

**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 88D3303
Calibrator 88	05530553 (124579)	10310376	C8833LA and C8833HA; C8834LA and C8834HA
Homocysteine (500 Test Kit)	09087913 (124578)	10310375	088154, 088156, and 088157
Homocysteine (100 Test Kit)	05370300 (124577)	10310374	088154, 088156 and 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) HCY Reagent Lot 088157/Cal 88 Lot 34	New Target and Range (µmol/L) 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

MCM Level	Previous Target and Range (µmol/L) HCY Reagent Lot 088157/Cal 88 Lot 34	New Target and Range (µmol/L) 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 5.1–9.65
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

MCM Level	ADVIA Centaur and ADVIA Centaur XP Target and Range (µmol/L) HCY Reagent Lot 088158/Cal 88 Lot 35	ADVIA Centaur CP Target and Range (µmol/L) HCY Reagent Lot 088158/Cal 88 Lot 35
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

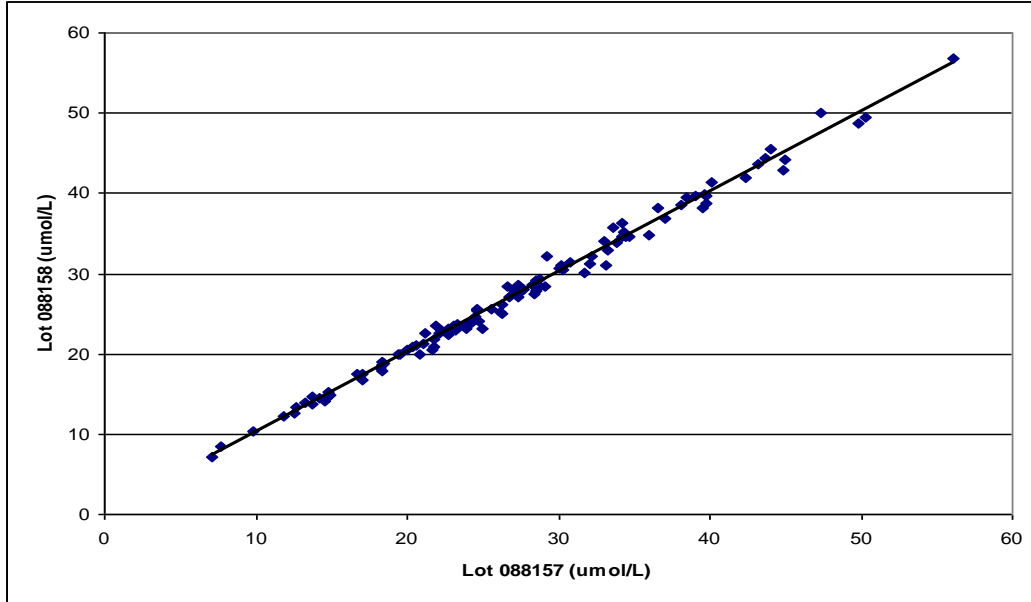
ADVIA Centaur and ADVIA Centaur XP Systems					ADVIA Centaur CP System			
Control	Assigned Value (µmol/L)	Range (µmol/L)	New Assigned Value (µmol/L)	New Range (µmol/L)	Assigned Value (µmol/L)	Range (µmol/L)	New Assigned Value (µmol/L)	New Range (µmol/L)
34931	8.00	6.40–9.60	8.67	6.94–10.4	8.78	7.02–10.5	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

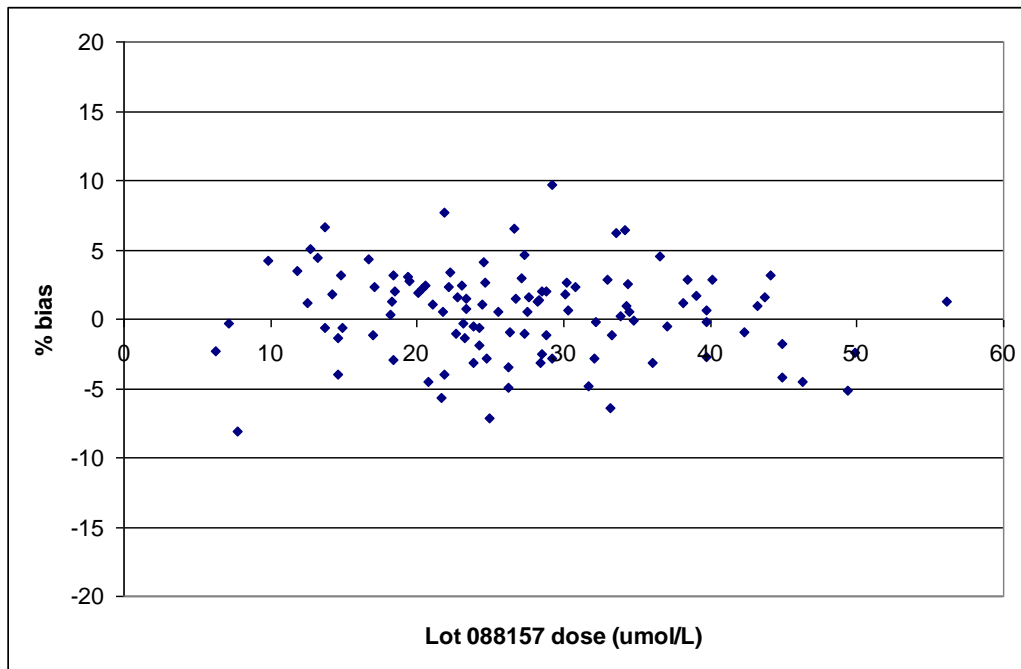
The following patient sample result comparisons are provided to show the relationship between previous reagent and calibrator combinations to HCY reagent lot 088158 and Calibrator 88 lot 35. Figure 1 through Figure 4 provide the regression analysis and bias plot data comparing HCY reagent lot 088157 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 $\mu\text{mol/L}$. $r = 0.99$

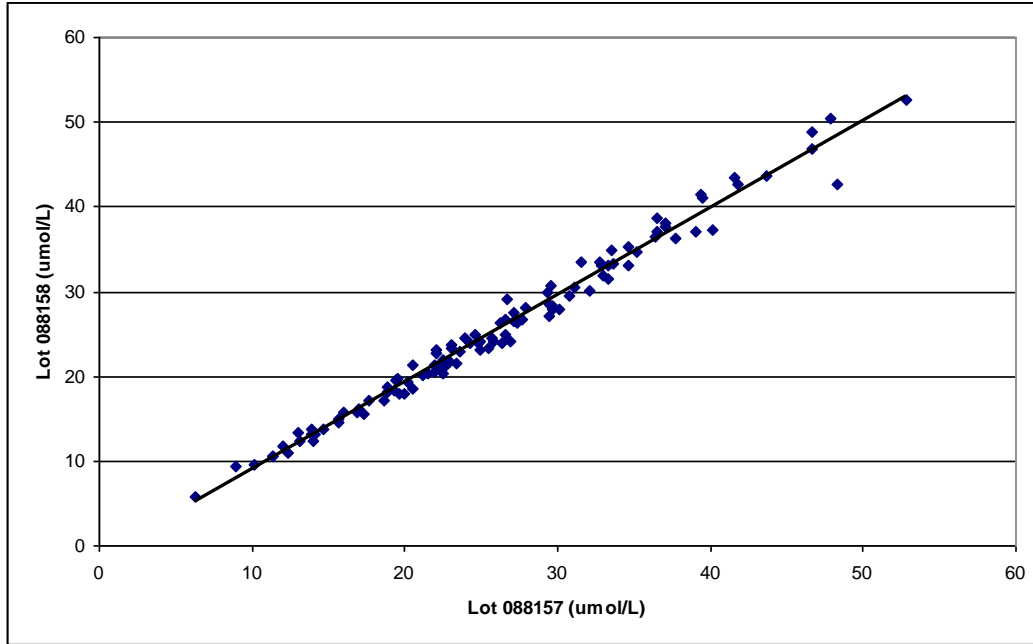


**Figure 2. ADVIA Centaur HCY Lot 088157/Cal 88 Lot 34 to
ADVIA Centaur HCY Lot 088158/Cal 88 Lot 35
Bias Plot Mean % Bias = 0.83%**



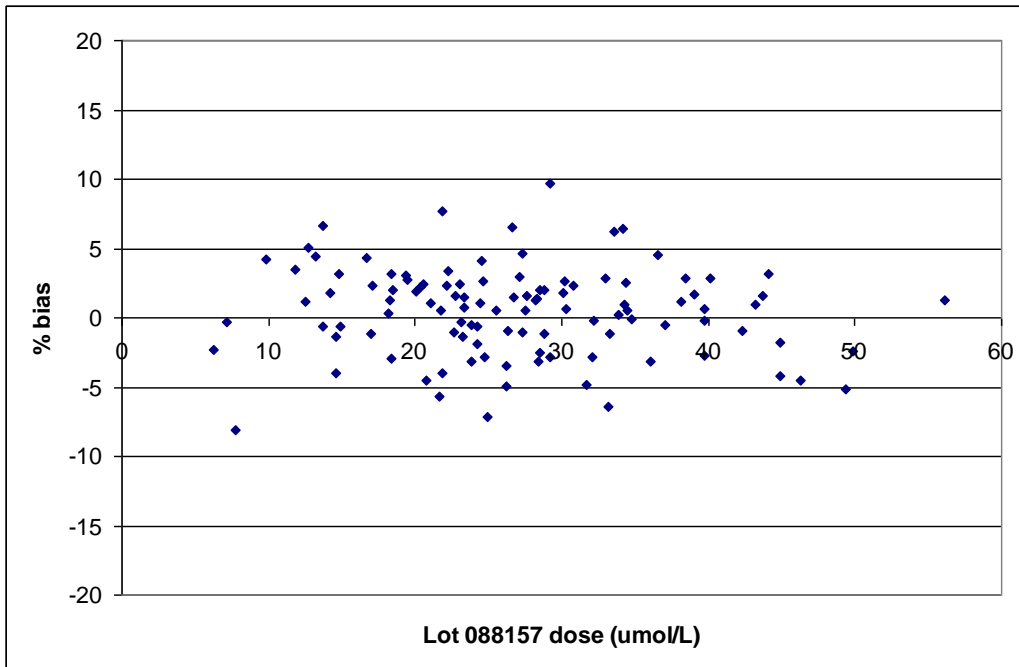
**Figure 3. ADVIA Centaur CP HCY Lot 088157/Cal 88 Lot 34 to
ADVIA Centaur CP HCY Lot 088158/Cal 88 Lot 35**

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

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

PLEASE FAX THIS COMPLETED FORM TO: 0845-605-6800

Homocysteine Dilution Recovery and Calibrator 88 Value Assignment Improvement

REF: CC 13-14

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: Block Capitals:
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Title:		Instrument Serial Number:	
Hospital:		Street:	
City:		Post Code	
Email:		Phone:	
Signed:		Date	

PLEASE FAX THIS COMPLETED FORM TO: 0845-605-6800

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