Fact Sheet

How to understand, verify and determine aPTT reference intervals

The activated partial thromboplastin time (aPTT) is a global coagulation assay. A prolongation of the aPTT clotting time indicates an abnormality of the intrinsic and final coagulation pathway.

Clinical relevance

- Monitoring of therapy with unfractionated heparin (UFH)
- Indicating Hemophilia A, B and C
- Indicating Coagulation factor inhibitors
- Indicating Phospholipid antibodies (lupus anticoagulants)

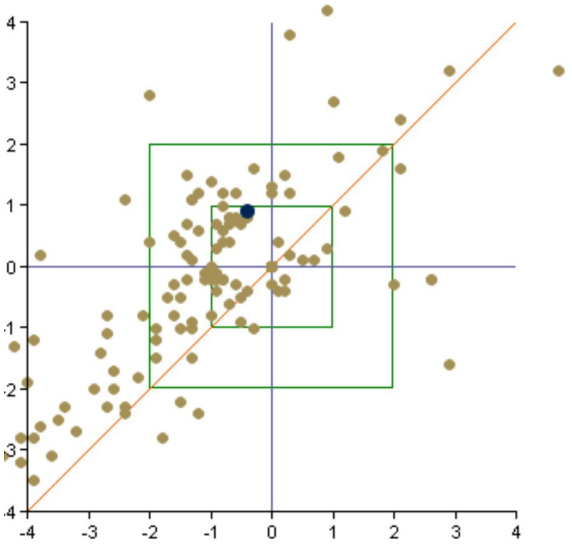
aPTT results are reported in seconds. Until now, there is no global standard e.g. by the WHO or international societies. Thus, the results are specific to the aPTT reagent of a manufacturer.

Variations of aPTT assays of the manufacturers

Manufacturers utilize different compositions for their aPTT assays. There are various activators applied, e.g. ellagic acid, kaolin, micronized silica or different phospholipid concentrations and sources, e.g. rabbit brain cephalin, soy bean phospholipid extract, or synthetic phospholipid mixtures.
Additionally, aPTT assay variants are designed for specific diagnostic purposes, e.g. for a high/low factor or lupus anticoagulants sensitivity. This results in a variation of sensitivity to aPTT-characteristic influences.

Reflection in results of ring-trials

The results of the various aPTTs of ring-trial participants are scattered broadly in the Youden Diagram:



Results of the external quality program ESfEQA (European Society for External Quality Assessment) 2020

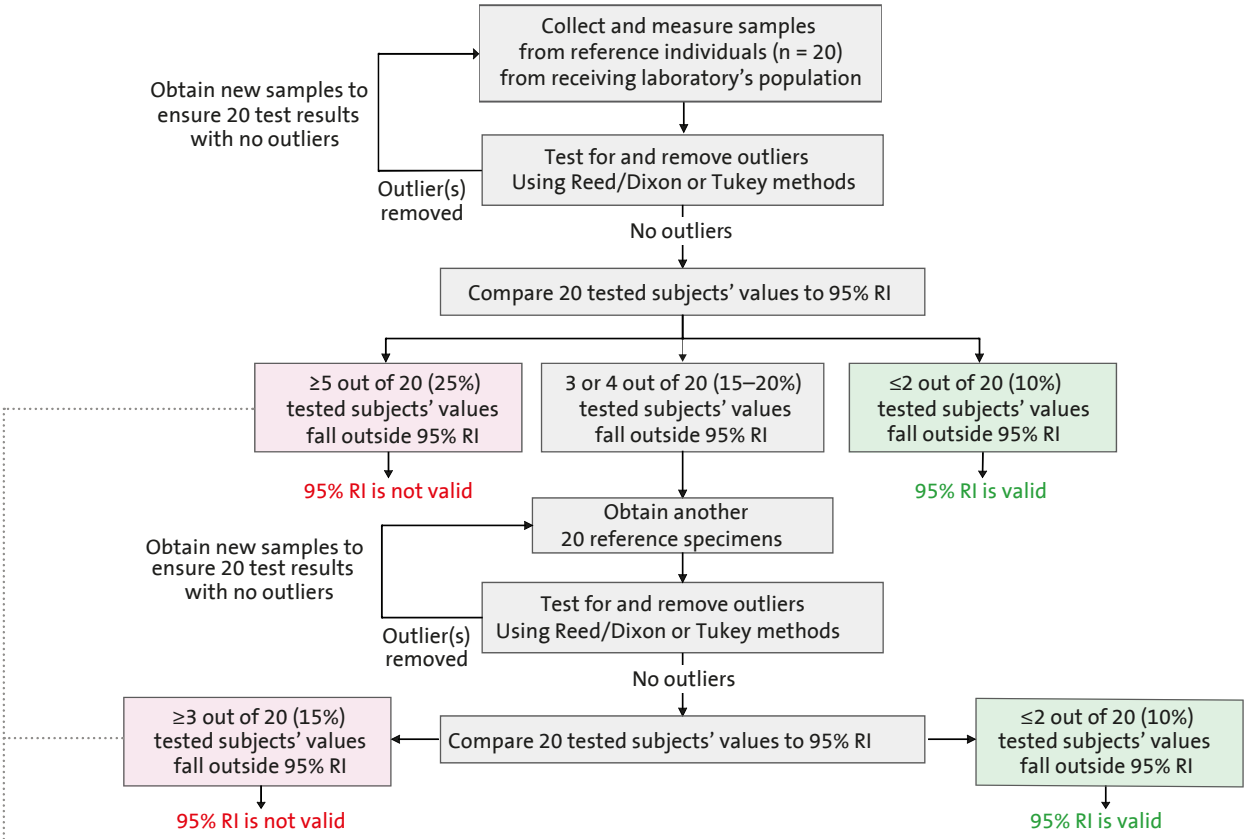
This aPTT-specific background comes on top to the regular diagnostic variances in a laboratory, as the population, equipment, instrument and reagent lot used. Hence, it is especially important that every laboratory establishes its own reference range or at least verify the reference range provided by the manufacturer.

Fact Sheet

Verification and close approximation of aPTT reference intervals

Verification of a reference interval (RI) acc. to CLSI guideline EP28-A3c22[1,2]

After confirmation that the preanalytical factors, analytical factors, and local populations are consistent with the conditions used for the respective reference range the recommended procedure can be applied. If these conditions differ substantially, the receiving laboratory should consider developing its own reference intervals.



Close approximation to reference interval with ≥20 individuals acc. to CLSI Guideline H47-A2[3]

If the reference intervals (RI) cannot be verified, a close approximation may be determined

« **7.10 Reference intervals** - *For full information on determination of the reference interval, see CLSI/NCCLS document C28. Each laboratory should establish a reference interval, and it should be verified with any change in reagent lot number, instrument, or collection system, or at least once a year. A minimum number of 120 subjects have been recommended for establishing the reference interval, and even more may be required for full statistical validity depending on the distribution of results. See CLSI/NCCLS document C28. This is important when manufacturers of PT/APTT reagents develop new methods. In routine PT and APTT testing, for practical purposes, a close approximation can be obtained by testing a minimum of 20 individuals that encompass the age range and sex patient testing will include, keeping in mind the reference interval is only a guide in conjunction with the patients clinical picture. In coagulation testing, the determination of the reference interval should be established with normal donors who meet specific criteria. The individual donor criteria include healthy individuals who are not on medication nor vigorously exercised within the last 18 to 24 hours.* »[3]

For further information regarding the expected range of the HEMOSTAT aPTT applications on the HumaClot instruments please refer to the instruction for use and application sheets.

References

1. Ozarda et al.: Verification of laboratory reference intervals *Clinical Chemistry and Laboratory Medicine 2018*
2. CSLI Guideline EP28-A3C: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory
3. CLSI Guideline H47-A2: One-Stage Prothrombin Time (PT) Test and Activated Partial Thromboplastin Time (APTT) Test