URGENT FIELD SAFETY NOTICE
IMMEDIATE ACTION REQUIRED

Ref No:	**CFSN VANC3 SBN-CPS-2019-006**
Date:	**11/07/2019**
Type of Action:	**Field Safety Corrective Action (FSCA)**

Product Affected: ONLINE TDM Vancomycin Gen.3

System Affected:

cobas c 311
cobas c 501
cobas c 502
cobas c 503
cobas c 701
cobas c 702

Software Version: N/A

Product No	Material No	Lot No
ONLINE TDM Vancomycin Gen.3 100 Tests (c311/501/502)	06779336190	N/A
ONLINE TDM Vancomycin Gen.3 200 Tests (c311/501/502)	06779344190	N/A
ONLINE TDM Vancomycin Gen.3 150 Tests (c701/702)	06781632190	N/A
ONLINE TDM Vancomycin Gen.3 100 Tests (c503)	08445605190	N/A
ONLINE TDM Vancomycin Gen.3 200 Tests (c503)	08508849190	N/A

Summary of Issue

ONLINE TDM Vancomycin Gen.3 incorrectly low results

Roche Diagnostics
Charles Avenue
Burgess Hill
West Sussex
RH15 9RY

√	Immediate Action Required
	Action Required
	Information Only

Registered No 571546

Reason for Notice

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.

Other results were erroneously low within the measuring range without any flag. Internal investigations using alternative reagent formats and techniques (e.g. LC-MS/MS) confirmed that these samples contained vancomycin and therefore the results obtained with ONLINE TDM Vancomycin Gen.3 were incorrect.

Root cause

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 unusual strong agglutination of the microparticles. This led to the incorrect results below the measuring range (<4.0 µg/mL) observed in the reported cases. With the competitive test format of VANC3 a lower aggregation kinetic would be expected for samples containing vancomycin.

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 & Severity

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.

The frequency of occurrence is remote based on the reported cases per number of tests performed.

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Actions taken by Roche Diagnostics

1. Introduction of a prozone check

In order to make customers aware of incorrect results below the measuring range, Roche will implement a 'prozone check' for the VANC3 applications ACN (8)159 for the **cobas c** 311 analyzer, **c** 501/502 and **c** 701/702 modules. This check detects samples with a stronger agglutination than that of a vancomycin-free sample or the zero calibrator. Such affected samples will be flagged with a ">Kin" flag. Updated e-library packages are expected to be available by the end of September 2019.

For the VANC3 application (ACN 21210) on **cobas c** 503 analytical unit a corresponding check (kinetic unstable check) has already been implemented with the launch version. The affected samples will be flagged with ">Kin3".

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

In general, the operator manuals for the **cobas c** systems recommend a dilution or a rerun with decreased sample volume for ">Kin" or ">Kin3" flagged samples. However, for samples with a low recovery below the measuring range a dilution of the affected samples would not correct the recovery and 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, expected to be available by the end of September 2019:

"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."

Investigation showed an agglutination of the microparticles that could not always be distinguished from unaffected samples. Therefore, samples with a low recovery within the measuring range cannot be detected by a prozone check. As interfering substances can also lead to an inhibition of the agglutination and consequently to incorrectly high results, it was decided to include the following disclaimer in the IfU:
"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."

Action Required

Actions to be taken by the customer/user

The prozone check settings cannot be changed manually but is included in the updated application.

For VANC3 on **cobas c** 311 analyzer and **cobas c** 501/502/701/702 modules we kindly ask you to download the updated VANC3-application. The updated IfU will be available in the e-content portal.

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

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Please complete and return the Acknowledgement Form which accompanies this Field Safety Notice by 26th July 2019.

Please bring this notice to the attention of all personnel in your hospital or Health Care facility who need to be aware of this safety issue.

If you have forwarded the affected product(s) listed above to another laboratory, please provide a copy of this notice to them.

Attachments CFSN VANC3 SBN-CPS-2019-006 Acknowledgment Form

This action is being conducted with the knowledge of the Medicines and Healthcare Products Regulatory Agency (MHRA), the Health Products Regulatory Authority (HPRA), and other International Regulatory Agencies.

Roche Diagnostics operates a vigilance system that complies with the IVD Directive 98/79 EC

A copy of this notice can also be found on the Roche Dialog Portal

If you require any further information please contact our

Technical Support Hotline

UK: 0808 100 19 20

Ireland: 1800 40 95 64

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ACKNOWLEDGEMENT

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Field Safety Notice Ref No: CFSN VANC3 SBN-CPS-2019-006 Acknowledgment Form.
Date: 11/07/2019
Type of Action: Field Safety Corrective Action (FSCA)

Kindly complete and return this form to the e mail address shown in the footer before 26th July 2019.

Product Catalogue No:	ONLINE TDM Vancomycin Gen.3 (06779336190) ONLINE TDM Vancomycin Gen.3 (06779344190) ONLINE TDM Vancomycin Gen.3 (06781632190) ONLINE TDM Vancomycin Gen.3 (08445605190) ONLINE TDM Vancomycin Gen.3 (08508849190)
System:	**cobas c** 311 **cobas c** 501 **cobas c** 502 **cobas c** 503 **cobas c** 701 **cobas c** 702
Customer Name & Dept:	
Address:	

Are the above contact details correct? *(Please circle)* Yes No *(If no please insert correct details below)*

Contact Name:

Department:

Telephone:

If you require an electronic copy of this field safety notice in addition to the hard copy please print your e-mail address below:

Email:

Please acknowledge receipt of information and awareness of any required actions described within the accompanying Field Safety Notice.

Please bring this notice to the attention of all personnel in your hospital or healthcare facility who need to be aware of this safety issue.

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email to burgesshill.techsupportdocs@roche.com

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I acknowledge receipt of this Field Safety Notice and have read, understood and implemented its content.

Name:

Signed:

Date:

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