

# Biocompatibility Testing

The table on the reverse side outlines the ISO/FDA test modalities frequently used to study the biological safety and biocompatibility of medical devices and combination products. These tests should be conducted on final product or representative samples according to the category of the device (based on anatomic location and duration of contact).

WuXi AppTec's comprehensive menu of services includes all the tests related to the table's "Tests for Consideration," as well as tests that may be required for Japanese (JMHLW) submissions.

For regulatory clearance purposes, most tests should be carried out under controlled laboratory conditions in compliance with Good Laboratory Practices (GLP).

WuXi AppTec is a global leader in providing discovery, testing and manufacturing services for the pharmaceutical, biotechnology and medical device industries. Research-driven and customer-focused, with operations in China and the U.S., WuXi AppTec offers a broad and integrated portfolio of services designed to assist our customers with cost-effective and efficient outsourcing solutions.

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WuXi AppTec's biocompatibility testing services include the following. Indicated [⊕] are those categories of assays most likely to require modifications to ensure proper testing of combination products.

- ⊕ **Cytotoxicity (*in vitro*)**
  - Agarose Overlay (USP, ISO)
  - MEM Elution (USP, ISO)
  - Direct Contact
  - Growth Inhibition
  - Extract Colony Assay (JMHLW)
- **Sensitization (*in vivo*)**
  - Guinea Pig Maximization
  - Guinea Pig Repeated Patch (Buehler)
  - Murine Local Lymph Node Assay (LLNA)
  - Maximization Sensitization Test (JMHLW)
- **Irritation/Intracutaneous Reactivity (*in vivo*)**
  - Intracutaneous (USP, ISO, JMHLW)
  - Primary Skin Irritation (ISO, JMHLW)
  - Ocular Irritation
  - Intraocular Irritation
  - Mucosal Irritation: Oral • Vaginal • Bladder
  - Acute Dermal Limit
- ⊕ **Systemic (Acute) Toxicity (*in vivo*)**
  - Acute Systemic Toxicity (USP, ISO, JMHLW)
  - Pyrogen–Materials Mediated (USP, ISO, JMHLW)
  - Mouse Safety & Abnormal Toxicity
- ⊕ **Subchronic (Subacute) Toxicity (*in vivo*)**
  - Subacute Toxicity
  - Intravenous • Intraperitoneal
  - Subchronic Toxicity (JMHLW)
- ⊕ **Genotoxicity (*in vitro and in vivo*)**
  - In vitro* Bacterial Mutagenicity (Ames)
  - In vitro* Mouse Lymphoma
  - In vitro* Chromosomal Aberration
  - In vivo* Mouse Micronucleus
  - Bacterial Reverse Mutation (JMHLW)
  - In vitro* Chromosome Aberration (JMHLW)
- **Implantation (*in vivo*)**
  - Intramuscular Implant (USP, ISO, JMHLW)
  - Subcutaneous Implant
  - Intraperitoneal Implant
- **Hemocompatibility (*in vitro and in vivo*)**
  - Hemolysis Test
    - Extract Method (ASTM or NIH)
    - Direct Contact Method (ASTM or NIH)
    - Hemolytic Toxicity (JMHLW)
  - Complement Activation
  - Coagulation Studies
  - Platelet and Leukocyte Counts
  - Intravascular Thrombogenicity
- ⊕ **Chronic Toxicity**
  - Subcutaneous • Intraperitoneal
  - Dermal • Intravenous • Oral
- **Carcinogenicity**
- **Clinical Pathology**
  - Chemistry – 18 Test Parameters
  - Hematology – 14 Test Parameters
- **Histopathology / Immunochemistry**
- **Other Biocompatibility Testing**
  - USP Rabbit Pyrogen Test
  - LAL Bacterial Endotoxin Tests for Pyrogenicity
  - USP Safety Test in Mice and Guinea Pigs
  - In Vivo Assay for Viral Contaminants
  - Cytotoxicity Screening of Dissolvable Materials
  - USP Class I-VI
- **Part 18 Risk Assessment and Analytical Chemistry**

**Customized assays, toxicology and custom implant studies also available.**

For more information on WuXi AppTec's services please contact:

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## TESTS FOR CONSIDERATION

[Based on ISO 10993-1:2009 and FDA G95-1 Guidelines]

DEVICE CATEGORIES		BIOLOGICAL EFFECT									
		Initial							Other <sup>4</sup>		
Body Contact	Contact Duration	Cytotoxicity	Sensitization	Irritation	Systemic Toxicity (Acute)	Subchronic Toxicity (Subacute)	Genotoxicity	Implantation	Hemocompatibility	Chronic Toxicity	Carcinogenicity
		A – Limited [≤ 24 hrs]	B – Prolonged [>24 hrs to ≤30 days]	C – Permanent [>30 days]							
SURFACE DEVICES	Skin	A	●	●	●						
		B	●	●	●						
		C	●	●	●						
	Mucosal Membranes	A	●	●	●						
		B	●	●	●	◇	◇		◇		
		C	●	●	●	◇	●	●	◇		◇
	Breached or Compromised Surfaces	A	●	●	●	◇					
		B	●	●	●	◇	◇		◇		
		C	●	●	●	◇	●	●	◇		◇
EXTERNAL COMMUNICATING DEVICES	Blood Path, Indirect <sup>3</sup>	A	●	●	●	●				●	
		B	●	●	●	●	◇			●	
		C	●	●	◇	●	●	●	◇	●	◇
	Tissue <sup>1</sup> /Bone/Dentin Communicating	A	●	●	●	◇					
		B	●	●	●	●	●	●	●		
		C	●	●	●	●	●	●	●		◇
	Circulating Blood <sup>3</sup>	A	●	●	●	●		◇ <sup>2</sup>		●	
		B	●	●	●	●	●	●	●	●	
		C	●	●	●	●	●	●	●	●	◇
IMPLANT DEVICES	Tissue / Bone	A	●	●	●	◇					
		B	●	●	●	●	●	●			
		C	●	●	●	●	●	●	●		◇
	Blood <sup>3</sup>	A	●	●	●	●	●		●	●	
		B	●	●	●	●	●	●	●	●	
		C	●	●	●	●	●	●	●	●	◇

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<sup>1</sup> "Tissue" includes tissue fluids and subcutaneous spaces.

<sup>2</sup> For all devices used in extracorporeal circuits.

<sup>3</sup> Pyrogenicity / Materials Mediated should be considered.

<sup>4</sup> Supplemental tests for consideration.

● – ISO Evaluation Tests for Consideration

◇ – Additional tests that the FDA considers may be applicable

For reproductive and biodegradation tests, contact your WuXi AppTec Account Manager.