



## Standard Practice For Selecting Tests for Determining the Propensity of Materials to Cause Immunotoxicity<sup>1</sup>

This standard is issued under the fixed designation F 1905; 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 (ε) indicates an editorial change since the last revision or reapproval.

### 1. Scope

1.1 This practice covers the introduction of foreign materials into the body that may have an impact on the immune system. One possible effect is that the immune system will be depressed or certain cell types may be affected. Immunotoxicity may be determined with blood and tissue samples from the animals used in the other biocompatibility test procedures such as implantation and blood contact test protocols. It is also possible to use these techniques with blood samples from human patients in a clinical trial. Any procedures with human subjects should follow the appropriate rules of the local institutional review board and the appropriate regulatory agencies. This document may serve as an annex to Practice F 748.

1.2 The material may affect the humoral immune response, the cell mediated response, or both.

1.3 *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 and health practices and determine the applicability of regulatory limitations prior to use.*

### 2. Referenced Documents

#### 2.1 ASTM Standards:<sup>2</sup>

F 619 Practice for Extraction of Medical Plastics

F 748 Practice for Selecting Generic Biological Test Methods for Materials and Devices

### 3. Terminology

#### 3.1 Definitions:

3.1.1 *antigens*—these are substances that stimulate the host to produce an immune response

3.1.2 *cell mediated immunity (CMI)*—some antigens stimulate the production of lymphocytes that react specifically with

the antigen. These cells do not circulate widely in the host and are generally located at the site of antigen deposition. The use of living lymphocytes is required to test for CMI to an antigen.

3.1.3 *complement*—this is a complex system of circulating proteins (enzymes, pro-enzymes, and co-factors) found in the blood. This system is usually activated by antigen-antibody reactions and is a reflection of humoral immunity. However it is apparent that other factors can activate the complement system. These include large polysaccharides and various materials and tissues. Activation of complement can affect the immune system, inflammation, and vascular activity with fever and shock as a consequence of complement activation in the host.

3.1.4 *humoral immunity*—some antigens stimulate the host to produce antibodies (immunoglobulins) which are specific for the antigen and react with the antigen. Antibodies circulate in the blood and tissue fluids. The antibodies produced can be detected using blood from the host.

3.1.5 *inflammatory factors*—various soluble substances may be produced by lymphocytes in response to an antigen. This may occur in humoral immune responses or in CMI. These substances may influence the function of other cells and are called cytokines. Many of these act on various white cells and are called interleukins. They are reflection of antigenic stimulation of the host.

### 4. Summary of Practice

4.1 Immunotoxicity testing is done using specimens from animals being tested according to the Practice F 748 matrix for irritation and sensitivity, or for implantation. Blood, organs, or tissues from the animals may be used. In predicting biocompatibility, tests using animals are recommended even though the material will eventually be used in humans. The use of human material is also feasible in this testing protocol for those laboratories having approval for such studies.

4.2 Immunologic testing is done using materials or extracts according to Practice F 619. These materials or extracts may be used for *in vivo* tests or for the *in vitro* tests.

<sup>1</sup> This practice 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> For referenced ASTM standards, visit the ASTM website, [www.astm.org](http://www.astm.org), or contact ASTM Customer Service at [service@astm.org](mailto:service@astm.org). For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.