

ADVIA Centaur®  
 ADVIA Centaur® XP  
 ADVIA Centaur® CP

### Homocysteine Dilution Recovery and Calibrator 88 Value Assignment Improvement

Our records indicate that you may have received the products listed in Table 1:

**Table 1. ADVIA Centaur Homocysteine (HCY) Part Numbers**

| Assay                       | Catalog Number    | Siemens Material Number (SMN) | Lot Number                                  |
|-----------------------------|-------------------|-------------------------------|---|
| ADVIA Centaur HCY Diluent   | 03302138 (124581) | 10318677                      | Expired                                     |
| HCY Diluent                 | 09877493 (124533) | 10310370                      | 88D1524<br>88D3303                          |
| Calibrator 88               | 05530553 (124579) | 10310376                      | C8833LA and C8833HA;<br>C8834LA and C8834HA |
| Homocysteine (500 Test Kit) | 09087913 (124578) | 10310375                      | 088154, 088156, and<br>088157               |
| Homocysteine (100 Test Kit) | 05370300 (124577) | 10310374                      | 088154, 088156 and<br>088157                |

### Reason for Correction

Siemens Healthcare Diagnostics is conducting a field correction for the ADVIA Centaur Homocysteine (HCY) assay for the 1:10 dilution recovery, used on the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur CP systems. Siemens identified the percent recovery for 1:10 diluted patient sample dilutions is lower than reported in the Instructions for Use (IFU).

Table 2 provides the range of 1:10 dilution recoveries in the IFU, and currently observed:

**Table 2. Dilution Recoveries in IFU Vs. Currently Observed**

| Observed  | ADVIA Centaur System | ADVIA Centaur CP System |
|-----------|----------------------|-------------------------|
| In IFU    | 88% to 91%           | 73% to 103%             |
| Currently | 64% to 72%           | 60% to 94%              |

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In addition to the field correction, Siemens is communicating an improvement to the HCY calibrator value assignment process. This improvement minimizes reagent lot-to-lot variability beginning with Calibrator 88 lot 35 and higher. As a consequence of this change, a modification to previously assigned Quality Control (QC) material and Master Curve Material (MCM) values is necessary. Revised values are provided in this communication.

Product is expected to be available to customers in early July 2013.

### **Risk to Health**

Dilution of patient samples is primarily to resolve above range results from hyperhomocysteinemic patients. Severe hyperhomocysteinemia may be due to marked deficiencies of the B complex vitamins, or is sometimes associated with chronic renal failure. More rarely, severe hyperhomocysteinemia and hyperhomocysteinuria is due to inherited genetic defects such as cystathionine beta synthase deficiency. Homocysteine is used as an adjunct assay with direct measurement of the specific B complex vitamin or genetic test. In these cases a negatively biased dilution recovery result would not impact subsequent treatment or mask an elevated value.

Since the determination of homocysteine levels is used as an aid in diagnosis of a B complex deficiency or inherited defect, and treatment is based on folic acid and vitamin B12 status and/or genetic testing, it is not necessary to review results from specimens that were previously diluted 1:10, nor is it necessary to repeat dilution testing on those patients.

### **Actions to be Taken by the Customer**

- Upon receipt of this communication, you must discontinue the use of 1:10 dilutions of samples with the ADVIA Centaur HCY assay run on ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur CP systems.
- Ensure that the 1:10 dilution is not selected manually or automatically when performing a dilution. Refer to *Entering Defining Automatic Dilutions* and *Entering Dilution Options* sections of your ADVIA Centaur system operator's guide.
- You can continue to use a 1:2 onboard or manual dilution for samples with results outside of the assay range. Siemens has confirmed that the performance at this dilution level meets IFU recoveries.
- A notecard will be included with the following products: ADVIA Centaur HCY reagent lot 088158 and higher, Calibrator 88 lot 35 and higher, and HCY Diluent lots 88D0145 and 08810145. What follows is the text of the notecard:

“In accordance with Urgent Field Safety Notice (UFSN) 10815312, use the ADVIA Centaur HCY reagent lots with the lots of the related products listed in the table below.”

| With HCY Reagent Lots      | Use HCY CAL Lots                         | Use HCY Diluent Lots         | Use HCY MCM Lots        |
|----------------------------|--|------------------------------|-------------------------|
| 088154, 088156, and 088157 | C8833LA and C8833HA; C8834LA and C8834HA | Not Available                | 13747 and 18160         |
| 088158 and higher          | C8835LA and higher; C8835HA and higher   | 88D0145; 08810145 and higher | 13747; 20096 and higher |

### Additional Information

Due to the improved value assignment of Calibrator 88 lot 35 (C8835LA and C8835HA) the values and ranges for MCM and QC material have been reassigned. The reassigned MCM values and ranges are provided in Table 3 through Table 5; the QC values and ranges are provided in Table 6. Bio-Rad will list assigned values as “For Use with HCY reagent lot 088154 and Calibrator 88 Lot 35 and above” in the insert sheet and Unity reports.

**Table 3. ADVIA Centaur and ADVIA Centaur XP HCY MCM Lot 13747**

| MCM Level | Previous Target and Range (µmol/L)<br>HCY Reagent Lot 088157/Cal 88 Lot 34 | New Target and Range (µmol/L)<br>HCY Reagent Lot 088158/Cal 88 Lot 35 |
|-----------|--|---|
| MCM1      | 0 < 1.50   | 0 < 1.50  |
| MCM2      | 4.68 3.28–6.08   | 4.16 2.91–5.41  |
| MCM3      | 8.22 5.75–10.7   | 7.42 5.19–9.65  |
| MCM4      | 32.7 26.2–39.2   | 30.2 24.2–36.2  |
| MCM5      | 51.0 40.8–61.2   | 46.2 37.0–55.4  |
| MCM6      | 74.3 > 59.4  | 73.4 > 58.7   |

**Table 4. ADVIA Centaur CP HCY MCM Lot 13747**

| <b>MCM Level</b> | <b>Previous Target and Range (µmol/L)<br/>HCY Reagent Lot 088157/Cal 88 Lot 34</b> | <b>New Target and Range (µmol/L)<br/>HCY Reagent Lot 088158/Cal 88 Lot 35</b> |
|------------------|--|---|
| MCM1             | 0 < 1.50   | 0 < 1.50  |
| MCM2             | 4.68 3.28–6.08   | 4.16 2.91–5.41  |
| MCM3             | 8.22 5.75–10.7   | 7.42 5.1–9.65   |
| MCM4             | 32.7 26.2–39.2   | 30.2 24.2–36.2  |
| MCM5             | 51.0 40.8–61.2   | 46.2 37.0–55.4  |
| MCM6             | 74.3 > 59.4  | 73.4 > 58.7   |

**Table 5. ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur CP HCY MCM Lot 20096**

| <b>MCM Level</b> | <b>ADVIA Centaur and ADVIA Centaur XP Target and Range (µmol/L)<br/>HCY Reagent Lot 088158/Cal 88 Lot 35</b> | <b>ADVIA Centaur CP Target and Range (µmol/L)<br/>HCY Reagent Lot 088158/Cal 88 Lot 35</b> |
|------------------|--|--|
| MCM1             | 0 < 1.50   | 0 > 1.50   |
| MCM2             | 3.65 2.56–4.75   | 3.65 2.56–4.75   |
| MCM3             | 6.52 4.56–8.48   | 6.52 4.56–8.48   |
| MCM4             | 26.7 21.4–32.0   | 26.7 21.4–32.0   |
| MCM5             | 40.5 32.4–48.6   | 40.5 32.4–48.6   |
| MCM6             | 67.4 > 53.9  | 67.4 > 53.9  |

**Table 6. Bio-Rad Quality Control Assigned Values and Ranges for the ADVIA Centaur HCY Assay**

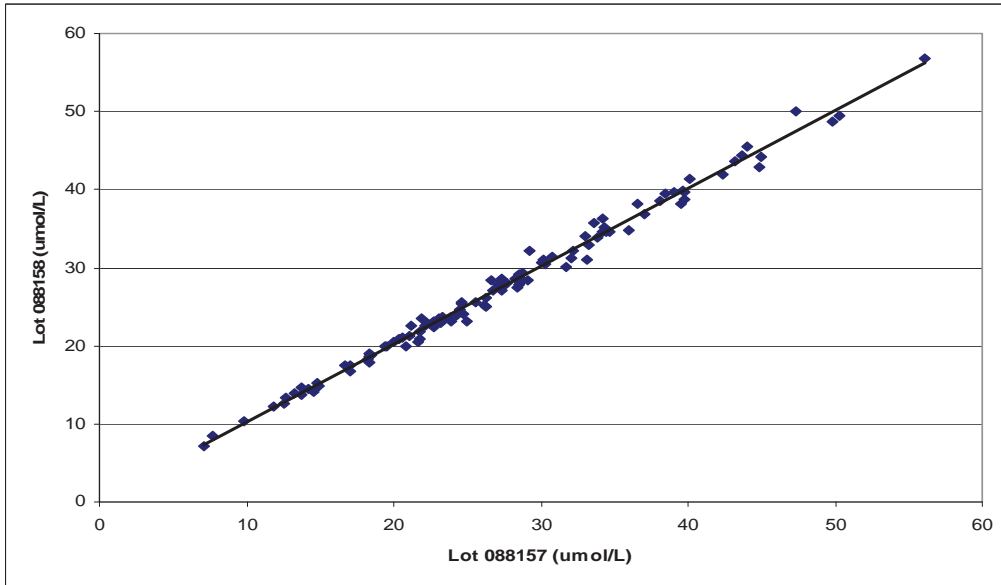
| ADVIA Centaur and ADVIA Centaur XP Systems |                         |                |                             |                    | ADVIA Centaur CP System |                |                             |                    |
|--|-------------------------|----------------|-----------------------------|--------------------|-------------------------|----------------|-----------------------------|--------------------|
| Control                                    | Assigned Value (µmol/L) | Range (µmol/L) | New Assigned Value (µmol/L) | New Range (µmol/L) | Assigned Value (µmol/L) | Range (µmol/L) | New Assigned Value (µmol/L) | New Range (µmol/L) |
| 34931                                      | 8.00                    | 6.40–9.60      | 8.67                        | 6.94–10.4          | 8.78                    | 7.02–10.5      | 9.20                        | 7.36–11.0          |
| 34932                                      | 20.6                    | 16.5–24.7      | 22.3                        | 17.8–26.8          | 21.6                    | 17.3–25.9      | 22.8                        | 18.2–27.4          |
| 34942                                      | 8.84                    | 7.07–10.6      | 8.92                        | 7.14–10.7          | 8.48                    | 6.78–10.2      | 8.85                        | 7.08–10.6          |
| 34943                                      | 20.2                    | 16.1–24.2      | 20.6                        | 16.5–24.7          | 20.1                    | 16.1–24.1      | 20.3                        | 16.2–24.4          |
| 34952                                      | 8.24                    | 6.59–9.90      | 8.76                        | 7.01–10.5          | 8.88                    | 7.10–10.7      | 8.63                        | 6.90–10.4          |
| 34953                                      | 21.4                    | 17.1–25.7      | 21.2                        | 17.0–25.4          | 20.7                    | 16.6–24.8      | 21.8                        | 17.4–26.2          |

**Patient Sample Result Comparisons**

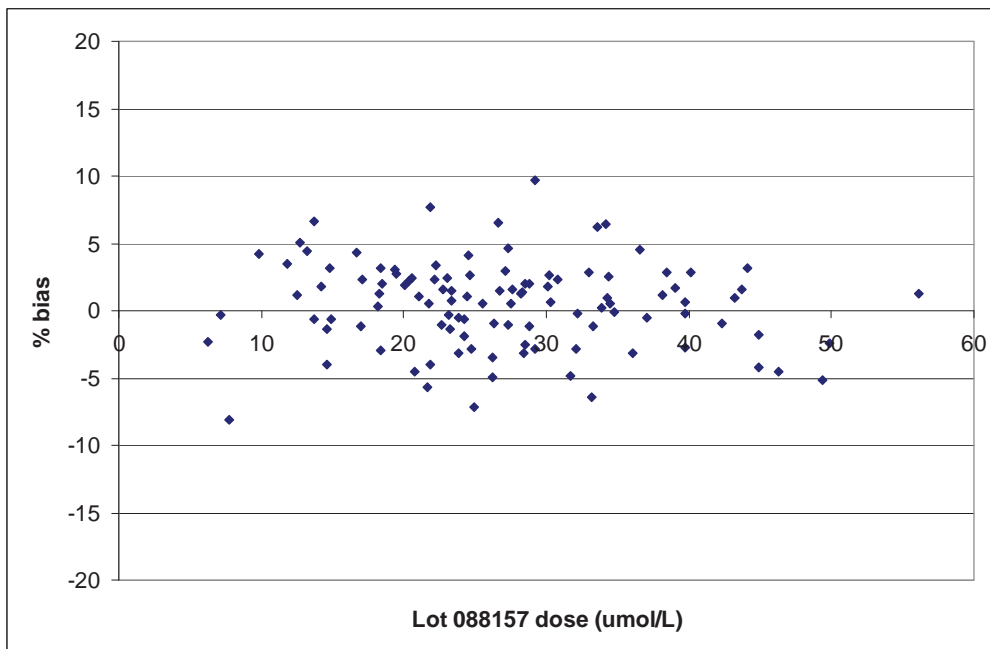
The following patient sample result comparisons are provided to show the relationship between previous reagent and calibrator combinations to HCY reagent lot 088158 and Calibrator 88 lot 35. Figure 1 through Figure 4 provide the regression analysis and bias plot data comparing HCY reagent lot 088157 and Calibrator 88 lot 34 to HCY reagent lot 088158 and Calibrator 88 lot 35 on the ADVIA Centaur and ADVIA Centaur CP systems. A total of 110 serum samples covering the assay range were used in this study. Each sample was processed in duplicate and the mean of the duplicates was used to generate a linear regression and the bias plots.

**Figure 1. ADVIA Centaur HCY Lot 088157/Cal 88 Lot 34 to  
ADVIA Centaur HCY Lot 088158/Cal 88 Lot 35**

Lot 088158/Cal 88 Lot 35 = 0.99 (Lot 088157/Cal 88 Lot 34) + 0.26  $\mu\text{mol/L}$ .  $r = 0.99$

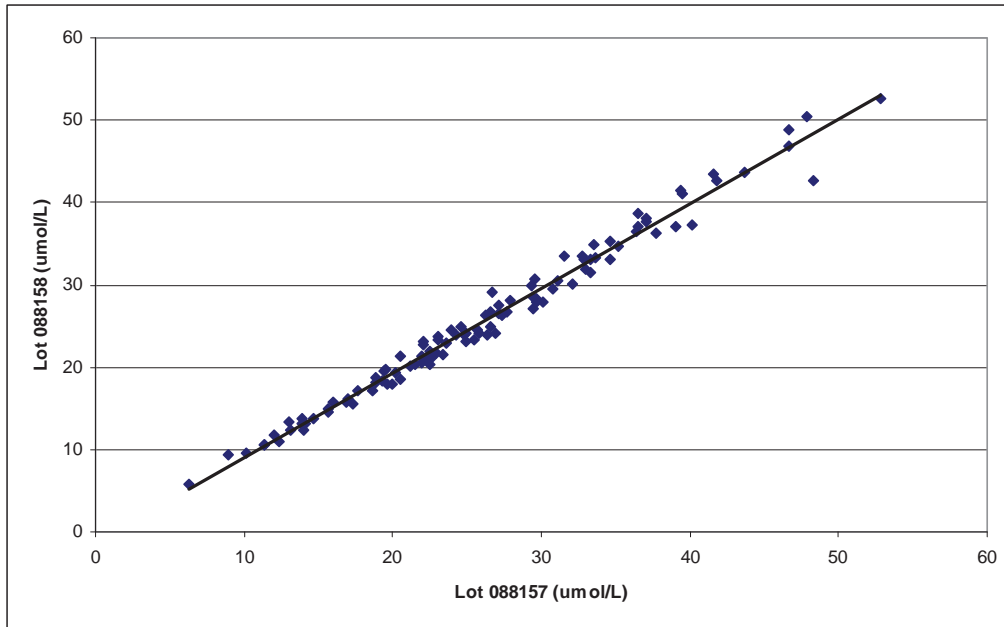


**Figure 2. ADVIA Centaur HCY Lot 088157/Cal 88 Lot 34 to  
ADVIA Centaur HCY Lot 088158/Cal 88 Lot 35  
Bias Plot Mean % Bias = 0.83%**

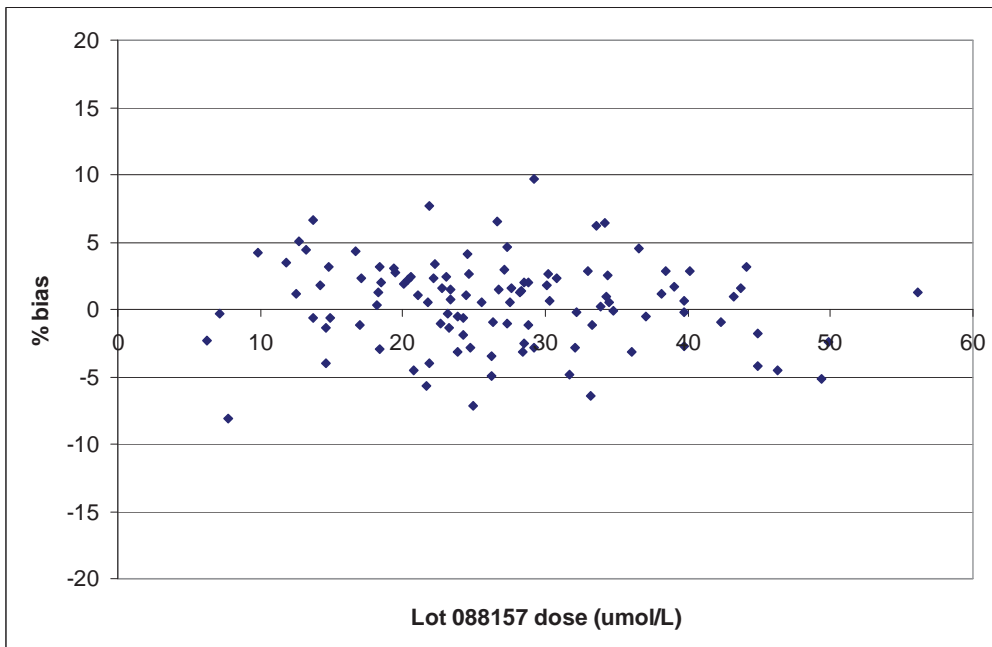


**Figure 3. ADVIA Centaur CP HCY Lot 088157/Cal 88 Lot 34 to  
ADVIA Centaur CP HCY Lot 088158/Cal 88 Lot 35**

Lot 088158/Cal 88 Lot 35 = 1.03 (Lot 088157/Cal 88 Lot 34) - 1.21  $\mu\text{mol/L}$ .  $r = 0.99$



**Figure 4. ADVIA Centaur CP HCY Lot 088157/Cal 88 Lot 34 to  
ADVIA Centaur CP HCY Lot 088158/Cal 88 Lot 35  
Bias Plot Mean % Bias = -2.64%**



## Homocysteine Dilution Recovery and Calibrator 88 Value Assignment Improvement

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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 has caused. If you have any questions, please contact your Siemens Technical Solutions Center or your local Siemens technical support representative.

ADVIA Centaur is a trademark of Siemens Healthcare Diagnostics.



**FIELD CORRECTION EFFECTIVENESS CHECK**

Homocysteine Dilution Recovery and Calibrator 88 Value Assignment Improvement

This response form is to confirm receipt of the enclosed Siemens Healthcare Diagnostics Urgent Field Safety Notice dated June 2013 regarding Homocysteine Dilution Recovery and Calibrator 88 Value Assignment Improvement. Please read the question below and indicate the appropriate answer. Fax this completed form to Siemens Healthcare diagnostics at the fax number indicated at the bottom of this page.

I have read and understood the Urgent Field Safety Notice instructions provided in the June 2013 letter. Yes  No

Name of person completing questionnaire:

Title:

Institution:

Instrument Serial Number:

Street:

City:

State:

Phone:

PLEASE FAX THIS COMPLETED FORM TO THE TECHNICAL SOLUTIONS CENTER AT (302) 631-7597.

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**Siemens Healthcare Diagnostics Inc.**

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