Consumer Letter

(CoaguChek XS PT Test PST, CoaguChek XS PT Test, CoaguChek PT Test)

Urgent Field Safety Notice

<Enter address here>

Location, Date

We are writing to inform you about an issue concerning your CoaguChek system and test strips. Please read this information carefully.

Dear Customer,

In order to ensure that your CoaguChek values can be compared to values of other devices (e.g. laboratory systems, Point-of-Care systems in your GP office/Coagulation clinic) we calibrate our test strips against the standard from the World-Health-Organization (WHO). This standard was renewed in 2016. Although manufacturers are not obliged to standardize against the newest standard, as a pioneer for the monitoring of so called “Blood Thinners” Roche Diagnostics decided to do so.
Roche Diagnostics has received an increase in complaints regarding deviations against laboratory methods during the last weeks. Therefore, we initiated an in-depth analysis in order to determine the reasons for the observed differences.

The results of the analysis were:

- For values between 0.8 and 4.5 INR: No significant differences are seen and your CoaguChek is reliable.
- For values above 4.5 INR: Greater than expected deviations to the laboratory methods were seen.

What does that mean to me as a patient self-tester?

Each patient has a so called “therapeutic range” she/he should be compliant to. The therapeutic range is defined by the indication you are receiving “Blood Thinners” (e.g. Atrial fibrillation, heart valve, VTE etc.) for. None of the medically used therapeutic ranges exceed the above mentioned value of INR 4.5. Therefore, your system is delivering reliable results for your relevant therapeutic range.

[COUNTRY ACTION: You are allowed to adopt the letter to your country specific situation, i. e. to insert or to remove the green text blocks below ([For countries performing patient-self testing] and [For countries performing patient-self management]) according to local procedures.

[For countries performing patient-self testing] However, according to the package insert you should contact your physician every time you are out of your therapeutic range:

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 limitation caused by this issue should be minimal, except of the fact that you should ask your health care professional for a laboratory cross-check for values above 4.5 INR.

[For countries performing patient-self management] You can continue using your CoaguChek device as you have done before with one limitation: As soon as you measure values above 4.5 INR, please contact your health care professional and ask for parallel testing with a laboratory method in order to decide on your further medication.

Which are the affected test strip lots?

The following lot numbers may be used up to an INR of 4.5. If the values exceed an INR of 4.5, please contact your health care professional.

Product	REF-Number	Lot Number (only valid up to 4.5 INR)
CoaguChek XS PT Test	04625315xxx* 04625358xxx* 07797826160 04625374xxx*	#272167 – 334498
CoaguChek XS PT PST Test	07671679190 07671687xxx* 07762798xxx*	#272167 – 334498

Table 1: Lot numbers affected by the limitation

[COUNTRY ACTION Note: xxx* refers to the different language versions → *countries: Please insert your respective SPV number, remove* and the remaining REF numbers.]*

Will this limitation be forever?

No – Roche Diagnostics has already started to produce new CoaguChek test strips, which will not have this limitation anymore and those strips will be available **beginning / mid of October 2018** as follows:

REF-Number	Product Name	Lot Number (Code Key)	Availability on stock (Mannheim)
07671679190	CoaguChek XS PT Test PST, 6 tests	≥334499 (S_344)	CW 40
07671687003	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 40
07671687016	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 40
07671687019	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 42
07671687070	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 40
07671687170	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 42
07762798003	CoaguChek XS PT Test PST, 2 x 24 tests	≥334499 (S_344)	CW 40
07762798016	CoaguChek XS PT Test PST, 2 x 24 tests	≥334499 (S_344)	CW 40
04625374160	CoaguChek XS PT Test, 6 tests USA	≥334499 (S_344)	CW 42
04625374190	CoaguChek XS PT Test, 6 tests International	≥334499 (S_344)	CW 40
04625358003	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625358016	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625358019	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 40
04625358070	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625358170	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42

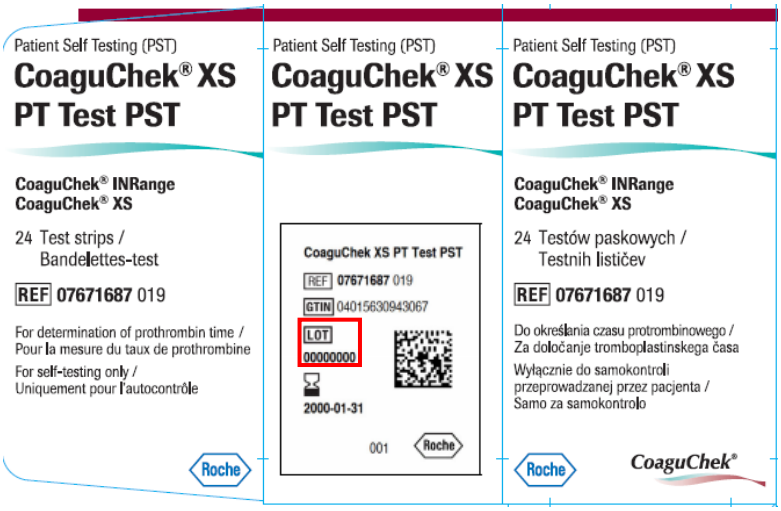
04625358172	CoaguChek XS PT Test , 24 tests	≥334499 (S_344)	CW 40
07797826160	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625315003	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 42
04625315016	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 40
04625315019	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 40
04625315070	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 42
04625315160	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 42
04625315172	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 40

Table 2: Availability of new lots

[COUNTRY ACTION. *Please remove REF number not available in your country]*

How do I recognize which CoaguChek test strip lot/code chip number I have?

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



LOT-Number

The code chip number is printed on the code chips (as shown below).

Code Chip Number

Who can I call for more advice?

Please contact your Roche Diagnostics Customer Care Center under the following number: [COUNTRY ACTION: insert number]

We apologize for any inconvenience caused by this issue to you.

Sincerely,

[COUNTRY ACTION: Insert signatures and company name]

Urgent Field Safety Notice

SBN-CPS-2018-014

CPS / Point of Care
Version 1
Aug-2018

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

Product Name / GMMI	CoaguChek XS PT Test PST	07671679xxx, 07671687xxx, 07762798xxx
	CoaguChek XS PT Test	04625374xxx, 04625358xxx, 07797826xxx 04625315xxx
	CoaguChek PT Test	06688721xxx
System	CoaguChek® XS system CoaguChek® INRange system CoaguChek® Vantus system CoaguChek® XS Plus system CoaguChek® XS Pro system CoaguChek® Pro II system	
Production Identifier (Lot No./Serial No.)	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
SW Version	N/A	
Type of Action	Field Safety Corrective Action (FSCA)	

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)*

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

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:

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

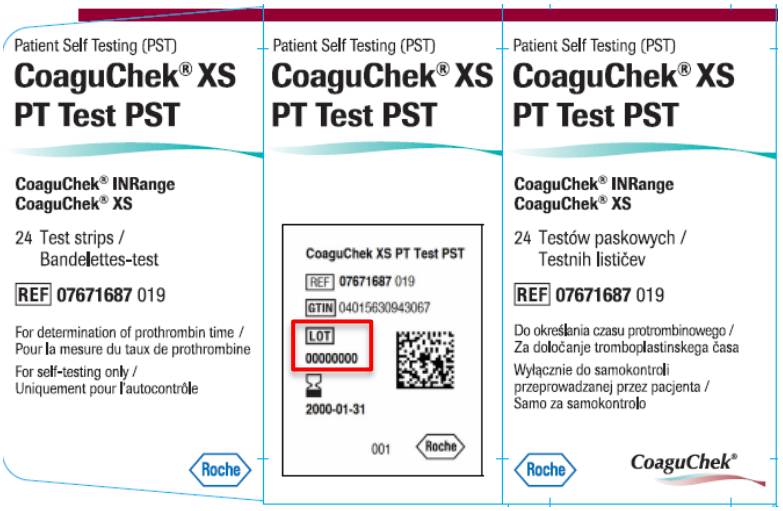
REF-Number	Product Name	Lot Number (Code Key)	Availability on stock (Mannheim)
07671679190	CoaguChek XS PT Test PST, 6 tests	≥334499 (S_344)	CW 40
07671687003	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 40
07671687016	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 40
07671687019	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 42
07671687070	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 40
07671687170	CoaguChek XS PT Test PST, 24 tests	≥334499 (S_344)	CW 42
07762798003	CoaguChek XS PT Test PST, 2 x 24 tests	≥334499 (S_344)	CW 40
07762798016	CoaguChek XS PT Test PST, 2 x 24 tests	≥334499 (S_344)	CW 40
04625374160	CoaguChek XS PT Test, 6 tests USA	≥334499 (S_344)	CW 42
04625374190	CoaguChek XS PT Test, 6 tests International	≥334499 (S_344)	CW 40
04625358003	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625358016	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625358019	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 40
04625358070	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625358170	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625358172	CoaguChek XS PT Test , 24 tests	≥334499 (S_344)	CW 40
07797826160	CoaguChek XS PT Test, 24 tests	≥334499 (S_344)	CW 42
04625315003	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 42
04625315016	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 40
04625315019	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 40
04625315070	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 42
04625315160	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 42
04625315172	CoaguChek XS PT Test, 2 x 24 tests	≥334499 (S_344)	CW 40
06688721003	CoaguChek PT Test, 2 x 24 tests	≥361433 (S_062)	CW 42
06688721016	CoaguChek PT Test, 2 x 24 tests	≥361433 (S_062)	CW 42
06688721019	CoaguChek PT Test, 2 x 24 tests	≥361433 (S_062)	CW 42
06688721070	CoaguChek PT Test, 2 x 24 tests	≥361433 (S_062)	CW 42
06688721170	CoaguChek PT Test, 2 x 24 tests	≥361433 (S_062)	CW 42

Table 2: Availability rTF/09 Lots

[COUNTRY ACTION: *Please remove REF numbers not available in your country. You are allowed to modify the column "Availability on stock (Mannheim)" according to your local delivery schedules.]*

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

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.

[COUNTRY ACTION: If you are not allowed by your local legislation, the following part can be deleted]

For countries selling directly to patients:

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.

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.

   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 […]

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

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. 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.

[COUNTRY ACTION: You are allowed to adopt the letter to your country specific situation, i. e. to insert or to remove the green text blocks below ([For countries performing patient-self testing] and [For countries performing patient-self management]) according to local procedures.

[For countries performing patient-self testing]

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.

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

[For countries performing patient-self management]

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 Field Safety Notice (if appropriate)

<If the recipient needs to forward the FSN to additional organizations/individuals then one or more of the following statements may be included:

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

Please transfer this notice to other organizations/individuals on which this action has an impact. (If appropriate).

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

The following statement is mandatory in FSNs for EEA countries but is not required for the rest of the World:

Include if applicable: The undersigned confirms that this notice has been notified to the appropriate Regulatory Agency.

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

<closing salutations>,

Contact Details

To be completed locally:
Name
Title
Company Name
Address
Tel. +xx-xxx-xxxx xxxx
Email name@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,

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

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.