Recall for Product Correction

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

Date: August 2018 **Bulletin Number: SBN-POC-2018-03** **Roche Reference: SBN-CPS-2018-014**

Affected Product(s):

CoaguChek XS PT Test PST	**07671679190, 07671687019**
CoaguChek XS PT Test	**04625358172, 04625315172**
CoaguChek PT Test	**06688721019**

Affected Lot(s):

CoaguChek XS PT Test PST	**from #272167 up to #334498**
CoaguChek XS PT Test	**from #272167 up to #334498**
CoaguChek PT Test	**from #272170 up to #353606**

System:

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

☐ **Information** ☐ **Information and Action** ☒ **Feedback form mandatory**

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.
- 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

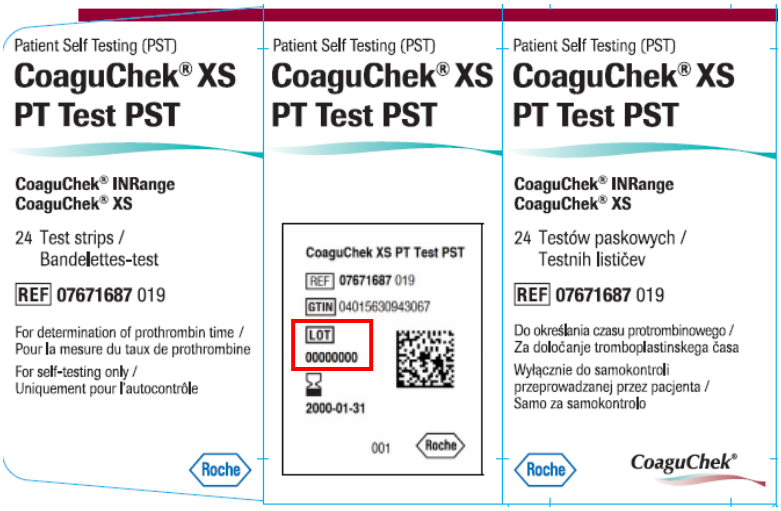
Since a medical risk, due to a possible Vitamin K treatment decision, for INR ranges >4.5 INR, cannot be excluded, it was decided to re-calculate the calibration for upcoming CoaguChek strip lots according to the previous WHO standard (rTF/09). Moreover, the current CoaguChek test strips, calibrated 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 **beginning / mid-October 2018** for the following lot numbers and availabilities:

Product Code	Product Name	Lot Number (Code Key)	Estimated Availability in stock (NZ)
07671679190	CoaguChek XS PT Test PST, 6 tests	≥334499 (S_344)	Oct 2018
07671687019	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	Nov 2018
04625358172	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	Oct 2018
04625315172	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	Oct 2018
06688721019	CoaguChek PT Test, 2 x 24 tests	≥361433 (S_062)	Nov 2018

Table 2: Availability rTF/09 Lots

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.

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/Pharmacy:
   - 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 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 don´t 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. Wholesalers, Retailers
   Please forward this notice and/or the attached “patient information letter” (where applicable) to all your affected customers.
   If patients contact you regarding INR results above their therapeutic range, please advise your customer to contact their local Health Care Professional.

4. All customers:
   - Read and familiarise all staff working with these Coaguchek products of the potential risk and follow the actions recommended in this letter.
   - Please retain this notice in a prominent place in your organisation until the new test strip lots are in use.
   - Please complete the attached acknowledgement form and return to Roche Diagnostics NZ by fax or email as soon as possible.

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

Please note with respect to the impact towards patients on patient self-testing:
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.

Please note with respect to the impact towards patients on patient self-management:
Patient self-managers are trained to contact their physicians as soon as they measure values above 4.5 INR. Therefore, patients can continue using their CoaguChek device as before with one limitation: When they measure values above 4.5 INR, they should ask their physician for a parallel testing with a laboratory method in order to decide on further medication. As a result, the above mentioned limitation of the measuring range (>4.5) will have only small impact to the current procedure of managing patients performing patient self-management. The risk of unnecessary Vitamin-K intake due to deviated high INR values (>4.5) is mitigated by the interaction with the physician.

Communication of this Product Correction

This notice must be passed on to all those who need to be aware within your organisation or to any organisation/individual where the potentially affected devices have been distributed/supplied.

Please transfer this notice to other organisations/individuals on which this action has an impact.

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

This action is being taken in consultation with Medsafe, Ministry of Health (Ref #23547)

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

Kind Regards,

Keryn Smith
Product Manager, Point of Care
Roche Diagnostics

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Auckland
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Email : keryn.smith@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.

Acknowledgement of In Vitro Diagnostics Device Notification

Please complete this form and return to: Roche Diagnostics NZ
Attention: Alison Rhodes

Recall for Product Correction

I have read and understood the instructions related to the following product**:**

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

Returning Organisation:

Name:

Address:

Telephone Number:

Fax:

Details of person making the declaration

Name:

Position:

Date:

Signature:

Fax to: 09 276 8917 or email to: keryn.smith@roche.com