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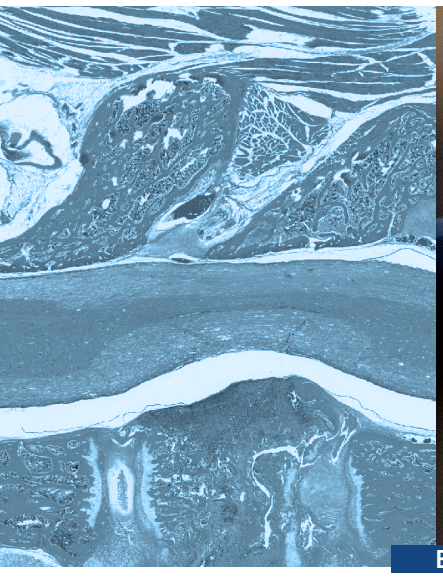

BIOLOGICS TESTING SOLUTIONS

Medical Device Testing

Sample Study Types

- Skin irritation
- Sensitization
- Hemolysis
- Implantation (including ocular and bone)
- Biodegradation
- Disinfectant efficacy and validation
- Bioburden
- Sterility
- Pyrogenicity (rabbit, LAL, or MAT)
- Specialized bone evaluations

The rise in use of medical devices as an interventional therapy or delivery tool is changing the preclinical development process. As with other forms of therapy, these devices are subject to an assessment of their safety in order to meet regulatory requirements. A number of factors (e.g., critical system/body part exposure, duration of contact) determine the extent of testing required to evaluate the device's overall risk. Charles River offers a range of safety evaluation and biocompatibility services for medical devices, including studies designed in accordance with ISO 10993, USP, FDA, OECD, and JMHLW guidelines. With capabilities to test many different types of medical devices across multiple therapeutic areas, we work with clients to design and deliver the most appropriate program for each product. We can also advise on any potential technical challenges, including preparation of eluates suitable for testing, and considerations relating to implantation techniques.

Toxicology, Pathology, and Related Services

Our experts draw from Charles River's comprehensive portfolio of toxicology (e.g., acute through chronic, genetic, reproductive, carcinogenicity, cytotoxicity) and pathology services, as well as specialized capabilities (e.g., biological reactivity testing) to develop each program.

Biocompatability Testing

Charles River offers medical device biocompatibility evaluation models that are fully GLP-compliant with ISO 10993 standards, as well as with FDA, OECD, and JMHLW guidelines. These models serve as efficient and cost-effective resources for evaluating test devices. Models include the guinea pig sensitization/maximization study, the skin irritation/intracutaneous reactivity study in rabbits, acute systemic toxicity study, hemocompatibility, biodegradation evaluations, subcutaneous or intramuscular implantation, subchronic and chronic toxicity, developmental and reproductive testing, and arcinogenicity. Charles River also has an established working relationship with an outside laboratory to subcontract cytotoxicity and genotoxicity assessments.

EVERY STEP OF THE WAY

Experience includes:

- Bandages
- Valves
- Breast implants
- Catheters
- Ingestible devices
- Bio-absorbable/bio-erodible mesh
- Cartilage and ligament repair
- Combination drug/device studies
- Vascular grafts/stent grafts
- Cautery devices
- Stents (vascular, airway, and urogenital)
- External communicating/ monitoring devices
- Deep-brain stimulating leads
- Hemostatic devices
- Satiogenic devices
- Orthopedic implants
- Sphincter bulking agent
- Hernia repair mesh
- Epidural/intrathecal electrodes
- Intramuscular implants

Viral Clearance

Class III medical devices that use material of animal origin (e.g., prosthetic valves) bear the risk of viral contamination, and thus may be subject to viral clearance studies. Frequently, such devices also require clinical trials before obtaining regulatory approval in Europe and the US. Charles River has over 20 years of experience in leading clients through the risk assessment, planning, and execution of viral and TSE clearance studies under ISO 22442-3 or FDA Guidance: Medical Devices Containing Materials Derived from Animal Sources (Draft 2014), including the feasibility studies that are often required before performing the actual study. To eliminate delays and optimize development, we support clients by preparing study concepts to be presented to regulatory agencies for discussion and ensuring acceptance prior to a study's execution.

Table 1. Required tests per ISO 10993

Medical Device Categorization			Biological Effect											
Nature of Body Contact		Contact Duration	Cytotoxicity	Sensitization	Irritation or Intracutaneous Reactivity	Systemic Toxicity (acute)	Subacute and Subchronic Toxicity	Genotoxicity	Implantation	Hemocompatibility	Chronic Toxicity	Carcinogenicity	Reproductive/ Developmental (for cause)	Biodegradation (for cause)
Category	Contact													
Surface Device	Skin	< 24 Hours	•	•	•									
		1 - 30 Days	•	•	•									
		> 30 Days	•	•	•									
	Mucosal Membrane	< 24 Hours	•	•	•									
		1 - 30 Days	•	•	•	□	□		□					
		> 30 Days	•	•	•	□	•	•	□		□			
	Breached or Compromised Surface	< 24 Hours	•	•	•	□								
		1 - 30 Days	•	•	•	□	□		□					
		> 30 Days	•	•	•	□	•	•	□		□			
External Communicating Device	Blood Path, Indirect	< 24 Hours	•	•	•	•				•				
		1 - 30 Days	•	•	•	•	□			•				
		> 30 Days	•	•	□	•	•	•	□	•	□	□		
	Tissue, Bone, Dentin[1]	< 24 Hours	•	•	•	□								
		1 - 30 Days	•	•	•	•	•	•	•					
		> 30 Days	•	•	•	•	•	•	•		□	□		
	Circulating Blood	< 24 Hours	•	•	•	•		□[2]		•				
		1 - 30 Days	•	•	•	•	•	•	•	•				
		> 30 Days	•	•	•	•	•	•	•	•	□	□		
Implant Device	Tissue, Bone	< 24 Hours	•	•	•	□								
		1 - 30 Days	•	•	•	•	•	•	•					
		> 30 Days	•	•	•	•	•	•	•		□	□		
	Blood	< 24 Hours	•	•	•	•	•		•	•				
		1 - 30 Days	•	•	•	•	•	•	•	•				
		> 30 Days	•	•	•	•	•	•	•	•	□	□		

Note: This table is a framework for the development of an assessment program and is not a checklist.

• = Tests per ISO 10993-1
□ = Additional tests that may be applicable in the United States

[1] Tissue includes tissue fluid and subcutaneous spaces
[2] For all devices used in extracorporeal circuits

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