



Designation: **F2382 – 04 (Reapproved 2010) F2382 – 17**

## Standard Test Method for Assessment of Intravascular-Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)<sup>1</sup>

This standard is issued under the fixed designation F2382; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon ( $\epsilon$ ) indicates an editorial change since the last revision or reapproval.

### 1. Scope

1.1 This test method covers the screening of ~~cardiovascular-circulating blood-contacting~~ device materials for their ability to induce blood coagulation via the intrinsic coagulation pathway. This assay should be part of the hemocompatibility evaluation for devices and materials contacting human blood, as per ANSI/AAMI/ISO 10993-4.

1.2 All safety policies and practices shall be observed during the performance of this test method.

1.3 All plasma and any materials that had contact with plasma will be bagged in a biohazard bag, properly ~~labeled~~ labelled with the contents, and disposed of by appropriate means. The plasma should be handled at the Biosafety Level 2 as recommended in the Centers for Disease Control/National Institutes of Health Manual Biosafety in Microbiological Laboratories.

1.4 The normal pooled human plasma must have tested negative for Hepatitis B (HBV) or Human Immunodeficiency (HIV) viruses. The plasmas should be treated like any patient plasma using ~~universal standard~~ precautions. The plasma should be handled at the Biosafety Level 2 as recommended in the Centers for Disease Control/National Institutes of Health Manual Biosafety in Microbiological Laboratories.

1.5 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.6 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate ~~safety~~ safety, health, and health environmental practices and determine the applicability of regulatory limitations prior to use.*

1.7 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

### 2. Referenced Documents

2.1 ~~ANSI~~ ANSI/AAMI Standard:

ANSI/AAMI/ISO 10993-4 Biological Evaluation of Medical Devices—Part 4: Selection of Tests for Interactions with Blood<sup>2</sup>

2.2 Other Document:

Centers for Disease Control/National Institutes of Health Manual—U.S. Department of Health and Human Services Biosafety in Microbiological Laboratories, and Biomedical Laboratories (BMBL), 5th ed., 1999<sup>3</sup>

### 3. Terminology

3.1 ~~Definitions:~~ Definitions of Terms Specific to This Standard:

3.1.1 *activator*—a medical material which demonstrates a shortened clotting time; an initiator of the intrinsic coagulation pathway.

<sup>1</sup> This test method is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.16 on Biocompatibility Test Methods.

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<sup>2</sup> Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, <http://www.ansi.org>.

<sup>3</sup> Available from National Institute of Health (NIH), 9000 Rockville Pike, Bethesda, MD 20892. The BMBL 5th Edition (December 2009) is available from the Government Printing Office or <https://www.cdc.gov/biosafety/publications/bmb15/bmb1.pdf>

3.1.2 *partial thromboplastin time (PTT) assay*—a modification of the Activated Partial Thromboplastin Time (APTT) assay; unlike the APTT test, the PTT assay uses reagent (rabbit brain cephalin) without activating substances (~~silica, such as silica, kaolin, elagic acid~~)acid. The material being tested acts as the activator.

3.1.3 *read time*—the time during which data is collected to detect a clot.

3.1.4 *blank time*—a period at the beginning of an assay when no data is taken. This is done to eliminate interference from premixing reagents, bubbles, and so forth.

3.1.5 *equilibration time*—the time allowed for the plasma samples to warm to 37°C. The ~~fibrometer~~coagulation analyzer can be set to zero if samples are pre-warmed to this temperature.

3.1.6 *duplicate flag*—the agreement between the results of duplicate samples in percent. For example, if set to “15,” the difference between the two channels must be less than or equal to ~~15 %~~15 %. If the variance in clot times exceeds this percentage, an asterisk “\*” will be printed by the average results on the report.

#### 4. Significance and Use

4.1 The purpose of this test method is to determine the time citrated plasma exposed to medical materials takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride. In this test method, the test article is the activator. The PTT assay is a general screening test for a medical material’s ability to activate the intrinsic coagulation pathway. Material samples that show a shortened PTT are activators of the intrinsic coagulation pathway.

4.2 ~~Test samples that show a shortened PTT are activators of the intrinsic coagulation pathway. The results are reported as a percent of the negative control. The~~ The test article, reference materials, and controls are exposed to human plasma. The plasma is tested on a coagulation device. Each sample tube is assayed in duplicate. The results are reported as a percentage of the negative control.

#### 5. Apparatus

5.1 *Polypropylene Test Tubes with Caps*, 12 by 75 mm.

5.2 *Automatic Pipets and Tips*, 100 and 1000  $\mu$ L.

5.3 *Ice Bath*.

5.4 *Coagulation Analyzer (Automated Fibrometer)*—(~~Siemens BFT II analyzer or other~~).

5.5 *Agitating Water Bath*,  $37 \pm 2^\circ\text{C}$ , capable of 60 rpm.

5.6 *Coagulation Analyzer Cuvettes*, or equivalent for specific analyzer.

#### 6. Reagents and Materials

6.1 *Calcium Chloride*, 25 ~~mm~~mM.

6.2 *Citrated Human Blood Plasma*, fresh (less than 4 h from draw) or freshly-frozen, maintained at minus 80°C, pooled.

6.3 *Lyophilized Rabbit Brain Cephalin (RBC)*.

6.4 *Positive Reference Control Material*, ~~Material (Optional)~~, see **Appendix X1**.

6.5 *Positive Control Material*, ~~Control~~, glass (Pasteur pipette tips or glass beads).

6.6 *Negative Reference Material* (e.g. High Density Polyethylene, HDPE).

6.7 *Marketed Comparator Device (Optional)*. A legally marketed, clinically acceptable device that has similar blood contact nature and clinical use as the material/device being investigated.

NOTE 1—It may be helpful to use a positive reference control material (n=1) per assay to assure continuity between runs.

#### 7. Hazards

7.1 The human blood plasma should be treated like any patient plasma using ~~universal standard~~ precautions. The plasma should be handled at the Biosafety Level 2 as recommended in the ~~Centers for Disease Control/National Institutes of Health Manual~~US Department of Health and Human Services Biosafety in Microbiological and Biomedical Laboratories.

#### 8. Preparation of Apparatus

8.1 Prepare each test article in triplicate. ~~The reference material(s), and the controls are prepared as singles.~~ article, the negative reference materials, marketed comparator device (if used) and controls in triplicate. If a positive reference control material is used, a single replicate is acceptable. All samples are prepared based on a ratio of 4 ~~either 4 or, preferably 6~~ cm<sup>2</sup> of material to 1 mL plasma and placed into polypropylene tubes. For device testing, if test sample quantity allows, use three separate ~~devices~~devices; otherwise, take three representative samples from one device.

8.2 Label duplicate polypropylene tubes and place in the ice bath.