

Instructions for Use

Intended Use:

star-TEM® is a ready-to-use liquid ROTEM® system reagent for recalcifying citrated blood or plasma. Recalcified blood or plasma will be analysed at NATEM using the ROTEM® analyser or using the activated tests INTEM and EXTEM.

Reagents:

Product Name:	star-TEM® 10	star-TEM® 20
Reference Number:	REF 503-01	REF 503-10
Package Size:	10 x 1 vials star-TEM® for 10 x 10 tests.	10 x 1 vials star-TEM® for 10 x 20 tests.

Constituents:
0.2 mol/l CaCl₂ in HEPES buffer pH 7.4 and 0.1% Na acid in 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 stable 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 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 (measurement cells; REF 700005 / REF 400050); pipette tips (REF 400041 / REF 400040 / REF 400044), if required activator such as in-TEM® (REF 503-02) or ex-TEM® (REF 503-03).
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:
star-TEM® contains an optimized amount of calcium chloride and is used for the recalcification of citrated blood for the thromboelastometric measurement (ROTEM®) (3,4). By adding star-TEM® to citrated blood the clotting process is started and continuously monitored by the ROTEM® analyser. There is an automatic calculation and documentation of the Clotting Time (CT), Clot Formation Time (CFT), the Maximum Clot Firmness (MCF) and further parameters. By these parameters total haemostasis through the clot activation, clot formation, clot polymerisation, clot stability and fibrinolysis can be registered. 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, sample storage time has not been found to influence the parameters measured for up to 4 hours (with EXTEM, INTEM) or 30 min. (with NATEM) 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 to eliminate storage sedimentation. Avoid foaming!
star-TEM® is mainly used as a trigger reagent. For further restrictions please refer to the package insert of the respective activator reagent.
Aspirin, clopidogrel and von Willebrand Factor have a very weak influence in the NATEM method.

Quality Control:
Use of control materials for regular quality control is recommended (e.g. REF 503-21 RO-TROL N / REF 503-24 ROTROL N / REF 503-25 ROTROL P). Further information may be found in the respective instructions for using these materials.

Expected Values:
Following provisional reference ranges have been obtained in blood samples from healthy Central European blood donors in the NATEM test with the star-TEM® on the ROTEM® (n=76): CT 300-1000 sec, CFT 150-700 sec, α-angle 30-70° and MCF 40-65 mm. For reference ranges for other tests please refer to the package inserts of the respective test. These values are for orientation only! They are not binding and may vary from lab to lab depending, as known from other clotting tests, 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 NATEM under the following clinical conditions:
→ Deficiency of coagulation factors (congenital or acquired)
→ Fibrinogen deficiency and / or fibrin polymerisation disorders (differentiation to platelet disorder possible with FIBTEM, refer to package insert fib-TEM®)
→ Platelet function disorders and / or thrombocytopenia (differentiation to fibrinogen disorder possible with FIBTEM, refer to package insert fib-TEM®)
→ Anti-coagulants: Heparin, LMWH, pentasaccharide, Hirudin, argatroban or other direct thrombo inhibitors (in high dosage)
→ Dilution effects (dilution coagulopathy)
→ Hyperfibrinolysis (confirmation possible with APTM, refer to package insert ap-TEM®)

Research applications:
Information on the use of the star-TEM® reagent in combination with native blood for research purposes can be requested from Pentapharm GmbH.

Warnings: For in vitro diagnostic use only
Precautions:
Human blood should be handled with care, following the precautions recommended for bio-hazardous material (6).

Procedure (NATEM assay):

- A. Mix the reagents carefully before use. Let the reagents reach room temperature prior to use (approx. 15 minutes for reagents from the refrigerator).
- B. Prepare a citrated blood specimen as recommended. Preheat the citrated blood to measuring temperature.
- C. NOTE: Follow the ROTEM® user manual for correct operation of the device .
- D. Choose a channel for measurement.
- E. Remove cup & pin (measurement cell) together from the pack and place the pin (stamp) upright in the cuvette firmly on to the measurement axis (It is essential not to touch it).
- F. Insert the cup (cuvette) in the pre-warmed cuvette holder and press it firmly into place with the MC-rod (REF 100017).

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

- **Manual Pipetting:**
Perform pipetting in a pre-warmed cuvette in the pre-warmed cuvette holder in the following sequence:
1. 20 µL star-TEM® reagent.
 2. 300 µL citrated blood (pre-warmed; with new pipette tip).
 3. Begin the measurement with the appropriate command (e.g. manual) in the desired pre-selected channel.
 4. Mix the sample and reagent by aspirating a 300 µL volume into the pipette once and slowly dispensing it.
 5. Finally, place the cup holder containing the sample mixture carefully and immediately on the appropriate channel.
 6. Stop the measurement at the desired time, remove the sample and dispose of it in conformity with local regulations.
 7. The channels may then be released for the next measurement using the appropriate command.

Performance Data:

Precision:

	CT VC (%)	CFT VC (%)	α-angle VC (%)	A10 VC (%)	MCF VC (%)
Day to day ¹	<13	<17	<2	<6	<5
Inter lab ²	15	21	3	3	3

¹ 1 measurement each over 10 days on one device
² Data from 3 centers
Blood samples from healthy donors or ROTROL N were used for the measurements.

Heparin responsiveness:
NATEM is highly sensitive to heparin. A use of the test in heparinised samples is only recommended to a limited extent.

Bibliography:

- (1) NCCLS Document H3-A4 Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture Fourth Edition; Approved Standard (1998)
- (2) DIN 58905-1, Blutentnahme: Teil 1: Gewinnung von venösem Citratplasma für hämostaseologische Analysen, Blutgerinnungsstudien mit der Thromboelastographie, einem neuen Untersuchungsverfahren. Härtel, H.: Klin. Wochenschrift 1948; 26: 577-583
- (4) Thromboelastographic Coagulation Monitoring during Cardiovascular Surgery with the ROTEM Coagulation Analyser, Calatzis, A. et al.: Management of Bleeding in Cardiovascular Surgery edited by Roque Pifarre; Hanley & Belfus, Inc. Philadelphia, PA, 2000
- (5) NCCLS Document H21-A2. Collection, transport, and processing of blood specimens for coagulation testing and performance of coagulation assays, 3rd ed. Approved Guideline 1998
- (6) Biosafety in Microbiological and Biomedical Laboratories, U.S. Department of Health and Human Services, Washington 1993 (HHS publication No. (CD) 93-8395)

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2004-03
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