Field Safety Notice

SBN-CPS-2019-006

CPS / ClinChem fully automated
Version 1
1-Aug-2019

ONLINE TDM Vancomycin Gen.3 incorrectly low results

Product Name	ONLINE TDM Vancomycin Gen.3 (VANC3)
System	cobas c 501/502 modules
GMMI / Part No **Device Identifier**	06779344190 ONLINE TDM Vancomycin Gen.3 200 Tests (c 311, c 501/502) *Note: There may be other affected identifiers that are affected globally. Please contact the product owner if the device is obtained from an overseas dealer.*
SW Version	Not applicable
Type of Action	Field Safety Corrective Action (FSCA)

Dear Valued Customer,

Description of Situation

Roche has received a small number of reports about incorrectly low results for vancomycin in individual patient samples measured with the ONLINE TDM Vancomycin Gen.3 assay on cobas c platforms (VANC3).

Some results were flagged as below the measuring range ("*<Test*"; defined by Limit of Quantification (LoQ) 4.0 µg/mL). As the patients were receiving vancomycin pharmacotherapy, the results below the measuring range were unexpected and thus implausible.

Some results were incorrectly low within the measuring range and were not flagged. Internal investigations using alternative reagent formats and techniques (e.g. LC-MS/MS) confirmed that these samples contained vancomycin. Hence, the affected sample results obtained with ONLINE TDM Vancomycin Gen.3 were incorrect.

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Root cause

Inaccurately low results below the measuring range

The VANC3 immunoassay uses a competitive assay format in which microparticles agglutinate (KIMS). In the reported cases, the VANC3 reagent reaction kinetic is impaired. The kinetics of the affected samples showed an unusually strong agglutination of the microparticles. This led to the incorrect results below the measuring range (<4.0 µg/mL) as observed in the reported cases. With the competitive test format of VANC3, a lower aggregation kinetic would be expected for samples containing vancomycin.

Inaccurately low results within the measuring range

From the reaction kinetics of the incorrectly low results within the measuring range (4.0–80 µg/mL), it is concluded that the affected patient samples contain one or more non-specific interfering substance(s) that enhance the agglutination. Despite several investigations, the interfering substance(s) could not be isolated. Immunofixation was performed on the available samples and a suspicious immunoglobulin pattern was observed. The exact target/epitope of these immunoglobulins could not be determined.

Detectability

The frequency of occurrence is remote based on the reported cases per number of tests performed.
For results below the measuring range, detection is probable, as this scenario is implausible and not expected during vancomycin pharmacotherapy.

For incorrectly low results within the measuring range, detection may be unreliable or difficult. Incorrectly low VANC3 test results within the measuring range are difficult to detect if not confirmed by an alternative method.

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Actions taken by Roche Diagnostics

1. Introduction of a prozone check

In order to detect samples with inaccurately low results below the measuring range, Roche will implement a prozone limit check for VANC3 applications (ACN 159 for cobas c 501 and ACN 8159 for cobas c 502 modules). This check detects samples with a stronger agglutination than that of a vancomycin-free sample or the zero calibrator. Affected samples will be flagged with the "*>Kin"* data alarm.

Updated e-library packages are expected to be available by the end of September 2019.

2. Update of the Instructions for Use (IfU) for VANC3 on all cobas c analyzer

For samples flagged ">Kin", the Operator's Manuals recommend dilution or rerun with a decreased sample volume. (Note: Decrease sample volume is not applicable to VANC3). However, dilution of the affected VANC3 samples does not correct the atypical agglutination. The recommended action for such a sample is to use another assay technique. Therefore, the Instructions for Use (IfU) will be updated to include the following information:

"A test result flagged with ">Kin", ">Kin3" indicates unusual reaction kinetics. There is a high probability that the sample contains an interfering substance which accelerates the reaction kinetics. For such very rare samples it is not possible to report a reliable analyte concentration with this assay."

During the investigation, the affected VANC3 samples showed a microparticle agglutination that could not be distinguished from unaffected samples. In principle, interferents can also lead to an inhibition of agglutination, and consequently to inaccurately high results. If the sample result is not consistent with the clinical picture or treatment regimen, assay vancomycin by a different method. Therefore, the Instructions for Use (IfU) will be updated to include the following information:

"In very rare cases (less than 1 reported case per 1 000 000 tests) certain immunoglobulins can unspecifically interfere with the agglutination reaction leading to unreliable results."

The updated and approved Instruction for use (IfU) will be available by Q1 2020.

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Actions to be taken by the customer/user

Download the updated VANC3 application

The prozone check settings cannot be changed manually but is included in the updated application.
We kindly ask you to download the updated VANC3-application (available by end of September 2019).

1. Before downloading the updated e-barcode, unload any cobas c packs already on board your analyser/module.
2. Go to Utility > Application > Download: then, select and download the application e-barcode version listed in the table below.

Application	Module	New e-barcode version
VANC3	cobas c501	01-02
	cobas c502	xx.xx-01-03*

* For cobas 8000 e-barcodes, xx.xx is used as a placeholder in this notification. The cobas link will automatically assign numbers to the e-barcodes upon release.

3. Load a new VANC3 cobas c pack on your cobas c analyser/module.

Samples showing incorrectly low VANC3 test results below and within the measuring range should be re-tested with alternative immunoassays or LC-MS/MS.

Consider the additional claims in the updated and approved IFU

The following claims will be included in the upcoming IFU for VANC3 (available by Q1 2020).

"A test result flagged with ">Kin", ">Kin3" indicates unusual reaction kinetics. There is a high probability that the sample contains an interfering substance which accelerates the reaction kinetics. For such very rare samples it is not possible to report a reliable analyte concentration with this assay."

"In very rare cases (less than 1 reported case per 1 000 000 tests) certain immunoglobulins can unspecifically interfere with the agglutination reaction leading to unreliable results."

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Communication of this Field Safety Notice

This notice must be passed on to all those who need to be aware within your organization or to any other organization/individual where the potentially affected devices have been distributed/supplied. Please pass on this notice to the Chairman Medical Board and Head of Department as well, as required by HSA.

Please maintain awareness of this notice and resulting action for an appropriate period to ensure the effectiveness of the corrective action

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

Sincerely,

Roche Diagnostics Asia Pacific Pte Ltd
Email: sg.regulatory@roche.com

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ACKNOWLEDGMENT RECEIPT

This is to acknowledge the receipt of Roche Field Safety Notice Reference No. SBN-CPS-2019-0006 dated 01 Aug 2019, regarding ONLINE TDM Vancomycin Gen.3 incorrectly low results.

Received by:

_____
Name & Signature

_____
Facility Stamp

_____
Date

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