Field Safety Notice

SBN-CPS-2018-014

CPS / Point of Care
Version 1
28-Aug-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) CoaguChek XS PT Test, 24 tests (04625358019) CoaguChek XS PT Test, 24 tests (04625358172) CoaguChek XS PT Test, 48 tests (04625315019) CoaguChek XS PT Test, 48 tests (04625315172)	272167 281241 **286319** 286320 286321 286322 286323 **286324** **294151** 294942 294943 294944 294945 294946	294947 **297787** **297788** 297790 297792 **297794** 304971 304972 304973 **304974** 304975 **314043** **314047** 314048	322640 322641 322642 **322643** 322644 330459 330460 330461 330462 330463 334496 334497 334498
CoaguChek XS PT PST Test (For use with INRange meter).	CoaguChek XS PT Test PST, 6 tests (07671679190) CoaguChek XS PT Test PST, 6 tests (07671687019)			
CoaguChek PT Test (For use with Pro II meter)	CoaguChek PT Test, 48 tests (06688721019)	**272170** **322039** 322040	**322646** **322647** 334502	353606

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

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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 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.

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- 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 locally by **November 2018** with the following lot no. :

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

Table 2: Availability rTF/09 Lots

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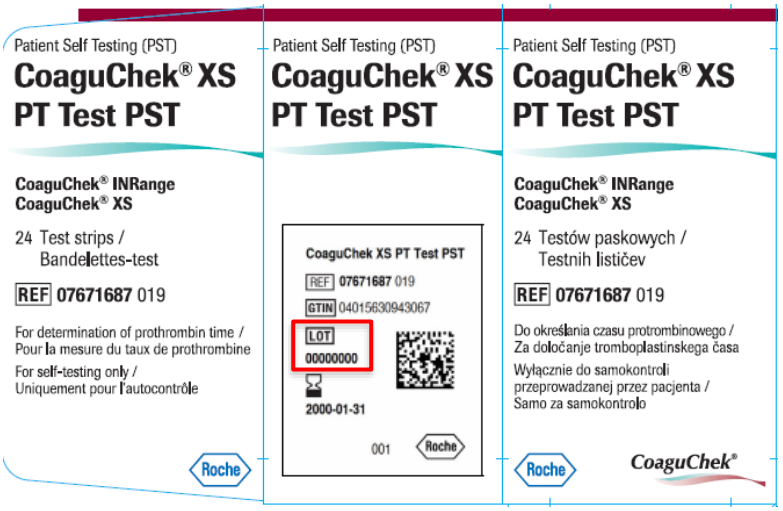
The lot number is printed on the label, which is applied to the test strip box at manufacturing:



*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.

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: 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.

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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: 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 "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
Email: sg.regulatory@roche.com

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, Tripodi A. International collaborative study for the calibration of proposed International Standards for thromboplastin, rabbit, plain, and for thromboplastin, recombinant, human, plain. J Thromb Haemost 2018; 16: 142–9.

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