Urgent Field Safety Notice
SBN-CPS-2016-009

CPS / ClinChem fully automated
Version 4
17-January-2017

UPDATE: Increased recovery of patient results with ONLINE TDM Gentamicin assay

Product Name	Gentamicin
Product Description	ONLINE TDM Gentamicin 100 Tests c 311, c 501/502 ONLINE TDM Gentamicin 100 Tests c 701/702
GMMI / Part No **Device Identifier**	04490843190 ONLINE TDM Gentamicin 100 Tests c 311, c 501/502 05841291190 ONLINE TDM Gentamicin 100 Tests c 701/702
Production Identifier (Lot No./Serial No.)	All current and future lots
SW Version	Not applicable
Type of Action	Field Safety Corrective Action (FSCA)

Dear Valued Customer,

Description of Situation

In the last version of this customer letter we informed you about the implementation of an instrument factor (IF) for ONLINE TDM Gentamicin that was - based on available data - the mitigation for the reported issue.

However, against initial data the correction of the instrument factor did not mitigate the issue. We received complaints from customers who implemented the IF, observing decreased sample recovery using the ONLINE TDM Gentamicin assay.

Since availability of fresh patient samples for gentamicin is very limited, frozen patient samples had to be used for internal investigations. Obviously, the internal results obtained with these samples and used for the implementation of the IF did not match with the external observations reported by customers. Further investigations were initiated at Roche to understand this mismatch. In order to verify the internal results a new panel of patient samples was collected (panel B, stored at -80°C) and compared to the panel that was used for the determination of the IF (panel A, stored at -20°C).

The outcome of this method comparison on **cobas c** 501 vs. COBAS INTEGRA was as follows:

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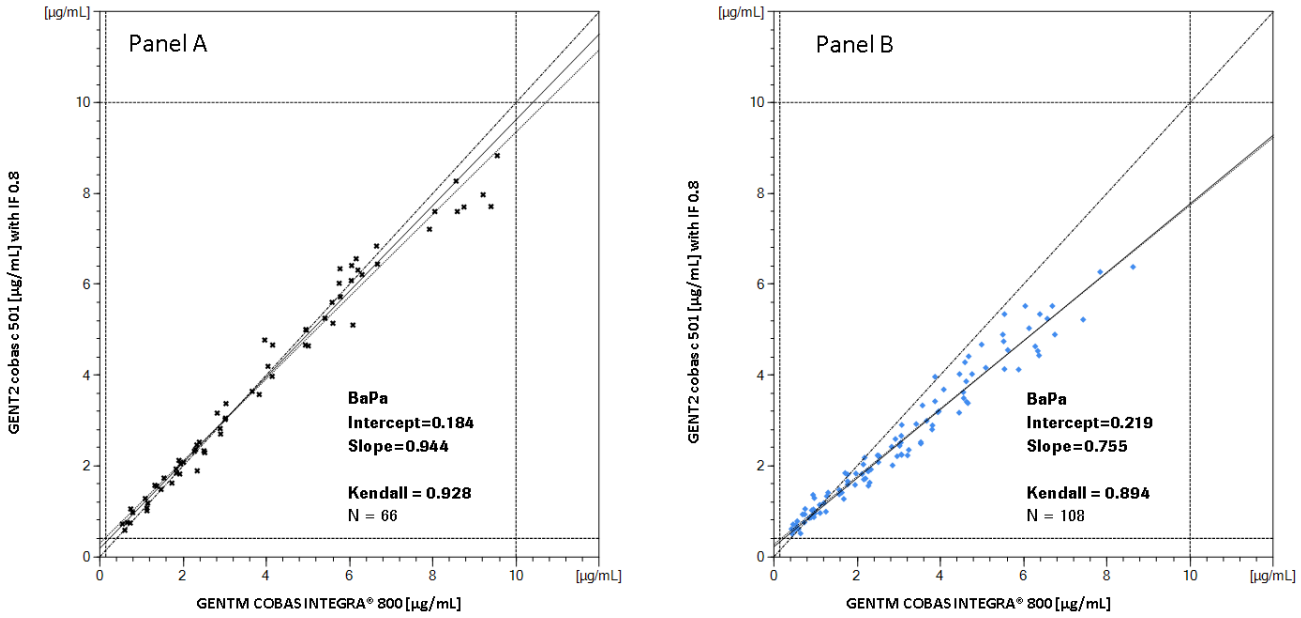
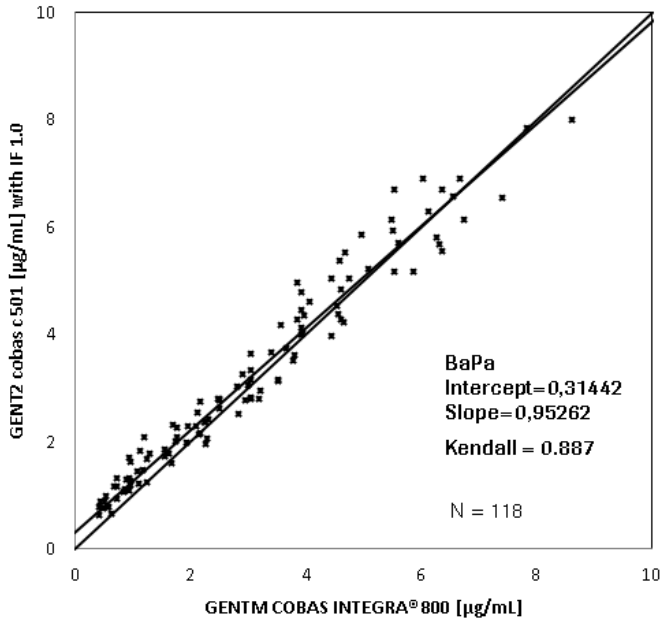
Method comparison GENT2 c 501 with IF vs. GENTM COBAS INTEGRA 800:



These recent results indicate that there is a different susceptibility of the ONLINE TDM Gentamicin assay against different storage conditions of patient samples.

Method comparison GENT2 c 501 w/o IF vs. GENTM COBAS INTEGRA 800 to verify the value recovery:



Recovery of sample panel B is comparable to the GENTM assay on COBAS INTEGRA which is internally considered as a reference method.

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Based on these findings (see above) it was decided to withdraw the IF to ensure that patient samples will be found correctly.

Underestimation of gentamicin may lead to an increased number of side effects. Severe over-dosage may lead to toxic concentrations of gentamicin with subsequent symptoms and potential harm to patients.

Gentamicin levels need to be tested according to guidelines, and the frequency depends on therapy and individual patient conditions (e.g. individual metabolism, renal failure). Levels can be subject to fluctuations over time. Considering this, no general recommendations with respect to the review and follow up were given. Any specific questions raised by the users should be addressed individually, considering all relevant clinical information.

Actions taken by Roche Diagnostics

Roche will make re-assigned values available via updated e-packages by mid of February 2017. In addition, we are still working on a long term solution to correct the matrix issue.

Actions to be taken by the customer

We kindly ask you to not implement the instrument factor of 0.8 on **cobas c** but re-set or leave the factor at 1.0.

- For **cobas c** 311/501/502/701/702 the instrument factor has to be set back to a = 1.
- The technical limit has to be set back to the original values.
- The re- assigned control values have to be implemented.

The re-assigned values for TDM Control Lots 125783 and 142573 are as follows for all **cobas c** systems:

Lot 125783	Short name	Method	ACN	Value	Range	1s	Unit
Level I	GENT2	KIMS	416	1.75	1.39 - 2.11	0.12	mg/ml
			8416	3.66	2.94 - 4.38	0.24	mmol/l
Level II				4.35	3.48 - 5.22	0.29	mg/ml
				9.09	7.26 -10.92	0.61	mmol/l
Level III				7.05	5.64 - 8.46	0.47	mg/ml
				14.7	11.7 - 17.7	1.0	mmol/l

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Lot 142573	Short name	Method	ACN	Value	Range	1s	Unit
Level I	GENT2	KIMS	416	1.71	1.38 - 2.04	0.11	mg/ml
			8416	3.57	2.85 - 4.29	0.24	mmol/l
Level II				4.26	3.42 - 5.10	0.28	mg/ml
				8.90	7.13 -10.67	0.59	mmol/l
Level III				6.64	5.32 - 7.96	0.44	mg/ml
				13.9	11.2 - 16.6	0.9	mmol/l

The following actions are required:

cobas c 311 analyzer and **cobas c** 501/502/701/702 modules:

1. Update of application settings:

   Option 1:

   Delete the GENT2 ACN (8)416 application and re-download the current application. In that case Instrument factor and technical range are reset to original values.

   Option 2 (*):

   To avoid deletion of calibration and controls data, the instrument factor and the technical limit have to be reset manually back to the original value.

   On the Calibration/Status/Instrument Factor display, update the instrument factor from a=0.8 to a=1 (On **cobas c** 701/702 for each module and each rotor).

   For **cobas c** 311/501/502: Technical range = measuring range to 0.4 – 10.0 µg/mL.

   For cobas c 701/702: Technical range is set to 0.6 – 10.0 µg/mL

   (For EP7 flagging keep in mind that the configuration is done on Data Manager)
2. Update the TDM Control target values and range with the re-assigned value manually or with e-bc if available
3. Perform a new calibration.

(*) NOTE:

The technical limit field on **cobas c** systems belongs to a group of settings that can be modified by the customer. These fields will not be overwritten by an updated e-barcode. This is the case even if the settings have not previously been manually edited. Only a complete re-installation would override the manually input fields.

New feature: **cobas** 8000 modular analyzer series customers who have already installed the new software version control unit 05-0x can choose if they want to overwrite the application parameter in case of a download.

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Communication of this Field Safety Notice (if appropriate)

This notice must be passed on to all those who need to be aware within your organization or to any organization/individual where the potentially affected devices have been distributed/supplied.

Please transfer this notice to other organizations/individuals on which this action has an impact.

The following statement is mandatory in FSNs for EEA countries but is not required for the rest of the World:

The undersigned confirms that this notice has been notified to the appropriate Regulatory Agency.

We apologize for any inconvenience this may cause and hope for your understanding and your support.

Best regards,

Contact Details

To be completed locally:
Name
Title
Company Name
Address
Tel. +xx-xxx-xxxx xxxx
Email name@roche.com