Beaumont Laboratory
Royal Oak

Effective Date: 03/30/2018
Supersedes: 04/15/2015
Related Documents:
RC.HM.CG.PR.001 Coagulation Tests: Specimen Collection and Handling (Non–Platelet Function Tests Only)
RC.HM.CG.PR.002 Coagulation Tests: Reportable Limits and Normal / Therapeutic Values
RC.HM.CG.PR.007 Coagulation Correlations
RC.HM.CG.PR.059 CA-7000 Operations Procedure
RC.HM.CG.PY.001 Autoverification Policy

SIEMENS INNOVANCE® D-DIMER
CA 7000

RC.HM.CG.PR.064.r02

Introduction

Coagulation activation results in the cleavage of fibrinogen to fibrin. The fibrin monomers spontaneously aggregate to fibrin and are cross-linked by Factor XIII; this produces a fibrin clot. In response to the coagulation process the fibrinolytic system is activated resulting in the conversion of plasminogen into plasmin, which cleaves fibrin (and fibrinogen) into the fragments D and E. Due to the cross-linkages between the D-domains in the fibrin clot, the action of plasmin releases fibrin degradation products with cross-linked D-domains. The smallest unit is the D-dimer. Detection of D-Dimers, which specifies cross-linked fibrin degradation products generated by reactive fibrinolysis, is an indicator of coagulation activity.

Elevated D-dimer levels are observed in all diseases and conditions with increased coagulation activation, e.g. thromboembolic disease, disseminated intravascular coagulopathy (DIC), acute aortic dissection, myocardial infarction, malignant diseases, obstetrical complications, third trimester of pregnancy, surgery or polytrauma.[1-6]

The relevance of the D-dimer assay is as an aid in the diagnosis of thromboembolic events. Elevated concentrations of D-dimer are indicative of the presence of a clot and have been reported in deep vein thrombosis, pulmonary embolism and disseminated intravascular coagulation.

The D-dimer assay is FDA approved for exclusion of deep vein thrombosis (DVT) and pulmonary embolism (PE).

Principle

Polystyrene particles covalently coated with monoclonal antibody (8D3)[8] are aggregated when mixed with samples containing D-dimer. D-dimer cross-linkage region has a stereosymmetrical structure, i.e. the epitope for the monoclonal occurs twice. Consequently, one antibody suffices in order to trigger an aggregation reaction, which is then detected turbimetrically via the increase in turbidity.

Specimen Collection and Handling

Refer to Coagulation Tests: Specimen Collection and Handling (Non-Platelet Function Tests Only) procedure

---

Supplies

EQUIPMENT / MATERIALS

1. Sysmex CA-7000 Instrument
2. Sysmex CA-7000 Instrument (lamp)
3. Sysmex CA-7000 racks
4. Reaction tubes
5. Sample cups

REAGENTS

All components of a kit are lot-specific except the D-dimer diluent. The combination of lots other than those specified for the particular kit lot may lead to incorrect results. In addition, once one reagent or buffer has been depleted on the instrument then the rest of the reagents/buffer must be discarded.

1. **Innovance® D-dimer REAGENT** – Lyophilized plasma containing polystyrene particles coated with monoclonal antibodies to D-dimer. Human serum album and preservatives. Dissolve with 4.0 mL distilled water. Invert 3 times. Leave vial for at least 15 minutes at 15 – 25 °C. Prior to placing on instrument mix well again by inverting 3 times. Avoid foam formation. Remove bubbles. After reconstitution the reagent is stable for 4 weeks at 2 – 8 °C and ≤ -18 °C. Onboard stability is 48h.

2. **Innovance® D-dimer BUFFER** – Ready to use.
   Stable for 4 weeks at 2 – 8 °C and ≤ -18 °C. Onboard stability is 48h.

3. **Innovance® D-dimer SUPPLEMENTAL** – Ready to use.
   Stable 4 weeks at 2 – 8 °C and ≤ -18 °C. Onboard stability is 48h.

4. **Innovance® D-dimer DILUENT** – Ready to use.
   Stable 4 weeks at 2 – 8 °C and ≤ -18 °C. Onboard stability is 48h.

5. **Innovance® D-dimer CALIBRATOR** – Lyophilized human plasma,
   D-dimer preparation and preservatives. Dissolve with 1.0 mL distilled water. Mix carefully without foam formation.
   Leave the vial for at least 15 minutes at 15 – 25 °C. Prior to placing on the system mix (again) carefully. Do not use if the vial contains a visible clot. After reconstitution the reagent is stable for 4h at 15 – 25 °C.

6. **Bleach** – 20% bleach solution. One part bleach to four parts distilled deionized water.

CONTROLS:

1. **Innovance® D-dimer Control 1** – Lyophilized human plasma based products containing D-dimer and preservatives. Dissolve with 1.0 mL distilled water. Mix carefully without foam formation. Allow to stand for at least 15 minutes at 15 – 25 °C. Mix carefully once more before using. After reconstitution the control is stable for 8 hours at 15 – 25 °C, 7 days at 2 – 8 °C and 4 weeks at ≤-18 °C.

2. **Innovance® D-dimer Control 2** – Lyophilized human plasma based products containing D-dimer and preservatives. Dissolve with 1.0 mL distilled water. Mix carefully without foam formation. Allow to stand for at least 15 minutes at 15 – 25 °C. Mix carefully once more before using. After reconstitution the control is stable for 8h at 15 – 25 °C, 7 days at 2 – 8 °C and 4 weeks at ≤-18 °C.

Maintenance

Refer to CA-7000 Operations procedure for CA 7000 maintenance including replacing and calibrating the lamp.

Quality Control

Quality control consists of Innovance® D-dimer Control 1 and 2.

FREQUENCY OF CONTROL USE

Innovance® D-dimer Control 1 and Innovance® D-dimer Control 2 are run once per shift, with newly reconstituted reagents, after changing the lamp on the instrument, each calibration, and after instrument troubleshooting.

Innovance® D-dimer control results go directly into control files of the CA-7000. Out-of-control situations are documented in the LIS. Hematology management reviews commercial control results every 30 days.

The CA-7000 is also monitored through the use of correlation specimens. These specimens consist of patient samples from the current day's run. The samples are compared to alternate instrumentation in the lab. Performed twice per year. (See Coagulation Correlations Procedure.)

Preparation of Standard Curve

Refer to CA-7000 Operations procedure.

Procedure

Refer to CA-7000 Operations procedure.

Expected Values

NORMAL RANGE

Refer to Coagulation Tests: Reportable Limits and Normal / Therapeutic Values procedure.

REPORTABLE RANGE

Refer to Coagulation Tests: Reportable Limits and Normal / Therapeutic Values procedure.

RESULTING IN LIS

1. Check all samples for a clot before placing on the instrument and resulting.
2. The LIS will multiply the D - dimer result by 1000 changing the units from mg/L FEU to ng/mL FEU.
3. Refer to autoverification policy.
4. Hemolyzed, lipemic, or icteric samples must be noted with the result.

TAT

1 hour

Notes

1. Any unreasonable result is to be repeated.
2. Over range result (****) will reflex to 1:8 dilution and numerical value is reported.
3. If unable to obtain numerical value, see instruction for over range values located in the CA 7000 binder for Error Flags. Follow instructions on how to process over range dimer results per Siemens.
3. The D-dimer concentration in mg/L is calculated automatically by the analyzer based on the reference curve. The D-dimer level is expressed as initial fibrinogen equivalent unit (FEU). An FEU is the quantity of fibrinogen initially present that leads to the observed D-dimer level. Increases in D-dimer concentration observed with thromboembolic events can be variable due to localization, extension and age of the thrombus. Therefore, a thromboembolic event cannot be excluded with certainty solely on the basis of a D-dimer concentration being within the reference range of ostensibly healthy persons.
4. The cut off value is 500 ng/mL FEU. Less than 500 ng/mL FEU is used to rule out DVT/PE. Greater than 500 ng/mL FEU has numerous causes such as old age, pregnancy, DIC, cancer, liver disease, infection, inflammation, and coronary disease.

Interfering Substances

Higher levels of lipids or turbid samples can lead to falsely elevated or decreased values. It is therefore recommended to perform an additional centrifugation step of the plasma (10 minutes at approx. 15.000 x g) before analyzing lipemic patient specimens. Lipemic samples or samples that contain particles, which cannot be clarified by centrifugation must not be used.

No interferences up to …	
Tryglycerides [mg/dL]	600
Hemoglobin [mg/dL]	200
Bilirubin [mg/dL]	60

References

SIEMENS Innovance® D-Dimer package insert, Siemens Healthcare Diagnostics Inc, Newark, DE, November 2008.

Authorized Reviewers

Medical Director, Coagulation

SIEMENS INNOVANCE® D-DIMER – CA 7000

Document Control

Location of Master: Coagulation Procedure Manual
Master electronic file stored on the Beaumont Laboratory server:
S:\HEMACOAG\Document Control\Procedure\Master Document\ Innovance D-dimer CA 7000
Number of Controlled Copies posted for educational purposes: 1
Number of circulating Controlled Copies: 0
Location of circulating Controlled Copies: NA

Document History

Signature	Date	Revision #		Related Documents Reviewed/ Updated
Prepared by: Karri Henderson MT(ASCP)	01/2011			
Approved by: Marc Smith, MD				
Reviewed by: (Signature)	**Date**	**Revision #**	**Modification**	**Related Documents Reviewed/ Updated**
Marc Smith, MD	01/20/2011	00	New procedure for new method on CA 7000.	Yes
Marc Smith, MD	06/18/2013		No Change	OK
Marc Smith, MD	04/15/2015	**01**	Removed Innovance D-dimer Training Checklist as related document.	OK
Marc Smith, MD	04/04/2017		No change	OK
Elizabeth Sykes, MD	02/22/2018			
Marc Smith, MD	03/30/2018	**02**	Pg 4 Added auto 1:8 dilution by CA 7000	OK

Printed copies of this document are not considered up-to-date. Please verify current version date with online document.