

Field Safety Notice

SBN-CPS-2018-014

CPS / Point of Care
Version 2
20-Sep-2018

Deviations of high (>4.5) CoaguChek INR values due to calibration with WHO reference standard rTF/16

Product name	REF-Number	Affected lot Number (only valid up to 4.5 INR)		
CoaguChek XS PT Test (For use with CoaguChek XS, XS Plus and XS Pro meter).	CoaguChek XS PT Test, 6 tests (04625374190)	272167	294947	322640
	CoaguChek XS PT Test, 24 tests (04625358019)	281241	297787	322641
	CoaguChek XS PT Test, 24 tests (04625358172)	286319	297788	322642
	CoaguChek XS PT Test, 24 tests (04625358172)	286320	297790	322643
	CoaguChek XS PT Test, 24 tests (04625358172)	286321	297792	322644
	CoaguChek XS PT Test, 48 tests (04625315019)	286322	297794	330459
	CoaguChek XS PT Test, 48 tests (04625315172)	286323	304971	330460
	CoaguChek XS PT Test, 48 tests (04625315172)	286324	304972	330461
	CoaguChek XS PT Test, 48 tests (04625315172)	294151	304973	330462
	CoaguChek XS PT Test, 48 tests (04625315172)	294942	304974	330463
CoaguChek XS PT PST Test (For use with INRange meter).	CoaguChek XS PT Test PST, 6 tests (07671679190)	294943	304975	334496
	CoaguChek XS PT Test PST, 6 tests (07671687019)	294944	314043	334497
	CoaguChek XS PT Test PST, 6 tests (07671687019)	294945	314047	334498
	CoaguChek XS PT Test PST, 6 tests (07671687019)	294946	314048	
CoaguChek PT Test (For use with Pro II meter)	CoaguChek PT Test, 48 tests (06688721019)	272170	322646	353606
		322039	322647	
		322040	334502	

There may be other affected identifiers that are affected globally. Please contact the product owner if the device is obtained from an overseas dealer.

Bold lot numbers are currently supplied in Singapore.

Type of Action Field Safety Corrective Action

Reason for Version 2 Additional information for clarification. Changes are highlighted in yellow.

Deviations of high (>4.5) CoaguChek INR values due to calibration with WHO reference standard rTF/16

Dear Valued Customer,

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)*

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

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.

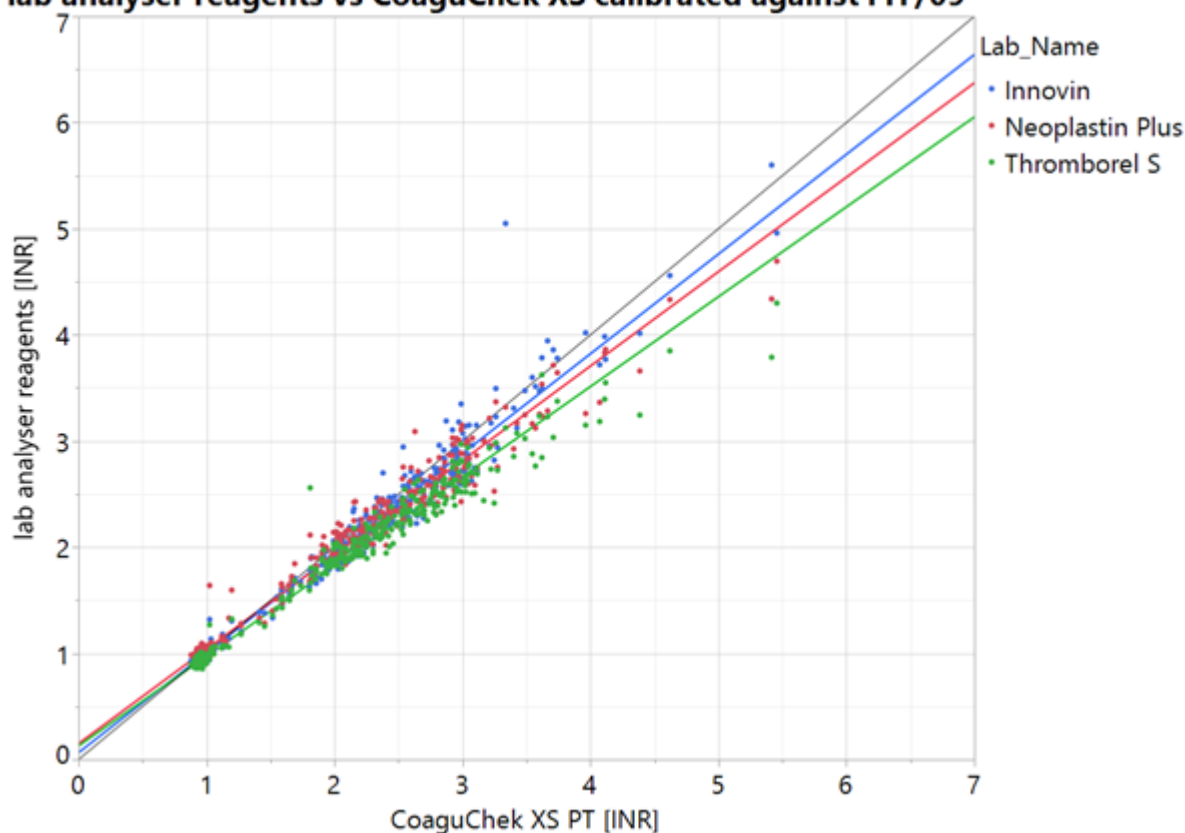
Our findings:

- For values up to 4.5 INR and calibrated to the new (rTF/16) WHO standard (1.5-4.5 INR), a mean difference of +6% was found when we compared in an internal validation study the new CoaguChek test strips against test strips calibrated to the previous (rTF/09) reference WHO standard.
- In our complaint investigation we have seen an unexpected additional increasing positive bias in the upper INR range (> 4.5 INR).

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- Due to these findings, it was decided to limit the use of the currently available CoaguChek (XS PT, XS PT PST, and PT) strips to the range of up to 4.5 INR which is in accordance to the validation of the WHO standard.
- In general, several influencing factors e.g. lot to lot differences, pre-analytics (e.g. sample tubes) can have a significant influence on the comparison of different methods (see graph below).

lab analyser reagents vs CoaguChek XS calibrated against rTF/09



Graph: Roche Diagnostics, External Masterlot calibration study CoaguChek XS PT, 2017

- No deviations have been experienced with the CoaguChek test strips referenced to the previous WHO standard rTF/09. Most laboratory methods are still calibrated against the previous (rTF/09) WHO standard.
- Internal analysis of complaints showed that after therapy changes (change of dosage, additional medication, hold of medication) the frequency of testing was not always adapted. Therefore, we recommend to follow the local medical guidelines regarding an increased testing frequency after therapy changes.

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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.

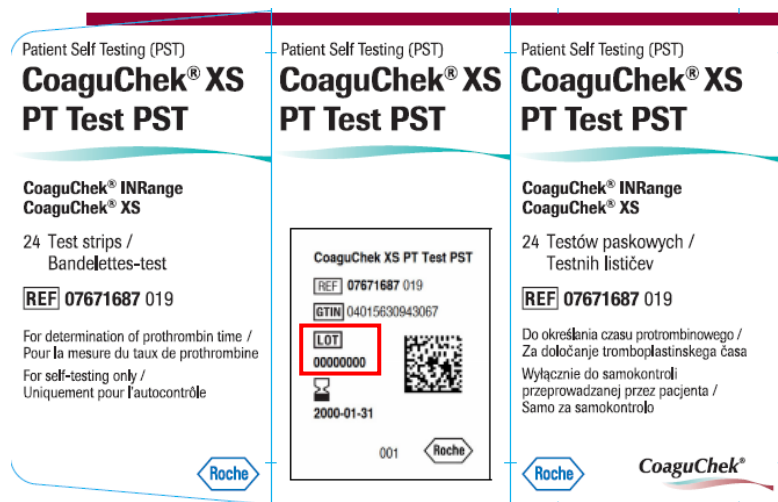
The first test strips re-calibrated to rTF/09 will be available locally by **November 2018** with the following lot no. :

Product	REF-Number	Lot Number
CoaguChek XS PT Test	04625374190 (6 tests)	≥334499
	04625358019 (24 tests)	
	04625358172 (24 tests)	
	04625315019 (48 tests)	
	04625315172 (48 tests)	
CoaguChek XS PT PST Test	07671679190 (6 tests)	≥361433
	07671687019 (24 tests)	
CoaguChek PT Test	06688721019 (48 tests)	≥361433

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

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.

In 2019 as an additional measure the respective CoaguChek test strip method sheets will be updated, with regard to method comparison.

Actions to be taken by the customer/user

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: If values >4.5 INR are measured a comparison measurement shall be performed with a laboratory method. In addition, the testing frequency shall be increased according to local medical guidelines until results in the therapeutic range of that individual are obtained until recalibrated material is available.

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Please note with respect to the impact towards patients on patient self-testing/self-management: All package inserts of CoaguChek test strips used by patients (XS PT/XS PT PST) contain the following advice:

CoaguChek XS PT Test:

"If the measured PT result is unusually high or low repeat the test. If the PT result is still outside the therapeutic range specified by your treating physician, immediately contact your physician and ask for the appropriate (anticoagulant) measures to take in order to reduce risks that could be encountered due to excessive anticoagulation (danger of bleeding) or insufficient anticoagulation (risk of thrombosis)."

CoaguChek XS PT Test PST:

"If the measured result is outside the therapeutic range specified by your treating physician, repeat the test. If the result is still outside the therapeutic range immediately contact your physician and ask for the appropriate (anticoagulant) measures to take."

Therefore, the above mentioned limitation of the measuring range will have only small impact to the current procedure of managing patients performing patient self-testing. The risk of unnecessary Vitamin-K intake due to deviated high INR values (>4.5) is mitigated by the interaction with the physician

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: If values >4.5 INR are measured a comparison measurement shall be performed with a laboratory. In addition, the testing frequency shall be increased according to local medical guidelines until results in the therapeutic range of that individual are obtained until recalibrated material is available.

You are requested to please **reactively** hand out the attached "Customer Letter" at your discretion, if patients use CoaguChek tests strips of the affected lots calibrated against rTF/16.

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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
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