CLINICAL AND LABORATORY STANDARDS INSTITUTE®

2nd Edition

H48

Determination of Coagulation Factor Activities Using the One-Stage Clotting Assay

This guideline provides recommendations regarding the proper collection and handling of specimens, reagents, controls, calibrators, and materials needed to optimize factor assay testing. It includes recommendations for good laboratory practices related to analyzer and reagent performance, reference intervals, lot-to-lot validation, and quality control. Assay limitations and sources of errors and variability are also included.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Determination of Coagulation Factor Activities Using the One-Stage Clotting Assay

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Abstract

Clinical and Laboratory Standards Institute guideline H48—*Determination of Coagulation Factor Activities Using the One-Stage Clotting Assay* provides information to be used in harmonizing laboratory testing of factor assays. It provides laboratories with guidelines to optimize factor assay testing by minimizing the effect of variation in preexamination, examination, and postexamination processes. It identifies good laboratory practices related to analyzer and reagent performance, reference intervals, lot-to-lot validation, quality assurance, and quality control issues. Standardizing assay performance provides patients with the best outcomes with regard to both diagnosis and treatment. This guideline is written for laboratorians and/or diagnostic testing personnel responsible for factor assay testing, physicians (eg, hematologists, pathologists) responsible for interpreting results, external quality assessment programs, and manufacturers of factor assay testing reagents and test systems.

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Contents

Foreword

Quantitative assays for measuring coagulant activity of both the intrinsic and extrinsic coagulation factors are important laboratory tools. The factor assay provides valuable information in:

- Patients found to have a prolonged activated partial thromboplastin time (APTT) or prothrombin time (PT)
- Patients with normal coagulation screening test values but a clinically suspected bleeding disorder
- Monitoring factor replacement therapy
- Risk assessment of premature atherosclerotic vascular disease in which elevated activity of Factors VII and VIII have been demonstrated

In addition, factor activity determinations are needed to evaluate the potency of therapeutic factor preparations such as fresh frozen plasma and factor concentrates.

This guideline provides recommendations for the routine performance of one-stage coagulation factor assays that are based upon the conventional APTT and PT coagulation tests described in CLSI document H47.[1] Recommendations on result reporting and safety precautions are also presented.

Overview of Changes

This guideline replaces the previous edition of the approved guideline, H48-A, published in 1997. Several changes were made in this edition including:

- Expanded terminology
- Use of factor assays to aid in diagnosis of coagulation disorders
- Enhanced preexamination, examination, and postexamination activities and sources of error
- Identification and reporting of inhibitors
- Anticoagulation effect on factor assays
- Reagents and reagent responsiveness
- Lot-to-lot verification

NOTE: The findings and conclusions in this guideline are those of the authors and are supported by the CLSI consensus process and do not necessarily reflect the views of the organizations the authors represent.

Key Words

Activated partial thromboplastin time, calibration, coagulation factor, extrinsic factor pathway, factor activity, factor assay curve, intrinsic factor pathway, inhibitor, prothrombin time

Determination of Coagulation Factor Activities Using the One-Stage Clotting Assay

Chapter 1: Introduction

This chapter includes:

- Guideline scope and applicable exclusions
- Background information pertinent to the guideline content
- Standard precautions information
- "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions
- Terms and definitions used in the guideline
- Abbreviations and acronyms used in the guideline

Historically, testing of blood plasma factors and platelets depended on seeing the clotting process directly or microscopically. Instrumentation later provided mechanical registration of clot development that allowed more reproducible timing and an expression of the clotting process.[2,3]

1.1 Scope

This guideline provides specifications for the one-stage clotting factor assay. It is intended to increase the diagnostic usefulness of the one-stage factor assay by providing the laboratory with necessary tools to minimize the effects of variables and to provide guidelines to enhance the precision and accuracy of patient results. Preexamination, examination, and postexamination issues specific to factor activity testing are covered.

This guideline is written for laboratory and/or diagnostic testing personnel responsible for factor assay testing including the performance, QC, and reporting of assays of coagulation factor activity, physicians (eg, hematologists, pathologists) responsible for interpreting results, external quality assessment (EQA) programs, and manufacturers of factor assay testing reagents and test systems.

This guideline does not cover chromogenic, two-stage clotting, antigenic, or manual methodologies for factor assays. Assays for fibrinogen, von Willebrand Factor (VWF), Factor XIII (FXIII), or contact factors of high molecular weight kininogen or prekallikrein are not covered in this guideline. Assays used to quantify inhibitors to specific factors are not covered in this guideline.

1.2 Background

The one-stage factor assay is based on the ability of the test plasma to correct the activated partial thromboplastin time (APTT) or prothrombin time (PT) of a specific factor-deficient plasma. The factor activity is quantified with a factor-specific calibration curve prepared using a referenced calibration plasma and a substrate plasma deficient in the factor being tested. Factor assays within the scope of this guideline include Factor II (prothrombin [FII]), Factor V (FV), Factor VII (FVII), Factor VIII (FVIII), Factor IX (FIX), Factor X (FX), Factor XI (FXI), and Factor XII (FXII).