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Urgent Field Safety Notice:

ADVIA® Chemistry 1800 / ADVIA Chemistry 2400 / ADVIA Chemistry XPT

Positive Bias Observed with Direct Bilirubin (DBIL_2) and Total Bilirubin (TBIL_2) Assays Following Calibration with Multiple Chemistry Calibrator Lots

Dear Sirs,

Our records indicate that you may have received the following product:

Table 1. ADVIA® Chemistry Systems Affected Product:

Calibrator	Siemens Material Number (SMN) /Reference Number (REF)	Lot Number	Expiration Date	Distribution Date
Chemistry Calibrator	10312279 / 09784096	534177	2021-09-30	2019-12-31
		534177A	2021-10-31	2020-03-28
		534177B	2021-12-31	2020-01-17
		534177C	2022-01-31	2020-02-24
		534177D	2022-03-31	2020-06
		960742	2022-05-31	2020-06

Reason for Correction

The purpose of this communication is to inform you of an issue with the Chemistry Calibrator (Chem Cal) lots indicated in Table 1 above and provide instructions on actions that your laboratory must take.

Siemens Healthcare Diagnostics has observed a positive bias with Quality Control (QC) and patient sample values for Direct Bilirubin (DBIL_2) and Total Bilirubin (TBIL_2) assays on the ADVIA Chemistry system following calibration with affected Chemistry Calibrator lots listed in Table 1. The bias has been attributed to bilirubin instability with these lots of Chemistry Calibrator. The positive bias may lead to QC results exceeding a laboratory's established ranges. Calibration errors may also be observed. See Table 2 below for representative QC performance from Siemens internal testing with affected Chem Cal lots. Testing of patient samples demonstrated similar performance.

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Table 2: Representative Internal QC Testing Recovery when using Affected Calibrator Lots vs. Expected Values

Assay	QC Product Lot	QC Level	Expected Mean mg/dL (µmol/L)	Expected Range mg/dL (µmol/L)	Recovery when using Affected Calibrator lots mg/dL (µmol/L)	% Bias
DBIL_2	Bio-Rad Multiqual Lot 47980	1	0.3 (5.1)	0.2 - 0.4 (3.4 - 6.8)	0.3 (5.1)	0%
		2	1.4 (23.9)	1.3 - 1.5 (22.2 - 25.7)	1.7 (29.1)	+21%
		3	2.4 (41.0)	2.0 - 2.8 (34.2 - 47.9)	3.2 (54.7)	+33%
	Bio-Rad Pediatric Control Lot 44350	2	7.5 (128.3)	7.2 - 7.8 (123.1 - 133.4)	10.1 (172.7)	+35%
TBIL_2	Bio-Rad Multiqual Lot 47980	1	0.7 (12.0)	0.6 - 0.8 (10.3 - 13.7)	0.8 (13.7)	+14%
		2	3.3 (56.4)	3.2 - 3.4 (54.7 - 58.1)	3.6 (61.6)	+9%
		3	7.6 (130.0)	7.2 - 8.1 (123.1 - 138.5)	8.4 (143.6)	+11%
	Bio-Rad Pediatric Control Lot 44350	2	18.0 (307.8)	17.4 - 18.6 (297.5 - 318.1)	19.8 (338.6)	+10%

All other analytes present in the Chem Cal continue to meet product standards.

All available lots of Chem Cal currently in Siemens inventory are similarly impacted. Siemens is working to restore the bilirubin stability of the Chem Cal. A follow up communication will be issued when a Chem Cal lot suitable for use with the DBIL_2 and TBIL_2 assays becomes available.

The root cause of this issue is under investigation.

Risk to Health

The calibrator issue described above may lead to an apparent delay in testing due to the inability to calibrate the assay or due to quality control results that do not meet acceptability criteria. If quality control results are within range when using an affected calibrator lot, the difference in patient results when compared to an unaffected calibration would not be expected to lead to a clinically significant difference in patient management. Siemens is not recommending a review of previously generated results.

Actions to be taken by the Customer

- Discontinue use of the Chem Cal lots listed in Table 1 for DBIL_2 and TBIL_2 calibration. The lots remain suitable for calibration of the other analytes contained in the Chem Cal.
- Reserve any unaffected lots of Chem Cal within the expiration date (not listed in Table 1) for calibration of only DBIL_2 and TBIL_2.
- If an unaffected lot of Chem Cal is not available, Siemens has evaluated the use of the RANDOX Calibration Serum Level 3 (CAL 3) Lot 1024UE as a suitable alternative. Siemens has verified the accuracy of this calibrator on the ADVIA Chemistry System by method comparison (see Figure 1 below). Results obtained at individual laboratories may vary. Siemens recommends that laboratories verify the accuracy of the results with acceptable QC performance when using the RANDOX CAL 3 calibrator, prior to reporting of patient samples. Please see instructions in the Additional Comments Section below. Product availability may vary by country.
- If the recommendations above are not suitable for your laboratory, alternative testing is recommended for the ADVIA Chemistry DBIL_2 and TBIL_2 assays.
- Complete and return the Field Correction Effectiveness Check attached to this letter within 30 days.
- Review this letter with your Medical Director.

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 Healthineers Customer Care Center or your local Siemens Healthineers technical support representative.

Sincerely yours,

Siemens Healthcare Diagnostics GmbH



i.V. Dipl. Ing. Franz Schwarz
Quality Management CEE



i.A. Dr.ⁱⁿ Brigitte Gassner
Product Manager Austria & SEE

Appendix 1: Additional Instructions:

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RANDOX CALIBRATION SERUM LEVEL 3 (CAL 3) Ordering information:

Product Name: RANDOX Calibration Serum Level 3 (CAL 3) Lot 1024UE
Siemens Material Number (SMN) / Reference Number (REF): 10328299 / 8492806
RANDOX Catalog Number CAL 2351 (if ordered directly from RANDOX)

RANDOX CALIBRATION SERUM LEVEL 3 (CAL 3) PRODUCT INFORMATION (as published in the RANDOX Product Insert):

Storage and Stability Requirements for Bilirubin:

Un-reconstituted: Un-reconstituted serum is stable up to the expiry date shown on the side of each individual bottle.

Reconstituted: Bilirubin in the serum is light sensitive and it is recommended that the serum is stored in the dark. Stored in the dark, it is stable for 1 day at +2°C to +8°C. Do not store at +15°C to +25°C. Do not freeze.

Preparation for Use:

Serum must only be reconstituted using the following procedure:

1. Open the vial carefully, avoiding any loss of material.
2. Reconstitute by pipetting exactly 5 ml of distilled water at +15°C to +25°C, into the vial.
3. Replace the rubber stopper and leave to stand for 30 minutes out of bright light before use.
4. Swirl gently several times during the reconstitution period to ensure that the contents are completely dissolved.
5. Prior to use, mix the contents by inverting the vial. Do not shake the vial as the formation of foam should be avoided.

Ensure that no lyophilized material remains un-reconstituted.

6. The serum is then ready for use with either a manual test or with an automated instrument.

Assigned Values

Refer to the SIEMENS ATELLICA / ADVIA 1200/1650/1800/2400® section of the RANDOX CAL 3 IFU for assigned values for TBIL_2 and DBIL_2.

Note: Siemens has only verified the use of the RANDOX Calibration Serum Level 3 (CAL 3) Lot 1024UE to calibrate Direct Bilirubin (DBIL_2) and Total Bilirubin (TBIL_2). Siemens has not verified the performance of the other analyte constituents contained in the RANDOX CAL 3 product. Siemens is only recommending the use of verified RANDOX CAL 3 lot 1024UE.

Refer to the RANDOX CAL 3 IFU for complete instructions for use of this product.

CALIBRATION:

Prior to using the RANDOX CAL 3 for the TBIL_2 and DBIL_2 assays, configure the calibrator definition and factor value (FV) in the ADVIA Chemistry instrument software using the steps outlined in the ADVIA Operator's Guide. Please contact your Siemens Customer Care Center for additional assistance, if needed.

FIGURE 1: Method Comparison / Correlation and Difference (%) plots of patient sample recoveries comparison between RANDOX CAL 3 and Chem Cal Master Lot for (A) ADVIA DBIL_2; and (B) ADVIA TBIL_2.

