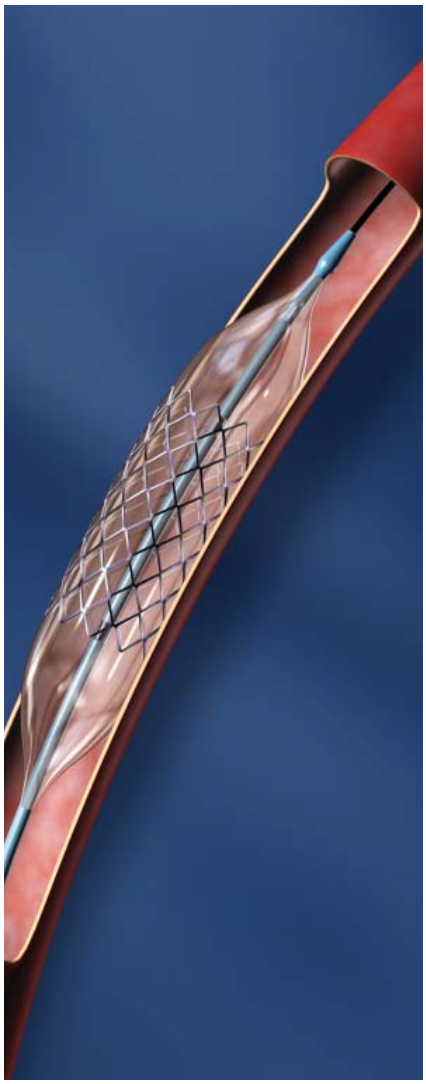
GUIDELINES FOR COMPLIANCE: MEDICAL EQUIPMENT MADE BY 3D PRINTING AND ADDITIVE MANUFACTURING

GUIDELINES FOR COMPLIANCE: MEDICAL EQUIPMENT MADE BY 3D PRINTING AND ADDITIVE MANUFACTURING TECHNIQUES

Additive manufacturing, also known as 3D printing, is a rapidly growing manufacturing process using specialized equipment to build a physical object from a three-dimensional digital model. This process typically places many thin layers of material, such as polymers, one above the last in succession as instructed by the digital design to create an object. This manufacturing method lends itself extremely well to applications in the medical devices industry.



The additive manufacturing designer can use virtually any 3D based modeling technique (CTscans, MRI scans or a combination of imaging modalities) to create a digital design which can then be produced using a variety of additive manufacturing techniques. This application of scanning and digital manufacturing can use a patient's own anatomy to create a truly personalized medical device or surgical guide for a particular procedure.

Additive manufacturing use in medicine presents a number of technical considerations that must be addressed to ensure patient safety -- the material selection, the additive manufacturing process, the design software associated with the modeling, and the cleaning and sterilization of the finished product.

This document contains guidelines for selecting the appropriate safety standards and routes to conformity for your device produced with 3D printing and additive manufacturing techniques.

The driver for this guide is to associate 3D printing and additive manufacturing techniques with the relevant existing safety standards for the various routes to conformity of medical equipment.

There are several standards publications, from the IEC, US, ISO and others, that adequately cover safety aspects of 3D printing and additive manufacturing equipment. The intent of this guide is not to introduce new requirements, but to explain appropriate existing standards with supplemental considerations to address the best route to conformity for medical devices and their chosen markets.

ROUTES TO CONFORMITY FOR DEVICES PRODUCED USING 3D PRINTING AND ADDITIVE MANUFACTURING

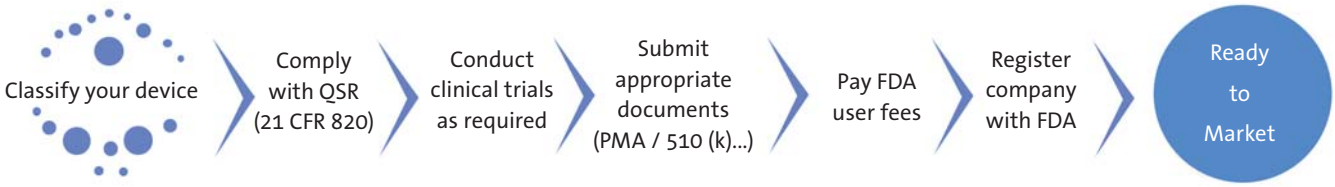


Figure 1: Route to Conformity for the US market

Figure 2: Route to Conformity for the Canadian market

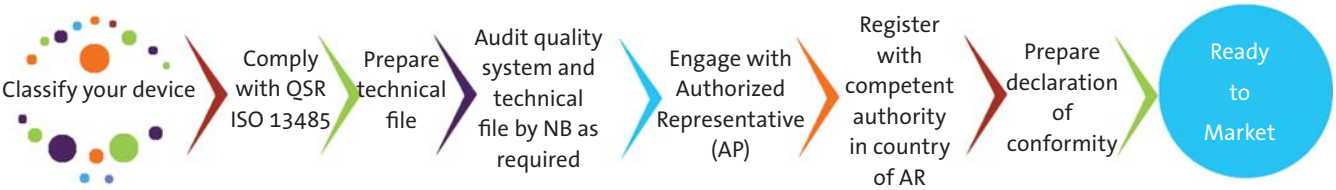


Figure 3: Route to Conformity for the EU market

Note: The above graphical representations are the critical high-level steps of very complex processes needed to bring a device to market. All submissions and registrations should be reviewed and approved by a company's regulatory department.

TESTING ASSURANCE

The ability to use 3D printing and additive manufacturing processes to specifically match a device to patients and their needs is impressive. Whether it is specifically matched for patients or mass-produced, it is incumbent on a manufacturer to address many safety and efficacy questions of its finished products. As an example, regulators do not "approve" materials for use in specific medical applications or devices. When tests are conducted in accordance with the consensus standards such as ISO 10993, the material can be recognized as biocompatible.

For the final product, it is a manufacturer's responsibility to assure the biocompatibility and general compliance with stated requirements of the finished product, for the intended use of the device. In addition, the manufacturer must assure that the device is compliant with the relevant General, Collateral and Particular standards applicable to the product. Some of these non-clinical test standards and their description are outlined briefly below.

Physico-Chemical Analyses

To demonstrate the suitability of a medical device having direct or indirect patient contact, a material characterization pursuant to ISO 10993-18 needs to be performed as a requirement in ISO 10993-1. Materials can be characterized using chemical, physical, morphological and mechanical test methods. Also, all leachable and extractable chemical substances should be identified and have their toxicity evaluated. Such kind of investigations should be performed before starting with biological testing.

Biocompatibility

For medical devices, the biocompatibility of a product has to be evaluated pursuant to the harmonized standard ISO 10993 series "Biological evaluation of medical devices." ISO 10993-1 classifies medical devices regarding the nature of their body contact, their contact duration, and by the names of the respective biological test methods and applicable standards.

Microbiological Basic Tests for Process Supervision

Medical devices contaminated with pathogens may be a source of infection for humans. According to regulators, devices must be designed and manufactured in such a way as to eliminate or reduce the risk of infection to the patient, user or third parties as much as possible. The microbiological basic tests inform the manufacturer about the microbiological status of their products at the end of the production process, support the evaluation of applicable sterilization efforts and disinfection properties and help to control the manufacturing processes.

Cleaning, Reprocessing, Sterilization

Typically, medical devices are subjected to a first-time cleaning process at the end of the manufacturing process. This cleaning process within the scope of the manufacturing process should be validated in order to consistently produce clean and biocompatible products. Reusable devices are subjected to a defined cleaning and disinfection process and are typically sterilized afterwards. Such processes need to be validated before including them in the Instructions For Use (IFU).

Shelf Life of Devices & Packages

According to ISO 11607-1, the specific properties of medical devices and their packaging systems must remain stable during their shelf life. Consequently, medical device manufacturers should perform appropriate validation studies in order to justify shelf life and transport stability of their devices. This includes the validation of the packaging processes, like forming and sealing process of sterile barrier systems, pursuant to ISO 11607-2. In the course of a combined stability and packaging validation study, packed (sterile) devices are subjected to a thermal accelerated and regular real-time aging and to a transport simulation (pursuant ISTA or ASTM standards).

Product Testing

For various medical devices, specific product standards exist. Such standards should be used in order to evaluate the performance and safety of the final product.

BIOLOGICAL CLASSIFICATION AND ASSOCIATED BIOLOGICAL EFFECTS

Medical device categorization by			Biological effect*							
Nature of body contact		Contact duration A - limited (≤24h) B - Prolonged (>24h - 30d) C- permanent (>30d)	Cytotoxicity	Sensitization	Irritation or intracutaneous reactivity	Systemictoxiity (acute)	Subchronic toxicity (subacute toxicity)	Genotoxicity	Implantation	Haemocopatibility
Category	Contact									
Surface device	Skin	A	X	X	X					
		B	X	X	X					
		C	X	X	X					
	Mucosal membrane	A	X	X	X					
		B	X	X	X					
		C	X	X	X		X	X		
	Breached or compromised surface	A	X	X	X					
		B	X	X	X					
		C	X	X	X		X	X		
External communicating device	Blood path, indirect	A	X	X	X	X				X
		B	X	X	X	X				X
		C	X	X		X	X	X		X
	Tissue, bone, dentin	A	X	X	X					
		B	X	X	X	X	X	X	X	
		C	X	X	X	X	X	X	X	
	Circulating blood	A	X	X	X	X				X
		B	X	X	X	X	X	X	X	X
		C	X	X	X	X	X	X	X	X
Inplant device	Tissue, bone	A	X	X	X					
		B	X	X	X	X	X	X	X	
		C	X	X	X	X	X	X	X	
	Blood	A	X	X	X	X	X		X	X
		B	X	X	X	X	X	X	X	X
		C	X	X	X	X	X	X	X	X

Table 1: Biological Classification and Associated Bilogical Effects

*Note: The "X" indicates data endpoint can be necessary for a biological safety evaluation, based on a risk analysis. Where existing data are adequate, additional testing is not required.

FDA DRAFT GUIDANCE DOCUMENT - INITIAL AND SUPPLEMENTARY TEST FOR CONSIDERATION

Medical device categorization by			Biological effect[a]											
Nature of body contact		Contact duration A - limited (≤24h) B - Prolonged (>24h - 30d) C- permanent (>30d)	Cytotoxicity	Sensitization	Irritation or intracutaneous reactivity	Systemic toxiity (acute)	Subchronic toxicity (subacute toxicity)	Genotoxicity	Implantation	Haemocopatibility	Chronic toxicity	Carciogenicity	Reproductive / Developmental	Biodegradation
Category	Contact													
Surface device	Skin	A	X	X	X									
		B	X	X	X									
		C	X	X	X									
	Mucosal membrane	A	X	X	X									
		B	X	X	X	O	O		O					
		C	X	X	X	O	X	X	O		O			
	Breached or compromised surface	A	X	X	X	O								
		B	X	X	X	O	O		O					
		C	X	X	X	O	X	X	O		O			
External communicating device	Blood path, indirect	A	X	X	X	X				X				
		B	X	X	X	X	O			X				
		C	X	X	O	X	X	X	O	X	O	O		
	Tissue, bone, dentin +	A	X	X	X	O								
		B	X	X	X	X	X	X	X					
		C	X	X	X	X	X	X	X		O	O		
	Circulating blood	A	X	X	X	X		O^		X				
		B	X	X	X	X	X	X	X	X				
		C	X	X	X	X	X	X	X	X	O	O		
Inplant device	Tissue, bone	A	X	X	X	O								
		B	X	X	X	X	X	X	X					
		C	X	X	X	X	X	X	X		O	O		
	Blood	A	X	X	X	X	X		X	X				
		B	X	X	X	X	X	X	X	X				
		C	X	X	X	X	X	X	X	X	O	O		

Table 2: FDA Draft Guidance Document - Initial and Supplementary Test for Consideration

Notes: X ISO Evaluation tests for condsideration

\+ Tissue includes tissue fluids and subcutaneous spaces

^ For all devices used in extracorporeal circuits

O Additional categories which should be addressed in FDA submissions, either by inclusion of the testing or a rationale for its omission

a The "X" indicates data endpoint that can be necessary for a biological safety evaluation, based on a risk analysis. Where existing data are adquate, additional testing is not required.

APPLICABLE STANDARDS FOR MEDICAL DEVICES

		United States	Canada	European Union
General Standards	**IEC 60601-1: 3rd Edition**		X	
	EN 60601-1: 3rd Edition			X
	ANSI60601-1: 2005	X		
Collateral Standards	**IEC 60601-1-2**	X	X	X
	IEC 60601-1-6	X	X	X
	IEC 60601-1-8	X	X	X
	IEC 60601-1-11	X	X	X
Particular Standards*	**IEC 60601-2-xx**	X	X	X
	IEC 80601-2-xx	X	X	X
Biocompatibility Standards	**ISO 10993**	X	X	X

Table 3: Applicable Standards for Medical Devices

*Note: There are national and international standards in force not referenced in this table that should also be used as applicable to your medical device.

Many medical device manufacturers are challenged during the development process to choose the right standards to evaluate their product/system design. It is incumbent on the device manufacturer to develop a comprehensive test plan for compliance to all the applicable testing and market entry requirements. This typically is accomplished by working with regulatory, design, manufacturing, clinical and consulting partners to develop the comprehensive testing plan. The testing should address the clinical, environmental, use and distribution hazards associated with the device and its use during the products end use life.

Resources:

IEC http://members.iecee.org/iecee/ieceemembers.nsf/IECEEScopeInStandard

ISO http://www.iso.org/iso/home.html

FDA http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/results.cfm

Health Canadahttp://hc-sc.gc.ca/dhp-mps/md-im/standards-normes/md_rec_stand_im_norm_lst-eng.php

Europe
http://ec.europa.eu/growth/single-market/european-standards/index_en.htm

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