# PENTAPHARM GmbH

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# r ex-TEM®

# Instructions for Use

## Intended Use:

For *in vitro* Diagnostic Use Only

r ex-TEM® is a ready to use liquid ROTEM® system reagent for the examination of the extrinsic coagulation system and its interaction with thrombocytes in citrated blood.

## Reagents:

**Product Name:** r ex-TEM®
**Reference Number:** REF 503-05
**Package Size:** 10 x 1 vials r ex-TEM® for 10 x 10 tests

**Constituents:**
Recombinant tissue factor and phospholipids, heparin inhibitor, preservatives and buffer in small glass vials.

**Preparation of the ready-to-use reagent:**
The reagent is ready-to-use after being mixed carefully but thoroughly.

**Storage and Stability:**
Store at +2 to +8 °C. The unopened reagent is stabl e until the expiry date indicated on the label.

**Stability after Initial Use:**
Opened vials must be used within 8 days after opening. Always enter the expiry date of the opened reagent in the field intended for this on the reagent vial. Store at +2 to +8 °C. Avoid contamination and always close the vials again immediately after each use to avoid evaporation.

**Additional Material:**
ROTEM® device; blood collection tubes (~0.106 M or ~0.129 M sodium citrate) for coagulation testing; cup and pin pro (measurement cells; REF 200011); pipette tips (REF 400041 / REF 400040), star-TEM® reagent (REF 503-01 or REF 503-10) for recalcification.

**Specimen:**
Freshly prepared citrated blood. Carefully mix 9 vol. of venous blood with 1 vol. sodium citrate (~0.106 M or ~0.129 M sodium citrate) (1, 2).

## Method:

**Analytical Principle:**
r ex-TEM® contains an optimized concentration of tissue factor and phospholipids which is used for a mild extrinsic activation of the coagulation system.
By adding r ex-TEM® to the sample, a standardised activation of extrinsic clotting cascade is triggered. The sample is recalcified with star-TEM®. In the thromboelastometric measurement, after addition of the reagents to the sample, the clotting process is started and continuously monitored by the ROTEM® analyser. There is an automatic analysis and documentation of the Clotting Time (CT), Clot Formation Time (CFT), the Maximum Clot Firmnes (MCF) and further parameters. Using these parameters, the clot activation, clot formation, clot polymerisation, clot stability and fibrolysis can be registered as well as the inhibition of the clotting cascade by anti-coagulants, hyperfibrinolysis, fibrin deficiency, fibrin polymerisation defects, thrombocytopenia and defects in platelet function (3, 4).
Clotting activation with r ex-TEM® is more rapid than with in-TEM®. Deviation of the parameters from the established reference ranges indicate a potential coagulation disturbance.

**Measurement Calculation:**
The ROTEM® device offers numerous parameters. Their mathematical and medical backgrounds are explained in the ROTEM® user manual.

**Limitation of the Procedure:**
Always use freshly prepared citrated blood samples. In tests of blood samples from healthy subjects using r ex-TEM®, sample storage time has been found not to influence the parameters measured for up to 4 hours after blood sampling. Store citrated blood at room temperature, NOT at +2 to +8 °C (5). Before analysis, bring citrated blood samples to 37 °C and, immediately prior to use, mix carefully and thoroughly. Avoid foaming! Acetylsalicylic acid, clopidogrel and von Willebrand Factor have no detectable influence in this method.
Abnormal patterns in the EXTEM test can also be caused by the influence of anti-coagulants such as hirudin or other direct thrombin inhibitors. The effect of oral anti-coagulants (coumarin) has a secondary influence on the results compared with the prothrombin time.
Local, non generalized fibrinolysis may be not detectable.

**Quality Control:**
Use of control materials for regular quality control is recommended (e.g. REF 503-24 ROTROL N / REF 503-25 ROTROL P). Further information may be found in the respective instructions for use of these materials.

**Expected Values:**
The reference ranges previously established for the EXTEM test using the liquid ex-TEM® reagent (REF 503-03) have been verified and confirmed for the r ex-TEM® reagent (REF 503-05): CT 38-79 sec, CFT 34-159 sec, α-angle 63-83 and MCF 50-72 mm. These values are for orientation only. They should be used with caution! They are not binding and may vary from lab to lab, depending on blood sampling technology and other pre-analytical factors. It is recommended to confirm these data by studying an own reference group in each hospital/laboratory.

**Pathological Results:**
Pathological results are often obtained with EXTEM under the following clinical conditions:

- → Serious deficiency of coagulation factors (congenital or acquired) or influence of vitamin K antagonists. In case of a very high dose of oral anti-coagulant therapy, it is possible to observe an extended CT. However, EXTEM shows considerably lower sensitivity compared with prothrombin tests.
- → Fibrinogen deficiency and/or fibrin polymerisation disorders (discrimination from platelet disorder possible using FIBTEM, refer to package insert fib-TEM®)
- → Platelet function disorders and/or thrombocytopenia (discrimination from fibrinogen disorder possible using FIBTEM, refer to package insert fib-TEM®)
- → Hirudin, argatroban or other direct thrombin inhibitors (in high dosage)
- → Dilution effects (dilution coagulopathy)
- → Hyperfibrinolysis (confirmation possible with APTEM, refer to package insert ap-TEM®)

**Warnings and Precautions:**

For *in vitro* diagnostic use only.
For professional use only.

Harmful if swallowed (R 22).
Wear suitable gloves (S 37).

Human blood should be handled with care, following the precautions recommended for bio-hazardous material (6).

## Procedure (EXTEM assay):

A. Mix the reagents carefully before use. Let the reagents reach room temperature prior to use (approx. 15 minutes).
B. Prepare a citrated blood specimen as recommended. Preheat the citrated blood if possible to measuring temperature.
C. NOTE: Follow the ROTEM® user manual for correct operation of the device.
D. Select a channel for measurement.
E. Remove cup & pin (measurement cell) together from the box and place the pin upright in the cuvette firmly onto the measurement axis (avoid touching it).
F. Insert the cup into the pre-warmed cup holder and press it firmly into place with the MC-rod (REF 400045).

→ **Automatic Pipetting:**
Follow each on-screen instruction when performing the EXTEM test using the automatic pipette.

→ **Manual Pipetting:**
Perform pipetting in a pre-warmed cup in the pre-warmed cup holder in the following sequence:

1. 20 µl star-TEM® reagent.
2. 20 µl r ex-TEM® reagent.
3. 300 µl citrated blood (pre-warmed; with new pipette tip).
4. Begin the measurement with the appropriate command (e.g. "START (MANUAL)") in the desired pre-selected channel.
5. Mix the sample and reagent by aspirating a 300 µl volume into the pipette once and slowly dispensing it.
6. Finally, place the cup holder containing the sample mixture carefully and immediately on the appropriate channel.
7. Stop the measurement at the desired time, remove the sample and dispose of it in conformity with local regulations.
8. The channels may then be cleared for the next measurement using the appropriate command.

## Performance Data:

**Precision:**

| | | CT CV (%) | CFT CV (%) | α-angle CV (%) | A 20 CV (%) |
|---|---|---|---|---|---|
| ROTROL N | Day to day[1] | 7 | / | 1 | 4 |
| ROTROL P | Day to day[1] | 8 | / | 2 | 3 |
| Blood samples | Inter channel[2] | 5 | 3 | 1 | 1 |
| Blood samples | Inter device[3] | 9 | 4 | 1 | 1 |

[1] Duplicate measurement each over 20 days
[2] Comparison of the 4 channels of a device
[3] Comparison of 2x4 channels of 2 independent devices

Blood samples from healthy donors, ROTROL N or ROTROL P were used for the measurements.

**Heparin responsiveness:**
r ex-TEM® contains a heparin inhibitor and is therefore largely insensitive to heparin. In *in vitro* experiments, addition of up to 5 IU/ml of unfractionated heparin to whole blood did not show any influence on the EXTEM test results.

**Bibliography:**


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thromboelastometry ROTEM®
The bleeding management system


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