

### DEVICES



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A	Limited Exposure (less than 24 hours)
B	Prolonged Exposure (24 hours to 30 days)
C	Permanent Exposure (More than 30 days)
■	Evaluation Required by FDA, ISO, and MHLW
□	Evaluation Required by FDA and ISO
●	Evaluation Required by FDA
◆	Evaluation Required by ISO

### FDA, ISO and Japanese MHLW Test Selection Chart

Device Categories	Biological Effects Initial Evaluation	Biological Tests Supplemental Evaluation												
		Contact Duration	Cytotoxicity	Sensitization	Irritation/Intracutaneous Reactivity	Acute Systemic Toxicity	Pyrogenicity	Subacute/Subchronic Toxicity	Genotoxicity	Implantation	Hemocompatibility	Chronic Toxicity	Carcinogenicity	Reproductive/ Developmental Toxicology
<b>Body Contact</b>														
<b>Surface Devices</b>														
Skin	A	■	■	■										
	B	■	■	■										
	C	■	■	■										
Mucosal Membranes	A	■	■	■										
	B	■	■	■	●	●	●		●					
	C	■	■	■	●	●	■	■	●		●			
Breached/Compromised Surfaces	A	■	■	■	●	●								
	B	■	■	■	●	●	●		●					
	C	■	■	■	●	●	■	■	●		●			
<b>External Communicating Devices</b>														
Blood Path, Indirect	A	■	■	■	■	■					■			
	B	■	■	■	■	■	●				■			
	C	■	■	●	■	■	■	■	●	■	■	■		
Tissues/Bones/Dentin	A	■	■	■	●	●								
	B	■	■	□	□	□	□	■	■					
	C	■	■	□	□	□	□	■	■		□	□		
Circulating Blood	A	■	■	■	■	■		●		■				
	B	■	■	■	■	■	□	■	□	■				
	C	■	■	■	■	■	■	■	□	■	■	■		
<b>Implant Devices</b>														
Tissues/Bones	A	■	■	■	●	●								
	B	■	■	□	□	□	□	■	■					
	C	■	■	□	□	□	□	■	■		■	■		
Blood	A	■	■	■	■	■	◆		■	■				
	B	■	■	■	■	■	□	■	■	■				
	C	■	■	■	■	■	■	■	■	■	■	■		

## Sample Requirements for Standard Studies



Cytotoxicity Tests	
Neutral Red Uptake (NRU)	30 cm <sup>2</sup> if < 0.5 mm thick, 15 cm <sup>2</sup> ≥ 0.5 mm, 1 gram
MEM Elution	USP: 120 cm <sup>2</sup> if < 0.5 mm thick; 4 grams
	ISO: 120 cm <sup>2</sup> if < 0.5 mm thick; 60 cm <sup>2</sup> if ≥ 0.5 mm thick; 4 grams
	MHLW: 8 grams; 120 cm <sup>2</sup> or 240 cm <sup>2</sup>
Agar Diffusion	USP: 2 pieces, each 1 cm x 1 cm
	ISO: 3 pieces, each 100 mm <sup>2</sup>
Genetox/Mutagenicity Tests	
Ames Assay	ISO: 240 cm <sup>2</sup> if < 0.5 mm thick; 120 cm <sup>2</sup> if ≥ 0.5 mm thick; 8 grams
	MHLW: 20 mL; 8 grams; 120 cm <sup>2</sup> ; 240 cm <sup>2</sup>
Mouse Micronucleus Assay	ISO: 200 cm <sup>2</sup> , 600 cm <sup>2</sup> , 25 grams
Chromosomal Aberration Assay	ISO: 240 cm <sup>2</sup> if < 0.5 mm thick; 120 cm <sup>2</sup> if ≥ 0.5 mm thick; 8 grams
	MHLW: 8 grams; 120 cm <sup>2</sup> or 240 cm <sup>2</sup>
Mouse Lymphoma Forward Mutation Assay	ISO: 240 cm <sup>2</sup> if < 0.5 mm thick; 120 cm <sup>2</sup> if ≥ 0.5 mm thick; 8 grams
Hemocompatibility Tests	
Hemolysis Complete (ASTM Method)	ISO: 500 cm <sup>2</sup> if < 0.5 mm thick; 250 cm <sup>2</sup> if ≥ 0.5 mm thick; 40 grams
Hemolysis Direct (ASTM Method)	ISO: 250 cm <sup>2</sup> if < 0.5 mm thick; 125 cm <sup>2</sup> if ≥ 0.5 mm thick; 20 grams
Hemolysis Indirect (ASTM Method)	ISO: 250 cm <sup>2</sup> if < 0.5 mm thick; 125 cm <sup>2</sup> if ≥ 0.5 mm thick; 20 grams
	MHLW: 600 cm <sup>2</sup> if < 0.5 mm thick; 300 cm <sup>2</sup> if ≥ 0.5 mm thick; 25 grams
Complement Activation Direct	ISO: 75 cm <sup>2</sup> if < 0.5 mm thick; 50 cm <sup>2</sup> if ≥ 0.5 mm thick; 2.5 grams
Complement Activation Indirect	ISO: 10 cm <sup>2</sup> if < 0.5 mm thick; 5 cm <sup>2</sup> if ≥ 0.5 mm thick; 1 grams
In Vitro Hemocompatibility Direct	ISO: 75 cm <sup>2</sup> if < 0.5 mm thick; 50 cm <sup>2</sup> if ≥ 0.5 mm thick; 2.5 grams
In Vitro Hemocompatibility Indirect	ISO: 10 cm <sup>2</sup> if < 0.5 mm thick; 5 cm <sup>2</sup> if ≥ 0.5 mm thick; 1 grams
Prothrombin Time Direct	ISO: 75 cm <sup>2</sup> if < 0.5 mm thick; 50 cm <sup>2</sup> if ≥ 0.5 mm thick; 2.5 grams
Prothrombin Time Indirect	ISO: 10 cm <sup>2</sup> if < 0.5 mm thick; 5 cm <sup>2</sup> if ≥ 0.5 mm thick; 1 grams
Thrombogenicity in Dogs	ISO: 2 units
In Vivo Tests	
Kligman Maximization	ISO: 720 cm <sup>2</sup> if < 0.5 mm thick; 360 cm <sup>2</sup> if ≥ 0.5 mm thick; 24 grams; 5 mL
	MHLW: Inquire
Buehler Closed Patch	ISO: 120 pieces of 2.5 cm x 2.5 cm patches each, or 17grams
Intracutaneous Injection	ISO: 240 cm <sup>2</sup> < 1 mm thick, 120 cm <sup>2</sup> ≥ 1 mm thick, or 8 grams
	MHLW: 16 grams; 240 cm <sup>2</sup> or 480 cm <sup>2</sup>
Primary Skin Irritation	ISO: 240 cm <sup>2</sup> < 0.5 mm thick, 120 cm <sup>2</sup> ≥ 0.5 mm thick, or 8 grams
Acute Systemic Injection	ISO: 240 cm <sup>2</sup> ≤ 0.5 mm thick, 120 cm <sup>2</sup> ≥ 0.5 mm thick, or 8 grams
Material Mediated Rabbit Pyrogen	USP: 600 cm <sup>2</sup> if < 0.5 mm thick; 300 cm <sup>2</sup> if ≥ 0.5 mm thick; 20 grams
	ISO: 600 cm <sup>2</sup> if < 0.5 mm thick; 300 cm <sup>2</sup> if ≥ 0.5 mm thick; 20 grams
	MHLW: 600 cm <sup>2</sup> if < 0.5 mm thick; 300 cm <sup>2</sup> if ≥ 0.5 mm thick; 20 grams
Class Tests per USP	Class I: 120 cm <sup>2</sup> < 0.5 mm thick, 60 cm <sup>2</sup> ≥ 0.5 mm thick, or 4 grams
	Class II: 240 cm <sup>2</sup> < 0.5 mm thick, 120 cm <sup>2</sup> ≥ 0.5 mm thick, or 8 grams
	Class III: 480 cm <sup>2</sup> < 0.5 mm thick, 1200 cm <sup>2</sup> ≥ 0.5 mm thick, or 16 grams
	Class IV: 360 cm <sup>2</sup> < 0.5 mm thick, 180 cm <sup>2</sup> ≥ 0.5 mm thick, or 12 grams
	Class V: 480 cm <sup>2</sup> < 0.5 mm thick, 240 cm <sup>2</sup> ≥ 0.5 mm thick, or 16 grams
	Class VI: 550 cm <sup>2</sup> < 0.5 mm thick, 275 cm <sup>2</sup> ≥ 0.5 mm thick, or 22 grams
Implants (Muscle, Subcutaneous, Bone, etc.)	▪ 2 Week
	▪ 4 Week
	▪ 6 Week
	▪ 8 Week
	▪ 12 Week
	▪ 13 Week
	▪ 26 Week
	▪ 52 Week
	▪ 1 & 4 Week Implant
	ISO: 18 strips per time point, each strip 10 mm x 1 mm. Sample should be supplied by sponsor in specified size, separately packaged and sterilized, and edges should be rounded and smooth.
	MHLW: 24 pieces, each 1 mm x 1 mm x 1 mm
General Chemistry Tests	
Physiochemical and other Compendia Tests	USP: 20 grams or 600 cm <sup>2</sup> / Inquire