URGENT FIELD SAFETY NOTICE
IMMEDIATE ACTION REQUIRED

Ref No:	**PFSN18 Deviations of high (>4.5) CoaguChek INR values due to calibration with WHO reference standard rTF/16 SBN-CPS-2018-014**
Date:	**22.08.2018**
Type of Action:	**Field Safety Corrective Action (FSCA)**
Product Affected:	CoaguChek XS PT Test PST CoaguChek XS PT Test CoaguChek PT Test
System Affected:	CoaguChek® XS system CoaguChek® INRange system CoaguChek® XS Plus system CoaguChek® XS Pro system CoaguChek® Pro II system
Software Version:	N/A

Product No	Material No	Lot No
CoaguChek XS PT Test PST	07671679190, 07671687019	from 272167 up to 334498
CoaguChek XS PT Test	04625374190, 04625358019, 04625315019	from 272167 up to 334498
CoaguChek PT Test	06688721019	from 272170 up to 353606

Summary of Issue

We need to inform you that Roche Diagnostics has decided to implement a temporary re-calibration of our CoaguChek PT, XS PT and XS PT PST test strips to the previous WHO Standard rTF*/09. At the same time, we can confirm that all CoaguChek test strips in the market which have been calibrated to the latest WHO standard rTF/16 (please refer to the lot numbers mentioned above) are safe to use for results between 0.8 to 4.5 INR.

**(rTF = human, recombinant thromboplastin / recombinant human tissue factor reagent)*

Reason for Notice

Description of Situation

Since market introduction of CoaguChek, test strips have been calibrated against standard reference thromboplastin provided by the WHO. In 2016, a new WHO reference Thromboplastin, rTF/16, was established. This new WHO reference standard is calibrated towards INR values between 1.5 and 4.5 INR and is derived from human tissue factors. Compared to the previous WHO standard of human based thromboplastin (rTF/09), it leads to an increase in INR values (6% bias) and shows a higher International Sensitivity Index (ISI):[1]

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WHO Standard	ISI
rTF/09	1.08
rTF/16	1.11

Table 1: ISI values of WHO standards

As the global leader for INR Point-of-Care solutions, Roche decided to switch to the new WHO standard and was one of the first companies who delivered CoaguChek test strips calibrated towards this new (rTF/16) standard to markets from January 2018.

Roche Diagnostics has received an increased number of complaints regarding deviations of CoaguChek test strips against non-Roche controls as well as laboratory methods during the last weeks. Therefore, we initiated an in-depth analysis in order to determine the reasons for the observed differences.

Our findings:

- For values within the common therapeutic ranges (up to 4.5 INR) and covered by the new (rTF/16) WHO standard (1.5-4.5 INR) a bias of 6% was verified when we compared the new CoaguChek test strips against Innovin-based thromboplastin from the previous (rTF/09) reference WHO standard. This bias is caused by the differences between the previous (rTF/09) and the new (rTF/16) WHO reference standards and was expected to be seen.
- For values >4.5 INR an unexpected increasing positive bias was found between CoaguChek test strips referenced to the latest WHO rTF/16 and Innovin-based laboratory methods referenced to rTF/09.
- No deviations have been experienced with the previous CoaguChek test strips referenced to the previous WHO standard rTF/09. Most laboratory methods are still calibrated against the previous (rTF/09) WHO standard.

Actions taken by Roche Diagnostics

Since a medical risk, due to a possible Vitamin K treatment decision, for INR ranges >4.5 INR, cannot be excluded, it was decided to re-calculate the calibration for upcoming CoaguChek strip lots according to the previous WHO standard (rTF/09). Moreover, the current CoaguChek test strips, calibrated to the new WHO standard rTF/16, can still be used but are limited to INR values up to 4.5 INR. All values above 4.5 INR, measured with CoaguChek test strips of the affected lot numbers (see above), should be double checked against a laboratory method. As mentioned in the method sheet of the test strips, methods using Innovin as Thromboplastin (Siemens) correlate very well with the CoaguChek system.

The first test strips re-calibrated to rTF/09 will be available from **November 2018** for the following lot numbers:

REF-Number	Product Name	Lot Number (Code Key)
07671679190	CoaguChek XS PT Test PST, 6 tests	≥334499 (S_344)
07671687019	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)
04625374190	CoaguChek XS PT Test, 6 tests International	≥334499 (S_344)
04625358019	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)
04625315019	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)
06688721019	CoaguChek PT Test, 2 x 24 tests	≥361433 (S_062)

Table 2: Availability rTF/09 Lots

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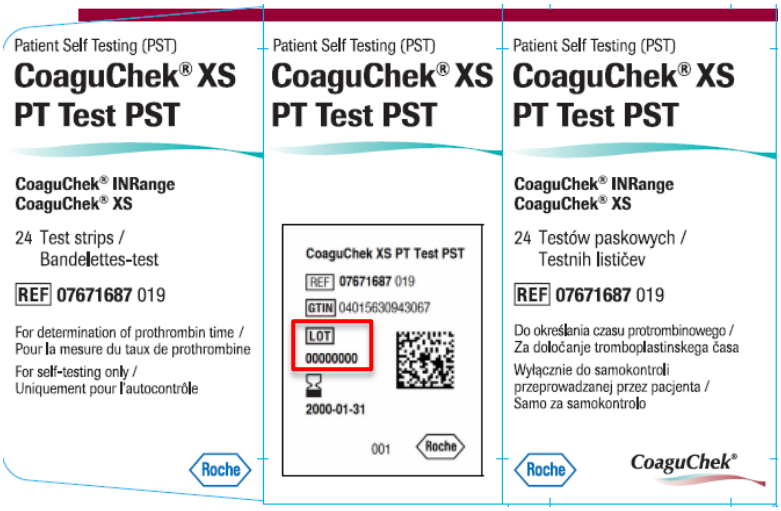
The lot number is printed on the label, which is applied to the test strip box at manufacturing:



*Example for box only

With the above mentioned lots in Table 2 the issue is resolved and values up to 8.0 INR are valid.

Until the new lots are available, rTF/16 calibrated test strips continue to be distributed for the following reasons:

- values are reliable from 0.8 to 4.5 INR
- the difference of 6%, caused by the new WHO standard, does not expose patients to a medical risk

A re-calibration to the new rTF/16 standard will be evaluated carefully.

The "Patient-Information-Letter" attached will be provided to patients that have purchased CoaguChek XS PT Test PST and CoaguChek XS PT Test strips directly from Roche.

Action Required

In order to prevent any risk to your and our valued patients we ask you for the following actions:

1. Health Care Professionals using one of the affected lots in their GP office/hospital:
   - Values ≤4.5 INR: Values are valid and can be used without lab comparison
   - Values >4.5 INR: Values should be compared with a laboratory method.

   As mentioned in the method sheet of the test strips, methods using Innovin as Thromboplastin (Siemens) correlate very well with the CoaguChek system.

Method Sheet CoaguChek XS PT, XS PT Test PST: […] Clinical studies were conducted in which venous and capillary blood results from the CoaguChek XS/XS Plus/XS Pro Systems were compared with venous blood results obtained using the laboratory reference method Innovin (Dade-Behring). The majority of slopes were found between 0.93 and 1.04 for venous results, and between 0.92 and 1.03 for capillary results […]

Method Sheet CoaguChek PT Test: […] A clinical study was conducted at 4 external sites in which venous

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blood results obtained with CoaguChek PT Test were compared to venous citrated plasma results obtained using the laboratory method Innovin (Siemens) [….]

Please note: Other methods that use e.g. Neoplastin Plus or Thromborel S do not correlate as well with the CoaguChek system.

2. Health Care Professionals (HCP) with patients performing self-testing/self-management:
   - Values ≤4.5 INR: Values are valid and can be used without lab comparison
   - Values >4.5 INR: Values should be compared with a laboratory method.

   As mentioned in the method sheet of the test strips, methods using Innovin as Thromboplastin (Siemens) correlate very well with the CoaguChek system.
   You are requested to please **reactively** hand out the attached "patient information letter" at your discretion, if patients use CoaguChek tests strips of the affected lots calibrated against rTF/16.

3. Insurers & Retailers (wholesalers, pharmacies etc.):
   If patients contact you regarding INR results above their therapeutic range, please advise your customer to contact their local Health Care Professional.

Once you have received the new rTF/09 calibrated test strip lots you can return to your usual testing and treatment procedures.

Please complete and return the Acknowledgement Form which accompanies this Field Safety Notice by Sept 5th 2018

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.

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

References:
1) van den Besselaar AMHP, Chantarangkul V, Angeloni F, Binder NB, Byrne M, Dauer R, Gudmundsdottir BR, Jespersen J, Kitchen S, Legnani C, Lindahl TL, Manning RA, Martinuzzo M, Panes O, Pengo V, Riddell A, Subramanian S, Szederjesi A, Tantanate C, Herbel P,

Attachments Consumer Letter

Acknowledgement Form

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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: PFSN18 Deviations of high (>4.5) CoaguChek INR values due to calibration with WHO reference standard rTF/16 SBN-CPS-2018-014
Date: 22/08/2018
Type of Action: Field Safety Corrective Action (FSCA)

Product Catalogue No:	CoaguChek XS PT	04625315019
		04625358019
		04625374190
	CoaguChek PT	06688721019
	CoaguChek XS PT PST	07671679190
		07671687019

System:
CoaguChek® XS
CoaguChek® INRange
CoaguChek® XS Plus
CoaguChek® XS Pro
CoaguChek® Pro II system

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:

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.fsn@roche.com

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

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

Name:

Signed:

Date:

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