SIEMENS

# Urgent Field Safety Notice

**CC 17-10.A.OUS**

**April 2017**

**ADVIA Centaur®**
**ADVIA Centaur® XP**
**ADVIA Centaur® XPT**
**ADVIA Centaur® CP**

## ADVIA Centaur Systems Insulin Assay: Standardization to WHO 1st IRP 66/304

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

**Table 1. ADVIA Centaur Affected Product(s)**

| Assay | Test Code | Catalog Number | Siemens Material Number (SMN) | Kit Lots ending | Expiration Date | Date of Manufacture |
|---|---|---|---|---|---|---|
| ADVIA Centaur Systems Insulin Calibrator | Calibrator IRI | 04618899 | 10310438 | 59 | 2017-Apr-05 | 2015-Sep-17 |
| | | | | 67 | 2017-Aug-22 | 2016-Mar-15 |
| | | | | 70 | 2017-Nov-27 | 2016-Jun-09 |
| | | | | 74 | 2017-Feb-26 | 2016-Aug-17 |
| ADVIA Centaur Systems Insulin ReadyPack | IRI | 02230141 | 10310439 | 169 | 2017-Apr-11 | 2016-Apr-11 |
| | | | | 170 | 2017-May-27 | 2016-May-27 |
| | | | | 173 | 2017-Jun-30 | 2016-Jun-30 |
| | | | | 174 | 2017-Aug-26 | 2016-Aug-26 |

## Reason for Correction

Siemens Healthcare Diagnostics is providing this Urgent Field Safety Notice to communicate the restoration of the ADVIA Centaur Systems Insulin (IRI) assay to World Health Organization (WHO) 1st IRP 66/304 standardization.

Siemens internal investigation has identified that current in-date lots of ADVIA Centaur Systems Insulin recover approximately 40% higher than the World Health Organization (WHO) 1st IRP 66/304 standardization based on slope values. The slope value was observed to be 1.40 on the ADVIA Centaur XP and 1.42 on the ADVIA Centaur CP.

Siemens has confirmed that the assay's reportable range, reference interval, precision, analytical sensitivity, hook effect and linearity are not impacted by this issue and continue to meet the assay performance characteristics stated in the assay Instructions for Use (IFU). Investigation also concluded that root cause of this issue is related to a raw material used during the manufacture of the IRI calibrators.

This issue has been corrected and standardization to WHO 1st IRP 66/304 has been restored beginning with ADVIA Centaur IRI ReadyPack kit lots ending in 201 when paired with IRI Calibrator kit lots ending in 02, which will be available by May 2017. For observed biases at specific clinical intervals that customers may observe after the correction is implemented, refer to Table 4 and Table 5 in this letter.





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## Risk to Health

With current in-date reagent lots, the potential exists for misinterpretation of insulin levels when comparing to standardization to the World Health Organization (WHO) 1st IRP 66/304. The reference interval for insulin is not impacted as a result of this issue. Insulin testing is not generally used in isolation in clinical practice. Additional laboratory testing is typically performed along with insulin, such as glucose, HbA1c, c-peptide, and proinsulin. Potential clinical impact is also mitigated by correlation to clinical history and symptomology. Siemens is not recommending a review of previously generated results.

## Actions to be Taken by the Customer

- Please review this letter with your Medical Director.
- Customers may continue to use existing product to report results until the re-standardized product is available. Corrected product, beginning with ADVIA Centaur Systems Insulin ReadyPack kit lots ending in 201 and IRI Calibrator kit lots ending in 02, will be available by May 2017.
- Upon receipt of ADVIA Centaur Systems Insulin ReadyPack kit lots ending in 201 (and future lots) and IRI Calibrator kit lots ending in 02 (and future lots), discontinue use of the product listed in Table 1.
- Use ADVIA Centaur Insulin Master Curve Material lots M0101 (and future lots) with ADVIA Centaur Systems Insulin ReadyPack lots ending in 201(and future lots) with IRI Calibrator lots ending in 02 (and future lots).
- Refer to the Bio-Rad website for revised control targets and ranges to be used with corrected product. For all other commercially available controls, evaluate the need for target reset.
- Review the Additional Information section of this letter for further details regarding expected performance.
- 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.

## Additional Information

Table 2 provides the results of the current state method comparison, using serum samples across the assay range. Current state refers to ReadyPack kit lots ending in 174 and below and Calibrator kit lots ending in 74 and below, as listed in Table 1 of this letter.

**Table 2: Current State Method Comparison: ADVIA Centaur Systems IRI vs. WHO**

| X-Axis | Y-Axis | N | Range of Samples (U/mL) | Slope | Intercept (U/mL) |
|---|---|---|---|---|---|
| WHO 1st IRP 66/304 Material | ADVIA Centaur/XP/XPT | 297 | 0.48 - 225 | 1.40 | -1.35 |
| WHO 1st IRP 66/304 Material | ADVIA Centaur CP | 296 | 0.57 - 215 | 1.42 | -1.44 |





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Table 3 provides the results of the re-standardized method comparison, using serum samples across the assay range. Re-standardized refers to ReadyPack kit lots ending in 201 and future lots with Calibrator kit lots ending in 02 and future lots.

**Table 3: Re-Standardized Method Comparison: ADVIA Centaur Systems IRI vs. WHO**

| X-Axis | Y-Axis | N | Range of Samples (U/mL) | Slope | Intercept (U/mL) |
|---|---|---|---|---|---|
| WHO 1st IRP 66/304 Material | ADVIA Centaur/XP/XPT | 304 | 0.48 - 239 | 1.01 | -0.05 |
| WHO 1st IRP 66/304 Material | ADVIA Centaur CP | 302 | 0.57 - 215 | 1.01 | 0.08 |

Table 4 and Table 5 provide serum sample results obtained during Siemens internal verification testing, comparing re-standardized product to current state. Based on this data set, the average % Bias expected in the range of 0.5 mU/L to 30 mU/L is approximately -23% on the ADVIA Centaur XP system and approximately -30% on the ADVIA Centaur CP system.

Customers should expect to see a change when they begin to use the re-standardized product. Slight differences in observed results may be attributed to different demographics of patient samples used by each laboratory.

**Table 4: ADVIA Centaur XP: Serum Sample Results (Re-Standardized vs. Current State)**

| Segment (mU/L) | N | Average Absolute Bias (mU/L) | Absolute Bias Range (mU/L) | Average % Bias | % Bias Range |
|---|---|---|---|---|---|
| 0.5 - 10 | 33 | -1.6 | -0.4 to -2.3 | -23.9% | -15.9% to -25.8% |
| >10 - 30 | 56 | -4.1 | -1.7 to -7.6 | -22.7% | -15.6% to -27.3% |
| >30 - 50 | 12 | -10.0 | -8.6 to -11.6 | -26.1% | -21.8% to -29.1% |
| >50 - 100 | 10 | -13.8 | -10.1 to -22.6 | -20.5% | -17.4% to -24.3% |
| >100 - 300 | 15 | -55.5 | -28.3 to -66.9 | -32.1% | -25.5% to -37.1% |

**Table 5: ADVIA Centaur CP: Serum Sample Results (Re-Standardized vs. Current State)**

| Segment (mU/L) | N | Average Absolute Bias (mU/L) | Absolute Bias Range (mU/L) | Average % Bias | % Bias Range |
|---|---|---|---|---|---|
| 0.5 - 10 | 33 | -1.6 | -0.6 to -2.5 | -32.4% | -27.1% to -41.1% |
| >10 - 30 | 56 | -4.1 | -1.8 to -8.2 | -28.5% | -19.0% to -39.7% |
| >30 - 50 | 12 | -10.1 | -7.5 to -11.4 | -35.0% | -30.1% to -39.6% |
| >50 - 100 | 10 | -15.5 | -9.9 to -30.8 | -28.1% | -19.1% to -41.4% |
| >100 - 300 | 15 | -56.8 | -26.7 to -71.6 | -49.5% | -33.2% to -67.3% |

A negative shift in quality control values will also be observed with the ADVIA Centaur Systems IRI ReadyPack kit lots ending in 201 (and future lots) when used in conjunction with IRI calibrator kit lots ending in 02 (and future lots). Please refer to the Bio-Rad website for revised targets and ranges for Bio-Rad control products.

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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## FIELD CORRECTION EFFECTIVENESS CHECK

ADVIA Centaur Systems Insulin Assay – Standardization to WHO 1st IRP 66/304

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice CC 17-10.A.OUS dated April 2017 regarding ADVIA Centaur Systems Insulin Assay Standardization to WHO 1st IRP 66/304.
Please read each question and indicate the appropriate answer.

Email this completed form to Siemens Healthcare Diagnostics at the email address 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** |
|---|---|---|
| ADVIA Centaur IRI Calibrator SMN 10310438 | | |
| ADVIA Centaur IRI ReadyPack SMN 10310439 | | |

Name of person completing questionnaire: _____

Title: _____

Institution: _____ Instrument Serial Number: _____

Street: _____

City: _____

Phone: _____ Country: _____

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

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





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