Guidance for Industry and FDA Reviewers/Staff

In Vitro Diagnostic Fibrin Monomer Paracoagulation Test

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U.S. Department Of Health And Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Hematology and Pathology Branch
Division of Clinical Laboratory Devices
Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to, Division of Clinical Laboratory Devices, Center for Devices and Radiological Health, HFZ-440, 9200 Corporate Boulevard, Rockville, MD 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Dr. Joseph Hackett at (301) 594-3084 or by electronic mail at JLH@cdrh.fda.gov.

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World Wide Web CDRH page: http://www.fda.gov/cdrh/ode/2242.pdf, or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 2242 when prompted for the document shelf number.

In Vitro Diagnostic Fibrin Monomer Paracoagulation Test

NOTE: As stated in the final rule reclassifying the Fibrin Monomer Paracoagulation Test *in vitro* diagnostic devices from Class III to Class II, this guidance document is the special control for this device.

This draft guidance document describes a means by which Fibrin Monomer Paracoagulation Test *in vitro* diagnostic devices may comply with the requirement of special controls for class II devices. Designation of this guidance document as a special control means that manufacturers attempting to establish that their device is substantially equivalent to a predicate device should demonstrate that the proposed device complies with either the specific recommendations of this guidance or some alternative control that provides equivalent assurances of safety and effectiveness.

This guidance document represents the agency's current thinking on Fibrin Monomer Paracoagulation Tests. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

I. Device Description

Common Name(s): Fibrin Monomer Paracoagulation Test
Class: II
Classification Panel: Hematology (81)
Product Codes: None
Regulation numbers: 21 CFR 864.7300

A fibrin monomer paracoagulation test is a device used to detect fibrin monomer in the diagnosis of disseminated intravascular coagulation (nonlocalized clotting within a blood vessel) or in the differential diagnosis between disseminated intravascular coagulation (DIC) and primary fibrinolysis (dissolution of the fibrin in a blood clot).

II. Indications for Use

Fibrin monomer tests are assays used to monitor the proteolytic cleavage of fibrinogen by thrombin and the resulting generation of soluble fibrin monomers. Fibrin monomer assays give direct evidence of thrombin activity on fibrinogen. It may aid in the diagnosis and/or exclusion of prethrombotic and thrombotic events such as pre-DIC, DIC or venous thrombosis. Additionally, soluble fibrin monomers can be used as aids for monitoring the response to DIC therapy.

Measurements obtained by this device are used in the diagnosis of disseminated intravascular coagulation. The intended patient population may be adult, pediatric, and neonatal, while the environment of use may be a hospital (e.g., respiratory care or laboratory department), urgent care situations (e.g., intensive care unit, surgery, emergency department), or bedside/near patient care situations.

III. Specific Performance Characteristics

A. Analytical Studies

The following performance characteristics should be included in the submission. Data should be provided that supports the use of the device in the intended population:

1. Precision
   - within-run (assay, and
   - between-run (assay), or
   - total
   - mean(s), standard deviation (s), and coefficient(s) of variation at medical decision levels and over entire range of values
   - total measurement error at selected decision points

2. Linearity
   - recovery or dilution

3. Sensitivity
   - minimum detection limit, or
   - analytical sensitivity

4. Interferences
   - endogenous, e.g., bilirubin, hemoglobin, lipids, etc.
   - exogenous, e.g., drugs, anticoagulants, etc.

5. Stability Summary
   - calibration interval
   - quality control interval
   - quality control materials
   - calibration materials

6. Software
   - validation information
   - certification information

7. Expected Values
   - population study, reference interval,
   - medical decision point(s) and/or
   - critical decision point(s)

8. Cut-off established to differentiate normal and abnormal samples.
   - describe method by which cut-off was established

9. Calibrators
   - data showing calibration against recognized standard

10. Analytical specificity
    - cross-reactivity

B. Clinical Studies

A method comparison study, comparing performance of the proposed device with that of the predicate device as well as an appropriate reference method should be conducted to demonstrate substantial equivalence. A sampling of patients from a population representing the proposed intended use should be included in the study.

1. Method Comparison
   a. Continuous data
      - slope and intercept can be analyzed by linear regression analysis
      - correlation coefficient, include confidence interval where appropriate
      - number and range of samples tested
      - standard error of the estimate
      - bias and bias plot
      - graphical representation of the data

   b. Dichotomous data can be presented in a 2x2 table comparing both methods.
      - estimates of sensitivity and specificity with confidence intervals should be included

IV. Labeling Considerations:

Refer to 21 CFR 809.10.

Checklist

Instructions: Use this checklist for premarket notification for Fibrin Monomer Paracoagulation Test as a guide in preparing your submission.

Truthful and Accurate statement verbatim as per 21 CFR 807.87(j).	
510(k) summary or statement per 21 CFR 807.92 or 21 CFR 807.93 respectively.	
Indications for use on a separate page.	
Labeling for in vitro diagnostic products (21 CFR 809.10 (b)	
Pre-Clinical Data:	
Interference Studies	
Linearity Studies	
Precision studies at medical decision levels	
Clinical Data (method comparison)	

REFERENCES:

Methodologies to assist sponsors in establishing the specific performance characteristics addressed in part III of this document may be obtained using NCCLS documents