SIEMENS

Urgent Field Safety Notice

Follow-up information
CC 17-12.B.OUS
June 2017

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

Follow-Up: ADVIA Centaur BR (CA 27.29) Assay Exclusion from Use with Multi-Diluent 1 Kit Lots Ending in 2577 and All Future Lots **– Mitigation Identified**

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

Table 1. ADVIA Centaur Product(s)

Assay	Test Code	Catalog Number	Siemens Material Number (SMN)	Lot Number
ADVIA Centaur BR assay (50 tests)	BR	02419937 (116734)	10333349	All lots
ADVIA Centaur BR assay (250 tests)	BR	03896216 (116735)	10334837	All lots

Reason for Urgent Field Safety Notice

Siemens Healthcare Diagnostics is communicating follow-up information to Urgent Field Safety Notice CC 17-12.A.OUS regarding BR (CA 27.29) assay exclusion from use with Multi-Diluent 1 Kit Lots ending in 2577 and all future lots.

This follow-up communication provides an investigation status update. While the investigation continues, Siemens has identified a mitigation to allow dilution testing with the BR (CA 27.29) assay on all ADVIA Centaur systems with patient samples > 450 U/mL using:

- BR (CA 27.29) assay kit Lots ending in 222 and above
- Calibrator G kit Lots ending in 37 (CG37) and above
- All available Multi-Diluent 1 Lots
- Overdilution point of 30 U/mL (Results for diluted patient specimens must be > 30 U/mL)

The mitigation included changes to the BR (CA 27.29) assay master curve associated with kit lots 222 and above and Calibrator G target values associated with lots CG37 and above. With this mitigation, Siemens is communicating mandatory lot pairing combinations in Table 2.

511 Benedict Avenue
Tarrytown, NY 10591

Follow-Up: *ADVIA Centaur BR (CA 27.29) Assay Exclusion from Use with Multi-Diluent 1 Kit Lots Ending in 2577 and All Future Lots* ***– Mitigation Identified***

Table 2. Mandatory Lot Combinations

Component	Mandatory Combination	Mandatory Combination
BR (CA 27.29) Reagent (kit lots ending in)	221	222 and above
Calibrator G (kit lots ending in)	36	37 and above

As a result of the mandatory lot pairing, Table 3 provides a summary of allowable actions for each combination.

Table 3. BR (CA 27.29) Reagent/Calibrator G Combinations & Allowable Actions

Actions	BR Reagent / Calibrator G kit Lots ending in	
	221 / 36	222 and above / 37 and above
Report undiluted sample results within the Analytical Measurement Range (AMR)	Yes	Yes
Perform on-board or manual sample dilutions for undiluted results above AMR	No	Yes, with an overdilution point of 30 U/mL

The mitigation will not correct dilution recovery for samples within the Analytical Measurement Range. As previously communicated in Urgent Field Safety Notice CC 17-12.A.OUS, on-board or manual dilutions of samples recovering within the Analytical Measurement Range **cannot be** performed with any Reagent and Calibrator G combination until further notice.

Customers should expect a difference in patient sample and control recoveries when moving from the current reagent and calibrator combination to BR (CA 27.29) assay kit Lots ending in 222 and Calibrator G kit Lots ending in 37. Refer to the *Additional Information* section for information related to patient samples and Bio-Rad controls.

Following Clinical Laboratory Standards Institute guidance, Siemens verified the Upper Limit of Normal (ULN), as defined in the ADVIA Centaur/XP/XPT and ADVIA Centaur CP systems Instructions for Use (IFU). The Upper Limit of Normal remains unchanged for both current and new combinations of Reagents and Calibrators as described above.

Siemens will provide a follow-up communication upon final resolution of this issue.

Risk to Health

Use of prior combinations of reagents and calibrators did not affect the clinical utility of the assay, based on the reference range verification and use of the assay for serial monitoring. Therefore, a review of previously generated results is not indicated.

A one-time difference may be observed when transitioning from the current lot combination (221/CG36) to the new lot combination (222/CG37). For ADVIA Centaur CP only, for patients previously tested who are being monitored serially (as stated in the IFU) and whose values using reagent lot 222/CG37 are $\leq$ 30 U/mL on ADVIA Centaur CP, it is recommended that these patients be re-baselined with the new lot 222/CG37.

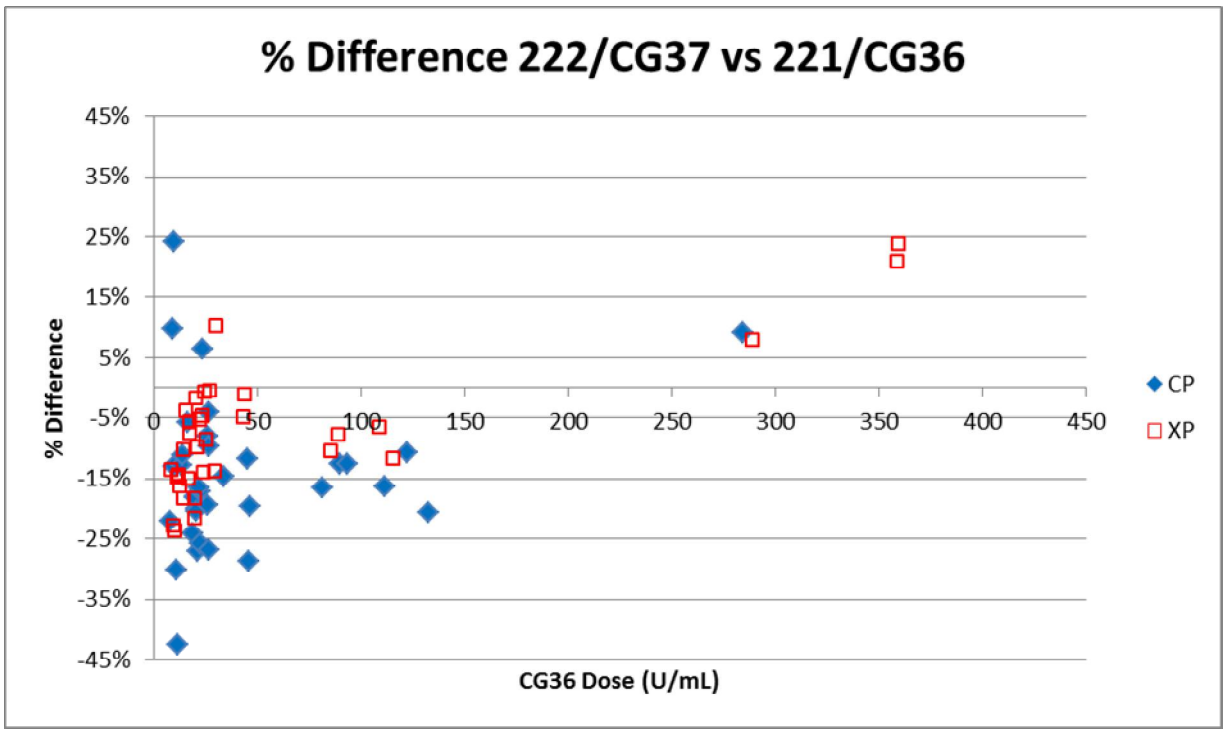
511 Benedict Avenue
Tarrytown, NY 10591

Follow-Up: *ADVIA Centaur BR (CA 27.29) Assay Exclusion from Use with Multi-Diluent 1 Kit Lots Ending in 2577 and All Future Lots* ***– Mitigation Identified***

Additional Information

Figure 1 demonstrates the patient difference observed during Siemens' internal investigation when comparing BR (CA 27.29) Lot 222/CG37 to Lot 221/CG36. Customers should expect similar performance upon transitioning to the new combination.

Figure 1. ADVIA Centaur Systems BR (CA 27.29) Patient Sample % Difference Lot 222/CG37 vs. Lot 221/CG36



Follow-Up: *ADVIA Centaur BR (CA 27.29) Assay Exclusion from Use with Multi-Diluent 1 Kit Lots Ending in 2577 and All Future Lots* ***– Mitigation Identified***

Table 4 provides the overdilution point instructions found in the applicable *Operator's Guide.*

Table 4. Overdilution Point Instructions

System	Instructions for Setting Overdilution Point
ADVIA Centaur/XP	Sign in as L1 1. At the workspace, select **Setup**. 2. Select **Test Definition Summary**. 3. At the Test – Summary window, select a **BR**. 4. Select **Ranges**. 5. At the Test – Ranges window, select **Edit**. 6. In the **Overdilution Point** field, enter the concentration of 30. 7. Select Save
ADVIA Centaur XPT	Sign in as a lab manager 1. Setup icon 2. Select Test Definition 3. Select Test 4. Select Ranges 5. Select dilution point tab 6. Select Edit (only if previous value exists in the fields) 7. Enter Overdilution point of 30 (Enter Within Range value (left side for Overdilution point, to right side dilution point)) 8. Select save **NOTE: To be able to edit these fields, move all open BR orders to Historical.**
ADVIA Centaur CP	Sign in as L1 Remove BR pack 1. At the workspace, select **Setup**. 2. Select the **Assay** tab. 3. Select BR. 4. Select **Details**. 5. Select **Ranges**. 6. Select **Auto Dilution**. 7. In the Overdilution Point field, enter the concentration of 30. 8. Select **OK** 9. Select **OK** 10. Select **Save** Reinstall BR pack

Follow-Up: *ADVIA Centaur BR (CA 27.29) Assay Exclusion from Use with Multi-Diluent 1 Kit Lots Ending in 2577 and All Future Lots* ***– Mitigation Identified***

Refer to Table 5 below for the revised Bio-Rad Control Targets and Ranges for currently available Bio-Rad control lots to be used with BR Reagent Kit Lots 222 (and above) and Calibrator G Kit Lots 37 (and above). The revised targets and ranges have been provided to Bio-Rad. Control lot 54600 was not available for Siemens to test and will not have revised targets and ranges.

Table 5. Revised Bio-Rad Control Targets and Ranges for Use with Lot 222 and above and CG37 and above

	ADVIA Centaur/XP/XPT		ADVIA Centaur CP	
Control Lot	Target (U/mL)	Range (U/mL)	Target (U/mL)	Range (U/mL)
23911	29.8	21.1 - 38.5	28.7	20.0 - 37.4
23912	82.9	67.1 - 98.7	87.9	71.3 - 105
23913	150	123 - 177	142	116 - 168
23921	28.1	19.5 – 36.7	28.3	19.7 – 36.9
23922	77.3	62.4 – 92.2	79.2	64.0 - 94.4
23923	152	125 – 179	158	130 - 186
23931	28.4	19.8 - 37.0	27.3	18.7 - 35.9
23932	74.3	59.8 - 88.8	77.7	62.7 - 92.7
23933	138	113 - 163	135	111 - 159
54611	22.8	14.2 - 31.4	21.0	12.4 - 29.6
54612	69.6	55.9 - 83.3	71.5	57.5 - 85.5
54613	143	117 - 169	147	121 - 173
54621	25.6	17.1 - 34.1	22.9	14.3 - 31.5
54622	82.3	66.6 - 98.0	83.6	67.7 - 99.5
54623	165	136 - 194	168	138 - 198
54631	26.5	17.9 - 35.1	29.5	20.8 - 38.2
54632	75.9	61.1 - 90.6	78.2	63.1 - 93.3
54633	149	122 - 176	142	116 - 168

Frequently Asked Questions (FAQs)

1. **Urgent Field Safety Notice CC 17-12.A.OUS said that BR (CA 27.29) assay did not dilute linearly when used with Multi-Diluent 1 kit lots ending in 2577 and all future lots. This indicated an issue with the Multi-Diluent 1. Why does the mitigation include changes to the BR (CA 27.29) assay master curve and Calibrator G?**

   The original issue appeared as specific lots of Multi-Diluent 1 failing specifications. Further investigations demonstrated an impact on the dilution recovery attributed to the reagent master curve and calibrator targets. Root cause remains under investigation.

2. **Why do I need to set an Overdilution Point?**

   Siemens' investigation found dilution recovery acceptable with samples where the dilution recovered > 30 U/mL. At this time, Siemens was unable to confirm acceptable dilution recovery for samples where the dilution recovered ≤ 30 U/mL. The investigation into this issue continues.

Follow-Up: *ADVIA Centaur BR (CA 27.29) Assay Exclusion from Use with Multi-Diluent 1 Kit Lots Ending in 2577 and All Future Lots* ***– Mitigation Identified***

3. **Do all patient samples tested on the ADVIA Centaur CP system with the new Reagent Lot 222/CG37 combination require re-baselining?**

   No. It is recommended that patients previously tested with an ADVIA Centaur CP system who are being monitored serially and whose values using **Reagent lot 222/CG37** are ≤ 30 U/mL, be re-baselined with the new lot Reagent Lot 222/CG37 combination.

4. **Can I alter the lot pairing combinations to match what I currently have in inventory?**

   No. The lot pairing combinations are mandatory as these are the combinations tested and approved by Siemens. No other combinations have been tested and approved.

Actions to be Taken by the Customer

BR (CA 27.29) Assay Customers that do not perform off-curve patient sample dilutions

- Please review this letter with your Medical Director
- Refer to Table 2 for mandatory lot pairing combinations.
- Continue to use BR (CA 27.29) assay kit Lots ending in 221 only with Calibrator G kit Lots ending in 36 to report results within the Analytical Measurement Range of the BR (CA 27.29) assay.
- Patient sample dilution can no longer be performed with BR (CA 27.29) assay kit Lots ending in 221 and Calibrator G Kit Lots ending in 36.
- When BR (CA 27.29) assay kit Lots ending in 221 and Calibrator G kit Lots ending in 36 are no longer available, customers should transition to BR (CA 27.29) assay kit Lots ending in 222 (and above) with Calibrator G kit Lots ending in 37 (and above). Refer to the transition instructions below for required transition information.
- All customers must 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.

BR (CA 27.29) Assay Customers that perform off-curve patient sample dilutions

- Please review this letter with your Medical Director
- Refer to Table 2 for mandatory lot pairing combinations.
- Transition to BR (CA 27.29) assay kit Lots ending in 222 (and above) and Calibrator G kit Lots ending in 37 (and above). This combination can be used to report results within the Analytical Measurement Range of the BR (CA 27.29) assay and to dilute patient samples > 450 U/mL. All diluent lots are acceptable for off-curve patient sample dilution

511 Benedict Avenue
Tarrytown, NY 10591

with this combination. Do not dilute samples ≤ 450 U/mL. Refer to the transition instructions below for required transition information.

- All customers must 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.

Transition Instructions for BR (CA 27.29) Assay kit lots ending in 222 (and above) and Calibrator G kit Lots ending in 37 (and above)

- For an automatic or manual dilution, the BR (CA 27.29) concentration in the diluted sample, prior to correction using the dilution factor, must be > 30 U/mL. Edit the overdilution point on the ADVIA Centaur Systems to 30 U/mL per the instructions found in the appropriate *Operator's Guide* or Table 4.
- Refer to Table 5 for revised control targets and ranges to be used with BR (CA 27.29) assay kit Lots ending in 222 (and above) and Calibrator G kit Lots ending in 37 (and above). For all other commercially available controls, evaluate the need for target reset.
- If using the ADVIA Centaur CP system, re-baseline patients as recommended in the *Risk to Health* section.

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.

511 Benedict Avenue
Tarrytown, NY 10591