Instrumentation Laboratory
A Werfen Company

ROTEM *delta* r ex-tem® Assay Field Correction

1. Correction/Removal Number: CAPA 04/17
   BfArM case number: 02553/17

   Manufacturer: Tem Innovations GmbH, Martin-Kollar Strasse, 13, Munich, Germany 81829, Registration Number 3005792925

   Initial Importers: **JASIKA d.o.o.** (Distributor), Remetinecka cesta 115, 10020 Zagreb, Croatia

   Person Responsible for conducting the field correction:
   Dr. Volker-Joachim Friemert
   Tem Innovations GmbH
   Instrumentation Laboratory
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   81829 Munich, Germany

2. Product Name and Use:
   Trade name: r-EXTEM Assay for ROTEM® delta Thromboelastometry System
   Classification name: Multipurpose for In-Vitro Coagulation Studies,

   Intended Use: For *in vitro* diagnostic use only.
   r ex-tem® is a ROTEM® system reagent for the assessment of the extrinsic coagulation pathway and its interaction with thrombocytes in citrated blood. It is always used in combination with star-tem®.

3. Part Numbers and Lot Numbers:
   Art.no.: 503-05, ex-tem®
   Lot.no.: 21734044, manufac. date: 2016-09, expiry date: 2017-10

4. Accounting for all affected product:
   Art.No. 503-05, ex-tem®
   Lot.No.: 21734044
   Total number produced and shipped: 3 boxes x 10 vials on 2017-01-17

5. Reason for the Field Correction:
   An unusual increase of CT values in patient samples as well as ROTROL control material when using r ex-tem reagent, art.no. 503-05, batch 21734044 was reported by Tem customers 4-6 weeks after the release of this r ex-tem batch.

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St.-Nr.: 143/185/60952 V001

First tests at Tem in January using retained samples have not confirmed the strong degradation of the material as reported by customers. However further investigation were performed in February. It was shown by increased CT values that since release in November / December 2016, the performance of r ex-tem batch 217334044 have been changing. The CT with whole blood from normal donors became longer by approx. 10 – 12 s, from a mean of 62 s to a mean of 72 – 74 s. In addition, approx. 10% of all whole blood measurements with retained r ex-tem, shown in this report, were outside the reference range of up to 79 s. All other parameters or performance (heparin neutralization, temperature stress robustness, sensitivity) remain unchanged.

Further increase of CT values as shown by customer samples was not found with retained samples. So additional worsening of the performance due to transport to or storage at customers cannot be excluded.

All ROTROL CTs reported here were close to the upper limit of the target ranges. Considering that all the tests were performed with retained r ex-tem samples, which performed better than the samples returned from customers, additional damage to the reagent would have led to ROTROL CTs outside the target range. This was reported by the customers and can be reproduced in the vial-to-vial study. Consequently, a r ex-tem vial that would have led to CTs outside the reference range for normal healthy donors would also have led to a ROTROL CT outside the target range. In this case the customer's failed QC would have provoked not to use that r ex-tem anymore for patient testing.

A greater than usual vial to vial variability was detected with occasional vials (approx. 5 % based on the precision data) showing extremely prolonged CTs (>200 s). Again, this result was also detected with ROTROL thereby attenuating the risk of false interpretation of patient results.

Because it cannot be excluded that degradation will continue, it is advised to inform all customers who have received this batch, that its use can lead to longer CTs with patient blood and therefore should not be used anymore.

6. Risk-Assessment (Injuries and Health Hazard Analysis):
   The risk of wrong decision-making in 0.7% (1:143, W3, probable) of the patient population despite an adequate customer quality control and following an evidence based bleeding management algorithm is high and result in combination with the severity of TEAs (S2-S3, moderate to critical) in a high risk level.
   Accordingly, all customers who have received the r ex-tem lot 21734044 have to be informed about potentially increased EXTEM CT results in blood samples analyzed with this lot. The sale of this lot has to be stopped immediately, and already delivered reagents have to be recalled.
   See "2017-03-12_Signed_Medical Statement kgo_Recall r ex-tem Lot 21734044"

7. Customer Communications:
   The customers affected will be notified by notification letter (see attachment "Important Customer Information ref 000503-05 lot 21734044" with a confirmation reply form to be sent back to the importer.
   Distributors will be notified by the notification letter and be instructed to inform their own users in local languages.

8. Recall Strategy:
   All affected customers were notified by sending a notification letter within 7 days Notifications were sent via mail and email on March 14, 2017. Customers were told to stop using the product and call for replacement product. Product will be replaced free of charge.

   Effectiveness checks:
   The number of customer confirmation replies will be monitored on a weekly basis.

9. Recall Classification:
   We classify the recall as FSCA reportable (MedDev 2.12/1 rev 7), because there is no situation in which the use of the batch ex-tem reagent, 21734044 are likely to cause death or dramatic health consequences. No Medical Device Reports will be submitted.

10. Timetable for Completion of the Field Correction:
    - Customer notification until 2017-03-14.
    - Return of all confirmation letters until 2017-03-31.

11. Further investigations and Corrective Actions:
    Root cause analysis on behavior of ex-tem reagent. Additional quality checks during release process.

12. Timelines for further Corrective Actions:
    - To be completed latest on July 31, 2017

Munich, 2017-03-14

Dr. Volker-Joachim Friemert
Tem Innovations GmbH
Instrumentation Laboratory

Addendum:
MEDDEV notice 02553_17.pdf
Distributor_information_r ex-tem, lot 21734044.pdf
Important Customer Information ref 000503-05 lot 21734044.pdf
2017-03-12_Medical Statement_Recall r ex-tem Lot 21734044
Package insert "r ex-tem_V0004"