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Biocompatibility Testing Matrix

Test for Consideration (Based on ISO 10993-1:2018 & FDA 2020 Guidance on ISO 10993-1)

DEVICE CATEGORY		BIOLOGICAL EFFECTS												
Body Contact	Contact Duration	Physical and/or Chemical Information	Cytotoxicity	Sensitization	Irritation	Acute Systemic Toxicity	Pyrogenicity	Subacute Toxicity	Subchronic Toxicity	Genotoxicity	Implantation	Hemocompatibility	Chronic Toxicity	Carcinogenicity
Surface Devices														
Skin	A	X	E	E	E									
	B	X	E	E	E									
	C	X	E	E	E									
Mucosal Membrane	A	X	E	E	E									
	B	X	E	E	E	E	◊	E	◊		E			
	C	X	E	E	E	E	◊	E	E	E	E		E	
Breached or Compromised	A	X	E	E	E	E	E							
	B	X	E	E	E	E	E	E	◊		E			
	C	X	E	E	E	E	E	E	E	E	E		E	E
Externally Communicating Devices														
Blood Path, Indirect	A	X	E	E	E	E	E					E		
	B	X	E	E	E	E	E	E	◊			E		
	C	X	E	E	E	E	E	E	E	E	E	E	E	E
Tissue/Bone/Dentin	A	X	E	E	E	E	E							
	B	X	E	E	E	E	E	E	◊	E	E			
	C	X	E	E	E	E	E	E	E	E	E		E	E
Circulating Blood	A	X	E	E	E	E	E			E*		E		
	B	X	E	E	E	E	E	E	◊	E	E	E		
	C	X	E	E	E	E	E	E	E	E	E	E	E	E
Implant Devices														
Tissue/Bone	A	X	E	E	E	E	E							
	B	X	E	E	E	E	E	E	◊	E	E			
	C	X	E	E	E	E	E	E	E	E	E		E	E
Blood	A	X	E	E	E	E	E			E	E	E		
	B	X	E	E	E	E	E	E	◊	E	E	E		
	C	X	E	E	E	E	E	E	E	E	E	E	E	E

*Only for devices used in extracorpereal circuits.

Exposure Duration	
A	Limited (≤ 24 hours)
B	Prolonged (>24 hours to ≤ 30 days)
C	Permanent (>30 days)

Regulatory Requirements	
X	Required
E	ISO Endpoints to be Evaluated
◊	Additional Tests Considered Applicable by FDA

Biocompatibility Testing Sample Requirements

Test Description	Sample Type	Method	< 0.5 mm Thickness Ratio: 6 cm^2/mL	≥ 0.5 mm Thickness Ratio: 3 cm^2/mL
PHYSICAL/CHEMICAL CHARACTERIZATION			**Sample Requirements**	**Sample Requirements**
Extractables & Leachables	3 Extracts	ISO 10993-18	8 devices (120 cm2 each)	4 devices (120 cm^2 each)
CYTOTOXICITY			**Sample Requirements**	**Sample Requirements**
Direct Contact Method	Liquid/Semi-Solid or 1 Extract	ISO 10993-5; USP <87>	1 device (72 cm^2)	1 device (36 cm^2)
Neutral Red Uptake (NRU) - Elution or Direct Contact	Liquid/Semi-Solid or 1 Extract	ISO 10993-5	1 device (72 cm^2)	1 device (36 cm^2)
XTT Dye Method - Elution or Direct Contact	Liquid/Semi-Solid or 1 Extract	ISO 10993-5	1 device (72 cm^2)	1 device (36 cm^2)
MTT - Elution or Direct Contact	Liquid/Semi-Solid or 1 Extract	ISO 10993-5	1 device (72 cm^2)	1 device (36 cm^2)
MEM Elution Method	Liquid/Semi-Solid or 1 Extract	ISO 10993-5; USP <87>	1 device (72 cm^2)	1 device (36 cm^2)
SENSITIZATION			**Sample Requirements**	**Sample Requirements**
Maximization Test (GPMT)	2 Extracts	ISO 10993-10	6 devices (120 cm^2 each)	6 devices (60 cm^2 each)
MHLW MaximizationTest (GPMT)	Exaggerated Extraction	MHLW	6 devices (120 cm^2 each)	6 devices (60 cm^2 each)
Murine Local Lymph Node Assay (LLNA)	2 Extracts	ISO 10993-10	6 devices (60 cm^2 each)	6 devices (30 cm^2 each)
Buehler Method	Fabric	ISO 10993-10	140 Fabric Samples (2.5 cm x 2.5 cm)	
EXTRACTIONS FOR MHLW (JAPAN)			**Sample Requirements**	**Sample Requirements**
Preliminary Test	Extraction in Acetone and Ethanol	MHLW	10 grams	
Main Test Extraction with Method 1 or 2	Extraction in Acetone or Ethanol	MHLW	Method 1 - TBD; Method 2 - 25 grams	
IRRITATION			**Sample Requirements**	**Sample Requirements**
Intracutaneous Reactivity	2 Extracts	ISO 10993-23	2 devices (120 cm^2 each)	2 devices (60 cm^2 each)
Primary Eye Irritation (72 hrs.)	2 Extracts	ISO 10993-23	2 devices (36 cm^2 each)	2 devices (18 cm^2)
Intracutaneous Reactivity	4 Extracts	USP <88>	4 devices (90 cm^2 each)	4 devices (60 cm^2 each)
Primary Skin Irritation (72 hrs.)	2 Extracts	ISO 10993-23	2 devices (36 cm^2 each)	2 devices (18 cm^2 each)
Buccal Mucosa w/ Histo. (48 hrs.)	2 Extracts	ISO 10993-23	3 devices (36 cm^2 each)	3 devices (18 cm^2 each)
SYSTEMIC TOXICITY			**Sample Requirements**	**Sample Requirements**
Acute Systemic Toxicity	2 Extracts	ISO 10993-11	2 devices (120 cm^2 each)	2 devices (60 cm^2 each)
Subacute Systemic Toxicity	Liquid/Semi-Solid or Extract	ISO 10993-11	TBD	TBD
Subchronic Systemic Toxicity	Liquid/Semi-Solid or Extract	ISO 10993-11	TBD	TBD
Chronic Systemic Toxicity	Liquid/Semi-Solid or Extract	ISO 10993-11	TBD	TBD
Material Mediated Pyrogen	1 Extract (Polar Only)	USP <151>	900 cm^2	450 cm^2
GENOTOXICITY			**Sample Requirements**	**Sample Requirements**
Ames Mutagenicity Test (1 concentration of each extract)	2 Extracts	ISO 10993-3 & 33; OECD 471	2 devices (60 cm^2 each)	4 devices (30 cm^2 each)
Ames Mutagenicity Test (5 concentration of each extract)	2 Extracts	ISO 10993-3 & 33; OECD 471	2 devices (60 cm^2 each)	4 devices (30 cm^2 each)
MLA Lymphoma Forward Mutation Assay	2 Extracts	ISO 10993-3; OCED 490	2 devices (240 cm^2)	
Chromosomal Aberration Assay	2 Extracts	ISO 10993-3; OECD 473	2 devices (240 cm^2)	2 devices (120 cm^2)
In Vivo - Peripheral Blood Micronucleus Test (Limit Test)	2 Extracts	ISO 10993-3 & 33; OECD 474	2 devices (120 cm^2 each)	2 devices (60 cm^2 each)
HEMOCOMPATIBILITY			**Sample Requirements**	**Sample Requirements**
ASTM Hemolysis (Static Design)	Blood Contact	Direct Contact - ASTM F756	3 devices (60 cm^2 each)	3 devices (30 cm^2 each)
ASTM Hemolysis (Static Design)	Blood Contact	Extract Method - ASTM F756	3 devices (60 cm^2 each)	3 devices (30 cm^2 each)
Hematology (Static Design); Platelet and Leukocyte	Blood Contact	ISO 10993-4	3 devices (60 cm^2 each)	3 devices (30 cm^2 each)
Partial Thromboplastin Time (PTT)	Blood Contact	ISO 10993-4	3 devices (60 cm^2 each) requires predicate device	
Complement Activation (SC5b-9)	Blood Contact	ISO 10993-4	6 cm^2	3 cm^2
Thrombogenicity	Blood Contact	ISO 10993-4	2 devices requires predicate device	
USP CLASS TESTING			**Sample Requirements**	**Sample Requirements**
Class VI (Implantation, Acute Sys. Tox, Intracut. Reac.)	Multiple Extracts	USP <88>	8 devices (90 cm^2 each)[A]	8 devices (45 cm^2 each)[A]
IMPLANTATION			**Sample Requirements**	**Sample Requirements**
Intramuscular, 5 Days of Implantation	Implant	USP <88>	8 devices + enough material for 10 implants that are 10-12 mm in diameter x 0.3-1 mm	
Subcutaneous, 7 Days of Implantation	Implant	USP <88>	8 devices + enough material for 8 implants that are 10-12 mm x 1-3 mm	
Subcutaneous, Muscle or Bone (4 week) w/ Histo	Implant	ISO 10993-6	15 samples per time point, each sample 10 mm x 1-3mm	
Subcutaneous, Muscle or Bone (13 week) w/ Histo	Implant	ISO 10993-6		
Subcutaneous, Muscle or Bone (26 week) w/ Histo	Implant	ISO 10993-6		
Subcutaneous, Muscle or Bone (52 week) w/ Histo	Implant	ISO 10993-6		

The above sample requirement chart is intended to highlight our most commonly ordered tests and does not represent all available tests. For sample requirements for tests not listed above, or questions about sample submission, please contact us at medical-device@eurofins.com.

[A]See the additional samples required for testing under implantation testing for the USP <88> method.

Testing Services

Biocompatibility & Toxicology • Cleaning & Reprocessing Validations
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Contact Us

North America: Medical-Device@BPT.EurofinsUS.com
Europe: Medical-Device@BPT.EurofinsEU.com
APAC: easl.cserv@BPJP.EurofinsAsia.com
www.Eurofins.com/Medical-Device