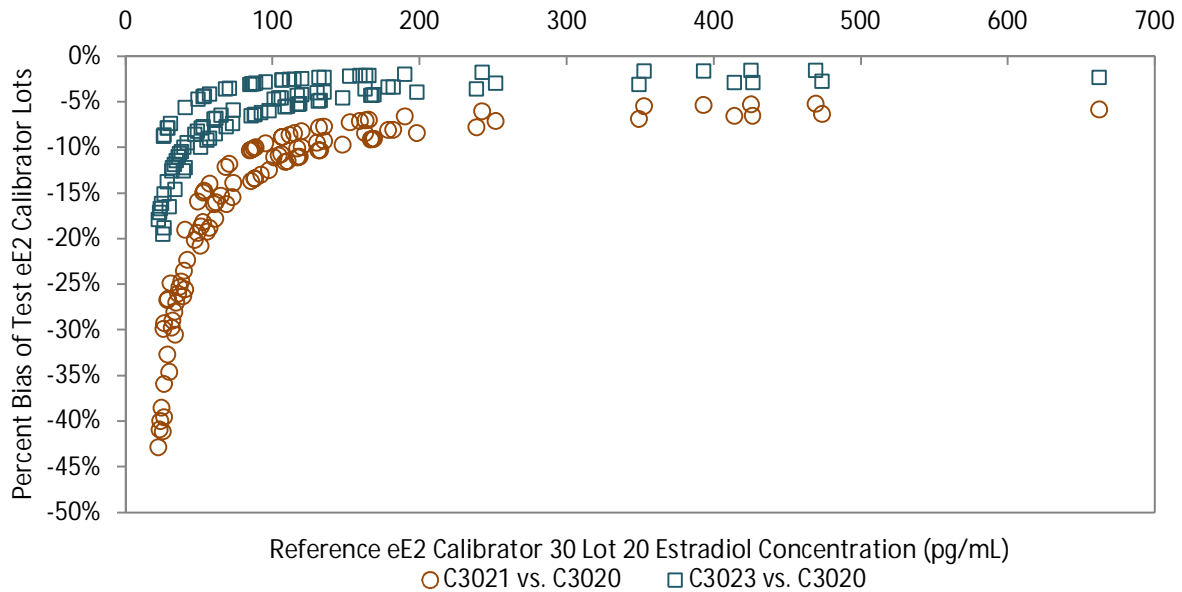
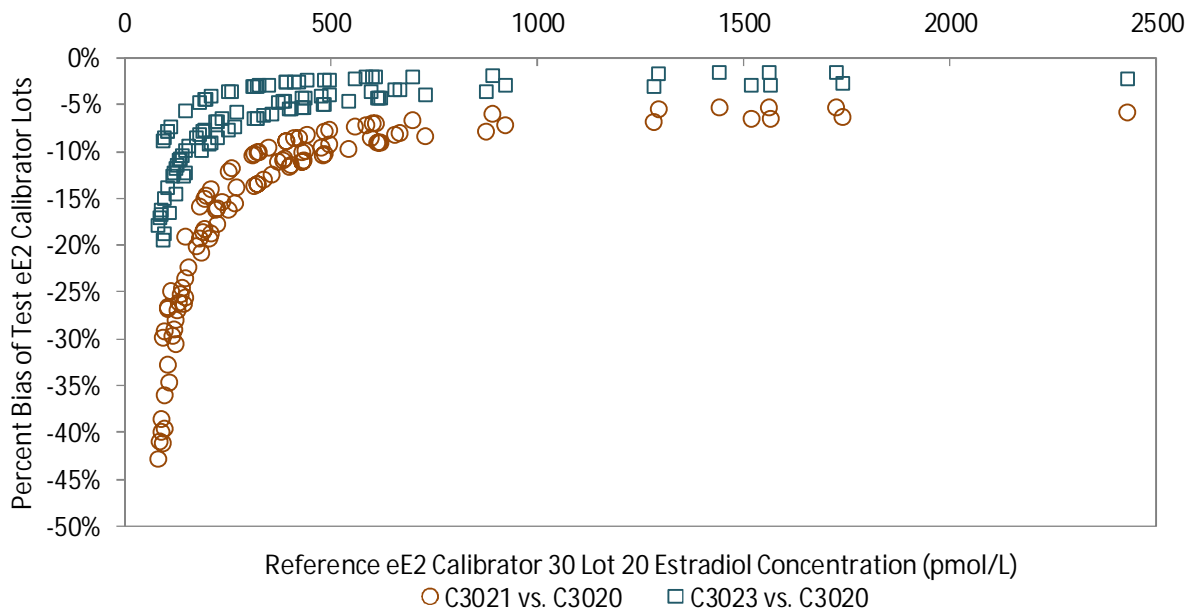


Figure 1b: Representative Bland-Altman Difference Plot in **pmol/L (SI Units)**:
ADVIA Centaur XP eE2 Calibrator Lot C3021 and C3023 versus C3020



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Figures 2a and 2b provide a representative method correlation between C3023 and C3020 for graphical presentation of the acceptability of these two lots.

Figure 2a: Representative Method Correlation in **pg/mL (Common Units):**
ADVIA Centaur XP eE2 Calibrator Lot C3023 versus C3020

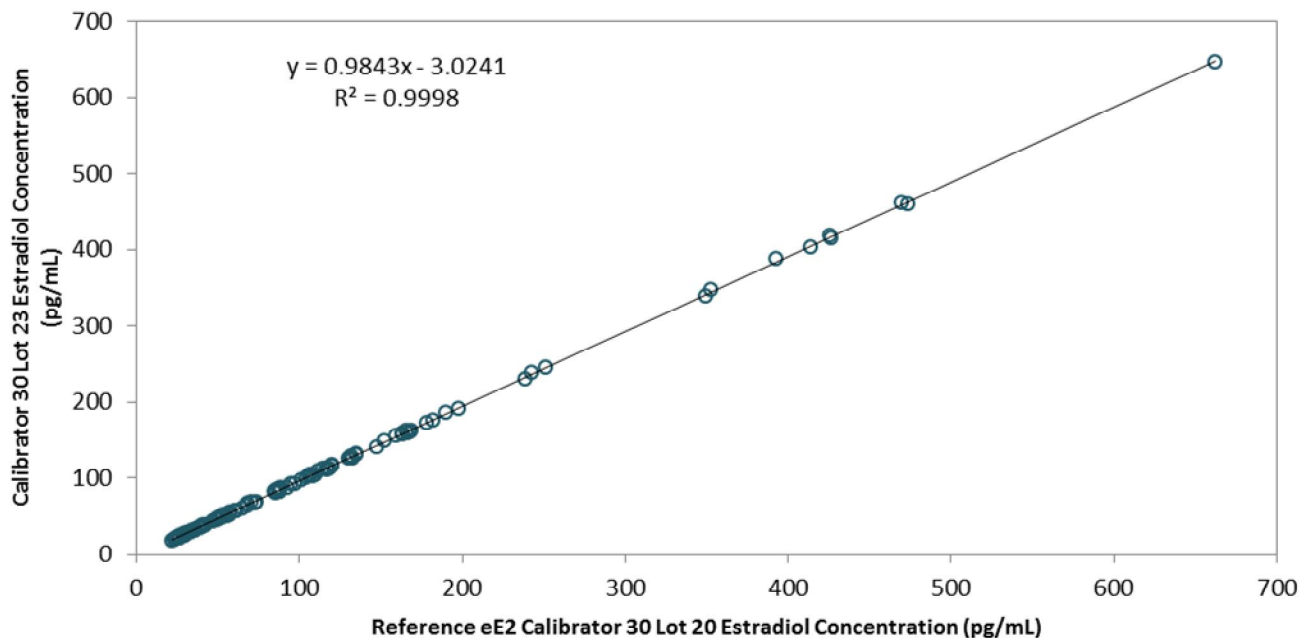
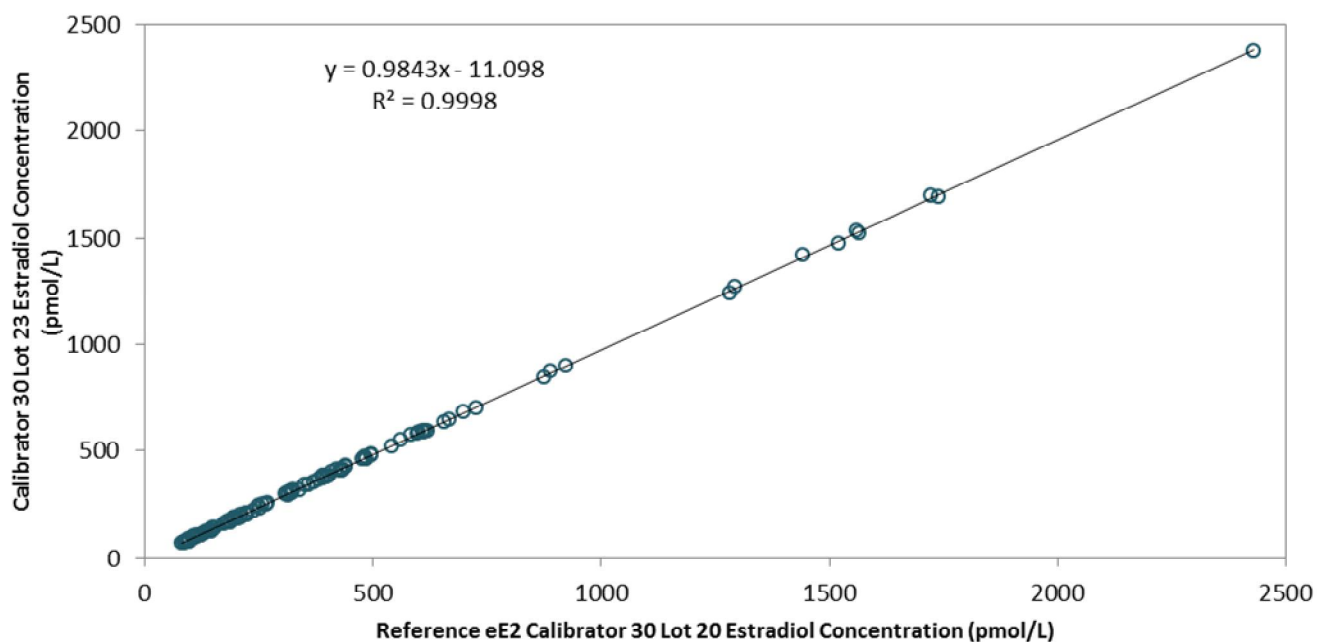


Figure 2b: Representative Method Correlation in **pmol/L (SI Units):**
ADVIA Centaur XP eE2 Calibrator Lot C3023 versus C3020



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FIELD CORRECTION EFFECTIVENESS CHECK

Enhanced Estradiol (eE2): Negative Bias Observed with Calibrator 30 Kit Lots Ending in 21

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice CC 17-15.A.OUS dated June 2017 regarding Enhanced Estradiol (eE2): Negative Bias Observed with Calibrator 30 Kit Lots Ending in 21. 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 use the eE2 assay on the ADVIA Centaur/XP/XPT systems? If Yes, complete question 3 below. If no, question 3 is not applicable. Yes No

3. 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 (if applicable)	Replacement Quantity Required
2 pack SMN 10379810 Lots: 00387A21, 16673A21, 36243A21		
6 pack SMN10379811 Lots: 00388A21, 15448A21, 51211A21		
Ref 2 pack SMN 10697756 Lot: 20640A21, 51024A21		

Name of person completing questionnaire: _____

Title: _____

Institution: _____ Instrument Serial Number: _____

Street: _____

City: _____ State: _____

Phone: _____ Country: _____

Customer Sold To #: _____ Customer Ship To #: _____

To fax this completed form please send it to the Customer Care Center at (XXX) XXX-XXXX. If you have any questions, contact your local Siemens technical support representative.

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