Reference Documents
For Biocompatibility and Class I-VI Testing

- **USP® United States Pharmacopeia / National Formulary (commonly sited references)**
  - **USP <87> Biological Reactivity Tests, In Vitro**
  - **USP <88> Biological Reactivity Tests, In Vivo**
  - **USP <1032> The Biocompatibility of Materials Used in Drug Containers, Medical Devices, and Implants**
  - **USP <1184> Sensitization Testing**
- **ANSI / AAMI / ISO 10993**
  - **Biological Evaluation of Medical Devices**

Extraction Conditions and Methods
(USP and ISO)

(37±1) ◦C for (24±2) hours
(37±1) ◦C for (72±2) hours
(50±2) ◦C for (72±2) hours
(70±2) ◦C for (24±2) hours
(121±2) ◦C for (1±0.1) hours

Biological Test Center
2525 McGaw Ave
Irvine, CA 92614-5895
Phone: 949-660-3185
www.biologicaltestcenter.com

Standard Surface Areas and Extract Volumes

Thickness mm	Extraction Ratio (surface area or mass/volume)	Forms of Materials
<0.5	6 cm^2 / mL	Film, sheet, tubing wall
0.5 to 1.0	3 cm^2 / mL	Tubing wall, slab, small molded items
> 1.0	1.25 cm^2 / mL	Larger molded items
Irregularly shaped solid devices	0.2 grams / mL	Powder, pellets, foam, non-absorbent, molded items
Irregularly shaped porous devices	0.1 grams / mL	Membranes

Biological Evaluation of Medical Devices
FDA ODE Memo #G95-1
ISO 10993

Biological evaluation of medical devices is performed to determine the potential toxicity resulting from contact of the component materials of the device with the body.

When selecting the appropriate tests for biological evaluation of a medical device, one must consider the chemical characteristics of the device materials and the nature, degree, frequency, and duration of its exposure to the body.

- **First, evaluate what type of contact the device has with the body**
- **Second, determine the expected contact duration**
- **Finally, using the test matrix select the appropriate test for evaluation of the device**

(Note: additional testing may be required by the regulatory agency for some devices)

Biological Test Center
2525 McGaw Ave
Irvine, CA 92614-5895
Phone: 949-660-3185
www.biologicaltestcenter.com

ODE General Program Memorandum #G95-1
(effective July 1, 1995)

Device Categories			Biological Tests											
			Initial Evaluation Tests								Supplementary Evaluation Tests			
Body Contact		Contact Duration A = Limited (< 24 hrs) B = Prolonged (24 hrs to 30 days) C = Permanent (> 30 days)	Cytotoxicity	Sensitization Assay	Irritation or Intracutaneous Reactivity	Acute Systemic Toxicity	Subchronic Toxicity	Genotoxicity	Implantation	Hemocompatibility/Hemolysis	Chronic Toxicity	Carcinogenesis Bioassay	Reproductive/Developmental	Biodegradation
Surface Devices	Intact Surface	A	X	X	X									
		B	X	X	X									
		C	X	X	X									
	Mucosal Membrane	A	X	X	X									
		B	X	X	X	0	0		0					
		C	X	X	X	0	X	X	0		0			
	Breached or Compromised Surface	A	X	X	X	0								
		B	X	X	X	0	0		0					
		C	X	X	X	0	X	X	0		0			
Externally Communicating Devices	Blood Path, Indirect	A	X	X	X	X				X				
		B	X	X	X	X	0			X				
		C	X	X	0	X	X	X	0	X	X	X		
	Tissue/bone/ Dentin Communicating	A	X	X	X	0								
		B	X	X	0	0	0	X	X					
		C	X	X	0	0	0	X	X		0	X		
	Circulating Blood	A	X	X	X	X		0		X				
		B	X	X	X	X	0	X	0	X				
		C	X	X	X	X	X	X	0	X	X	X		
Implant Devices	Tissue/Bone	A	X	X	X	0								
		B	X	X	0	0	0	X	X					
		C	X	X	0	0	0	X	X		X	X		
	Blood	A	X	X	X	X			X	X				
		B	X	X	X	X	0	X	X	X				
		C	X	X	X	X	X	X	X	X	X	X		

X = ISO Evaluation test for consideration 0 = Additional test which may be applicable