WHITE PAPER

The Ultimate Guide to Quality Assurance and Regulatory Affairs in Medical 3D Printing

This document aims to guide users in the medical device industry through every stage of the product development process, from evaluating manufacturing methods and 3D printing technologies to specific regulatory requirements for commercializing and marketing end-use 3D printed medical devices. Throughout the document are Formlabs and Greenlight Guru resources to support users in each step of the process.

formlabs | medical greenlight guru

Contents

POINT-OF-CARE OR HOSPITAL-BASED MANUFACTURING

The use of additive manufacturing within hospitals is accelerating, with hundreds of clinical publications highlighting the use of Formlabs technology to develop surgical tools, including patient-specific preoperative planning anatomical models, implant sizing templates, and cutting and drilling guides. The scope of this document is for medical device manufacturers that are subject to regulation, audits, and other requirements specific to commercial entities that are marketing devices. Hospitals that produce instruments under the practice of medicine may not be subject to the same regulatory requirements (requirements vary by region). However, the same principles behind a QMS still apply. Several sections and tables, including the Technical Considerations table and the MDR: Custom Devices section in Chapter 5, speak specifically about point-of-care requirements. Still, this document is not written to be a comprehensive guide for hospital-based 3D printing.

Outside of this guide, the US FDA's Center for Devices and Radiological Health (CDRH) has an Additive Manufacturing Working Group conducting a stakeholder engagement process for its Conceptual Framework. For the latest information on 3D printing at the point-of-care, please consider the following links:

- Pew Charitable Trusts, What Is Medical 3D Printing—and How Is it Regulated?
- American Society of Mechanical Engineers (ASME) - 3D Printing at the Point of Care
- Formlabs Clinical Innovator Content Series: Resources from imaging to sterilization, presented by clinicians
- Regulatory Information for Preoperative Planning Models

In the EU, point-of-care manufacturing for health institutions may fall under the exemptions in Article 5 of the EU MDR. While Article 5 exempts health institutions from specific requirements, a QMS and Annex I General Safety and Performance Requirements still apply. For those manufactures that do not qualify for an exemption, their device may be considered custom. For more information on if your device is a custom device or patient-matched, please see the MDCG guidance document. Please see the MDCG checklist Formlabs has prepared as a guide to determine if your device is a custom device.

Please contact Formlabs (healthcare@formlabs.com) with any specific questions on this topic.

ABOUT FORMLABS

Formlabs is expanding access to digital fabrication so that anyone can make anything. It has become the all-time best-selling 3D printer for professionals within ten years, with over 80,000 SLA and SLS machines sold, hundreds of thousands of surgeries supported, and over 70 million end-use medical supplies printed by customers in the last 18 months alone. By combining clinically validated 3D printing technology, in-house QA/RA services, and accessible pricing and user-friendliness, the company enables healthcare professionals and medical device engineers to enhance surgery, radiology, orthotics and prosthetics, device development, and device manufacturing. Formlabs has FDA-registered, ISO 13485-certified manufacturing facilities that it uses to produce a range of biocompatible, sterilizable materials. Its solutions have been used in hundreds of clinical publications and are trusted by the world's leading health systems and medical device manufacturers. For more information, visit https://formlabs.com/medical/.

greenlight guru

ABOUT GREENLIGHT GURU

Greenlight Guru is the only quality management software platform designed specifically for medical device companies. The platform helps companies bring safer products to market faster, simplifies FDA and ISO regulatory compliance, and provides a single source of truth by connecting the management of all quality processes like CAPAs, risk, audits, and more. Greenlight Guru's platform is used by thousands of organizations across the globe to push beyond baseline compliance and achieve True Quality for their medical devices. For more information, visit www.greenlight.guru.

1. Consider Your Product Requirements

PRODUCT TYPE

Products can naturally be produced for various applications and intended uses, including prototyping, hybrid manufacturing, tooling and manufacturing aid, and end-use (or final-use) devices. The type and purpose of the product can affect materials used, the volume of production, machining technique, lead time, cost, design flexibility, quality flexibility, etc. Various manufacturing methods are available to cover a wide range of applications, geometries, materials, and specifications. When choosing a method, all of the factors listed above must be considered to optimize production.

MATERIAL PROPERTIES

Once the purpose of your product is defined, you'll need to consider the material properties required to fulfill the specified purpose. Mechanical and physical properties can affect the materials capable of producing your manufactured part. Examples of material properties include conductivity, density, ductility, hardness, toughness, tensile strength, fatigue strength, and color. Please visit the Formlabs website for a complete list of the most common mechanical and thermal material properties, along with their definitions and functional values. Further, certain materials are compatible with specific manufacturing methods, requiring a holistic approach at the onset of the development process.

For more information on material compatibility with specific manufacturing methods, please read the "Manufacturing Methods" section in chapter 2. For more information on additive manufacturing material properties, please refer to chapter 3.

VOLUME + THROUGHPUT REQUIREMENTS

As briefly mentioned above, your part may have particular volume and throughput requirements depending on the product type and purpose. Different manufacturing methods are optimized for varying volume and throughput requirements, impacting each technique's cost, quality, and manufacturability of specific devices. For more information on each manufacturing method and their optimal use cases, including volume and throughput considerations, please refer to the "Manufacturing Methods" section in chapter 2.

2. Evaluate All Manufacturing Methods

IDENTIFYING PRODUCTION FACTORS AND CONSIDERATIONS

When evaluating manufacturing processes' feasibility and selecting one for your product or component, consider the following factors:

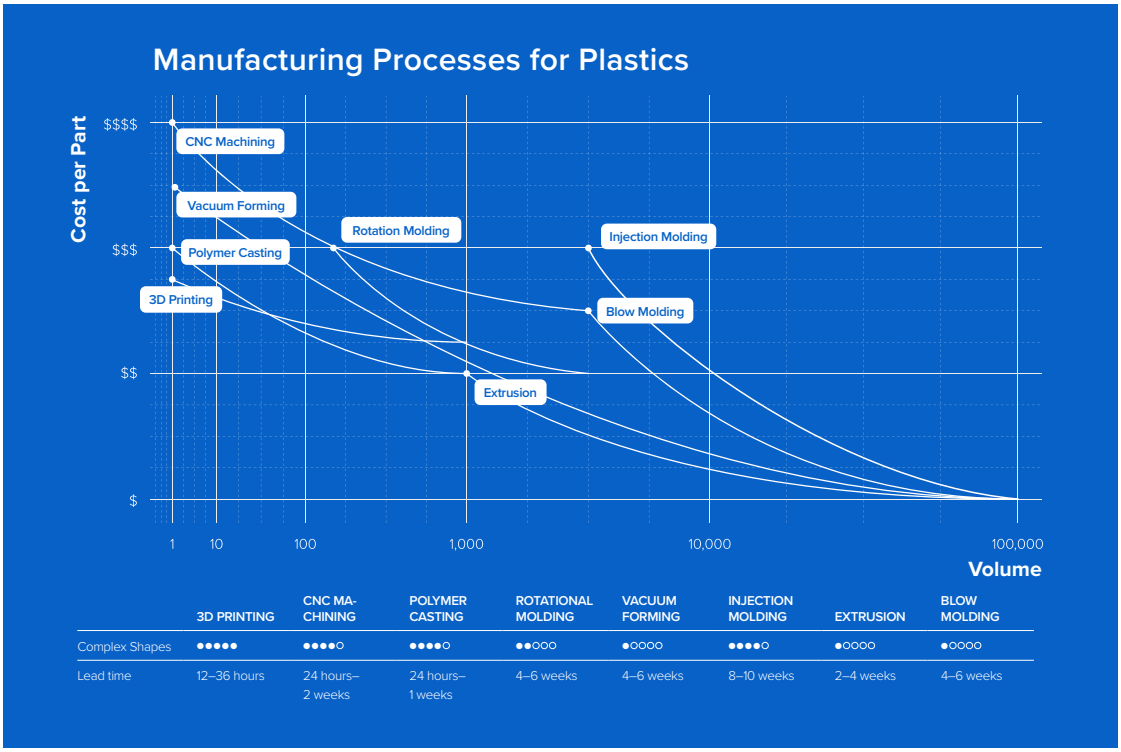
Form: Do your parts have complex internal features or tight tolerance requirements? Depending on the geometry of a design, manufacturing options may be limited, or they may require significant design for manufacturing (DFM) optimization to make them economical to produce.

Volume/cost: What's the total or the annual volume of parts you're planning to manufacture? Some manufacturing processes have high front costs for tooling and setup but produce inexpensive parts on a per-part basis. In contrast, low-volume manufacturing processes have low startup costs. Still, due to slower cycle times, less automation, and manual labor, cost per part remains constant or decreases marginally when volume increases.

Lead time: How quickly do you need parts or finished goods produced? Some processes create the first parts within 24 hours, while tooling and setup for certain high-volume production processes take months.

Material: What stresses and strains will your product need to stand up to? Several factors determine the optimal material for a given application (see the "Material Properties" section in Chapter 1 if you need a refresher). Manufacturers must also balance cost against functional and aesthetic requirements. Consider the ideal characteristics for your specific application and compare them with the available choices in a given manufacturing process.

MANUFACTURING METHODS



	3D PRINTING	CNC MACHINING	POLYMER CASTING	ROTATIONAL MOLDING	VACUUM FORMING	INJECTION MOLDING	EXTRUSION	BLOW MOLDING
Complex Shapes	●●●●●	●●●●○	●●●●○	●●○○○	●○○○○	●●●●○	●○○○○	●○○○○
Lead time	12–36 hours	24 hours–2 weeks	24 hours–1 weeks	4–6 weeks	4–6 weeks	8–10 weeks	2–4 weeks	4–6 weeks

Compare different manufacturing methods by considering cost per part, volume, lead time, and ability to manufacture complex parts. Read below for more details on each of these processes.

3D Printing

3D printers create three-dimensional parts directly from CAD models by building material layer by layer until a complete physical part is formed. They can be compatible with both plastics and select metals. For more information on 3D printing materials, please refer to the “Print Materials and Properties” section of Chapter 3.

As 3D printers require no tooling and minimal setup time for a new design, the cost of producing a custom part is negligible in comparison with traditional manufacturing processes. However, 3D printing processes are generally slower and more labor-intensive than manufacturing processes used for mass production. As 3D printing technologies improve, cost per part continues to fall, opening up a more comprehensive range of low- to mid-volume applications.

CNC Machining

CNC machining includes mills, lathes, and other computer-controlled subtractive processes. These processes start with solid blocks, bars, or rods of metal, plastic, or wood shaped by removing material through cutting, boring, drilling, and grinding.

Unlike most other plastic manufacturing processes, CNC machining is a subtractive process where the material is removed by either a spinning tool and fixed part (milling) or a spinning part with a fixed tool (lathe).

Machining is ideal for low-volume applications that require tight tolerances and geometries that are difficult to mold. Typical applications include prototyping and end-use parts like pulleys, gears, and bushings.

Polymer Casting

In polymer casting, a reactive liquid resin or rubber fills a mold which reacts chemically and solidifies. Typical polymers for casting include polyurethane, epoxy, silicone, and acrylic. RTV silicone molds can reproduce even the smallest details, yielding high-quality cast parts.

Rotational Molding

Rotational molding (also called rotomolding) is a process that involves heating a hollow mold filled with powdered thermoplastic and rotated around two axes to produce mainly large hollow objects. Methods for rotomolding thermoset plastics are available as well, however less common. The molds can be fabricated, CNC machined, cast, or formed from epoxy or aluminum at a lower cost and much faster than tooling for other molding processes, especially for large parts.

Rotomolding has some design constraints, and finished products have looser tolerances. As the entire mold has to be heated and cooled down, the process also has long cycle times and is quite labor-intensive, limiting its efficiency for higher volume applications.

Vacuum Forming

Vacuum forming is a manufacturing method where plastic is heated and formed, typically using a mold. Vacuum forming machines vary in size and complexity from low-cost desktop devices to automated industrial machinery. Commonly vacuum-formed parts include product packaging, shower trays, car door liners, boat hulls, and custom products like dental aligners.

For more information on vacuum forming, please visit the Formlabs website.

Injection Molding

Injection molding (IM) works by injecting molten thermoplastic or powdered metal into a mold. It is the most widely used process for mass manufacturing plastic parts. Injection molding can produce highly complex parts, but certain geometries will significantly increase the cost.

Extrusion

Extrusion molding works by pushing plastic or metal through a die. The shape of the die is a cross-section of the final part. Forms and shapes manufactured with extrusion are limited to products with continuous profiles, such as T-sections, I-sections, L-sections, U-sections, and square or circular sections. Typical applications include pipes, hoses, straws, and window frame moldings.

Blow Molding

Blow molding is a manufacturing technique used to create hollow plastic parts by inflating a heated plastic tube inside a mold until it forms into the desired shape. Blow molding is the most common process for creating hollow plastic products at scale. Typical applications include bottles, toys, automotive components, industrial parts, and packaging.

Please visit the Formlabs Guide to Manufacturing Processes for Plastics for more detailed information on each of these processes.

Sand Casting

In the sand casting process, a foundry worker fills mold boxes or flasks with a mixture of sand and binder, then packs sand around the pattern. The pattern is removed to leave a negative impression of the pattern behind, and molten metal is poured into the cavity.

An open-faced mold may be used for parts with features on a single side. Parts with features on multiple surfaces require closed cavity molds with upper and lower mold boxes.

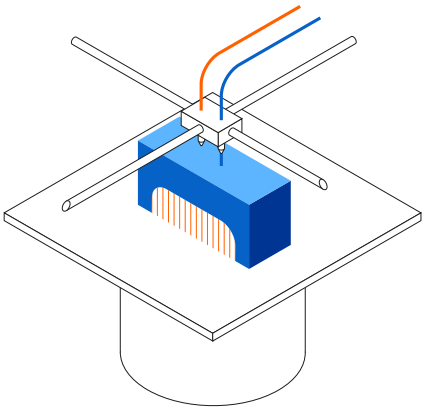
For more information on sand casting and investment casting, please visit the Formlabs article on Metal 3D Printing Alternatives.

3. Compare Additive Manufacturing Methods And Materials

Now that we have discussed a few manufacturing methods, we will focus on one of the newer and most rapidly evolving ones: 3D printing. The 3D printing or additive manufacturing market has undergone rapid change in recent years. No longer primarily the domain of hobbyists, sophisticated desktop machines have developed into essential tools for businesses. After becoming the go-to tool for prototyping and product development, 3D printing has expanded across manufacturing, dentistry, jewelry, and more. Please read below for more information on the most common 3D printing methods, including how they work and their pros and cons.

PRINT METHODS

Fused Deposition Modeling (FDM)



FDM

Fused Deposition Modeling

- Melts and extrudes thermoplastic filament
- Lowest price of entry and materials
- Lowest resolution and accuracy

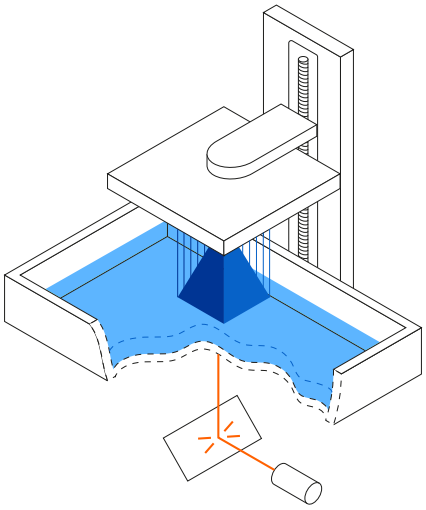
BEST FOR:

Basic proof-of-concept models and simple prototyping

FDM is the most widely used type of 3D printing at the consumer level. The FDM 3D printer functions by extruding molten thermoplastic (or metal) in layers onto a build area or platform until the 3D object is formed. Industrial-grade FDM 3D printers make use of a variety of thermoplastics.

PROS	CONS
• FDM 3D printing is the quickest printing process compared to other technologies. This makes it an excellent solution for 3D printing prototypes and iterative prototyping. • FDM works with diverse materials which support experimentation and prototyping • Industrial-grade FDM 3D printers can be equipped with relatively large build volumes that allow them to produce larger 3D models.	• FDM sports a lower resolution and accuracy level compared to other 3D printing technologies. Finished prints come with layer lines and require extensive post-processing activities to get high-quality printed objects. • FDM struggles to produce components with complex geometries at the high accuracy levels that medical devices require • Suppose attention to detail is a crucial requirement for producing a functional medical device. In that case, an FDM 3D printer will struggle to achieve excellent detailing due to its layered extrusion of filament.

Stereolithography (SLA)



SLA

Stereolithography

- Laser cures photopolymer resin
- Highly versatile material selection
- Highest resolution and accuracy, fine details

BEST FOR:

Functional prototyping, patterns, molds and tooling

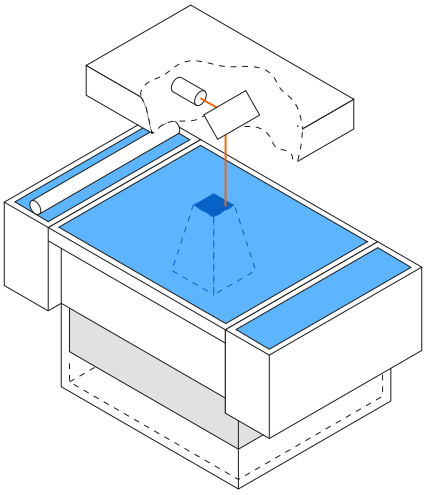
Another common 3D printing technology, SLA, involves using a laser to cure liquid resin within a vat into the 3D object. The curing process is known as photopolymerization, and it is capable of producing objects at very high resolutions. SLA resin 3D printers have become vastly popular for their ability to make high-accuracy, isotropic, and watertight prototypes and parts in a range of advanced materials with fine features and smooth surface finish. SLA resin formulations offer a wide range of optical, mechanical, and thermal properties to match those of standard, engineering, and industrial thermoplastics.

Traditionally, SLA 3D printers are relatively more expensive than many FDM offerings, but the technique brings some extensive features to the table. SLA 3D printers have the highest resolution and accuracy levels compared to other desktop 3D printers. SLA 3D printed parts are truly industrial-grade and can be used commercially as end-use products.

PROS	CONS
• SLA produces highly accurate objects at high resolutions, making it an excellent tool for prototyping and developing functional parts. • Excellent surface finishes (without lines and other defects that define FDM 3D printing) reduce the number of post-processing activities required. • Capable of producing a wide range of objects with great aesthetics and functional components, which is excellent for manufacturing precision devices. • Wide selection of biocompatible materials are available.	• Finished products must be stored properly as they are sensitive to UV light which, over time, causes the printed part to disintegrate. • Materials for 3D printing medical devices are relatively more expensive compared to FDM 3D printers.

For a comparison of FDM and SLA 3D printing technologies, please review the Formlabs comparison.

Selective Laser Sintering (SLS)



SLS

Selective Laser Sintering

- Laser fuses polymer powder
- Low cost per part, high productivity, and no support structures
- Excellent mechanical properties resembling injection-molded parts

BEST FOR:

Functional prototyping and end-use production

SLS is known across the industrial sector for its ability to produce high-performing end-use products. The SLS process involves using a powerful laser to fuse small particles of polymer powder into forming the finished part. During the 3D printing process, particles that are not fused support the fused structure, which means there is no need for additional support fixtures, unlike FDM and SLA printing.

The lack of supporting structures and the fusing process makes SLS ideal for developing complex medical device models. Coupled with the materials used, SLS can produce complex parts with a high tensile strength that can be put to practical use.

PROS	CONS
• SLS produces high-performing parts that are functional and can serve as prototypes and end-use products for commercial use • The design freedom that comes with a lack of need for supporting structures makes SLS an excellent technique for 3D printing complex parts with high resolution and accuracy • The industrial-grade prints SLS produces require little post-processing, which assists products go-to-market quicker	• The material limitations associated with SLS 3D printing mean manufacturers end up relying on nylon to satisfy the manufacturing process • SLS 3D printers are relatively more expensive compared to FDM and SLA 3D printers

	FUSED DEPOSITION MODELING (FDM)	STEREOLITHOGRAPHY (SLA)	SELECTIVE LASER SINTERING (SLS)
Resolution	●●○○○	●●●●●	●●●●○
Accuracy	●●●●○	●●●●●	●●●●●
Surface Finish	●●○○○	●●●●●	●●●●○
Throughput	●●●●○	●●●●○	●●●●●
Complex Designs	●●●○○	●●●●○	●●●●●
Ease of Use	●●●●●	●●●●●	●●●●○
Equipment Costs	Budget printers and 3D printer kits start at a few hundred dollars. Higher quality mid-range desktop printers start around $2,000, and industrial systems are available from $15,000.	Professional desktop printers start at $3,500, large-format benchtop printers at $11,000, and large-scale industrial machines are available from $80,000.	Benchtop industrial systems start at $18,500, and traditional industrial printers are available from $100,000.
Material Costs	$50-$150/kg for most standard and engineering filaments, and $100-200/kg for support materials.	$149-$200/L for most standard and engineering resins.	$100/kg for nylon. SLS requires no support structures, and unfused powder can be reused, which lowers material costs.
Labor Needs	Manual support removal (can be mostly automated for industrial systems with soluble supports). Lengthy post-processing is required for a high-quality finish.	Washing and post-curing (both can be mostly automated). Simple post-processing to remove support marks.	Simple cleaning to remove excess powder.

For a more in-depth comparison of FDM, SLA, and SLS technologies, please visit the Formlabs guide to 3D Printing Technology Comparison: FDM vs. SLA vs. SLS.

Selective Laser Melting (SLM) and Direct Metal Laser Sintering (DMLS)

SLM and DMLS printers work similarly to SLS printers, but instead of fusing polymer powders, they fuse metal powder particles together layer by layer using a laser. SLM and DMLS 3D printers can create strong, accurate, and complex metal products, making this process ideal for aerospace, automotive, and medical applications.

PROS	CONS
• DMLS is capable of producing high-performing end-use parts from metal • DMLS can reproduce complex geometries from metal. Thus, the finished product is strong and durable for commercial use.	• The start-up cost associated with purchasing a DMLS printer is costly compared to other 3D printing technologies. • DMLS is equipped with relatively small build volumes, which limits the size of parts that can be 3D printed

PRINT MATERIALS AND PROPERTIES

Now that you understand the different types of 3D printing technologies, it is essential to know which materials are compatible with the technology. This knowledge will help inform your decision on which 3D printing technology and material to select for manufacturing your device.

FDM

Plastic extrusion 3D printers work with a range of standard thermoplastic filaments, such as ABS, PLA, and their various blends. The popularity of FDM 3D printing in the hobbyist space has led to an abundance of color options; various experimental plastic filament blends also exist to create parts with wood- or metal-like surfaces.

Engineering materials, such as Nylon, PETG, PA, or TPU, and high-performance thermoplastics like PEEK or PEI are also available. Still, they are often limited to select professional FDM printers that support them.

Properties and comparisons of the most common FDM materials can be seen below.

MATERIAL	FEATURES	APPLICATIONS
ABS (acrylonitrile butadiene styrene)	Tough and durable Heat and impact resistant Requires a heated bed to print Requires ventilation	Functional prototypes
PLA (polylactic acid)	The easiest FDM materials to print Rigid, strong, but brittle Less resistant to heat and chemicals Biodegradable Odorless	Concept models Looks-like prototypes
PETG (polyethylene terephthalate glycol)	Compatible with lower printing temperatures for faster production Humidity and chemical resistant High transparency Can be food safe	Waterproof applications Snap-fit components
Nylon	Strong, durable, and lightweight Tough and partially flexible Heat and impact resistant Very complex to print on FDM	Functional prototypes Wear resistant parts
TPU (thermoplastic polyurethane)	Flexible and stretchable Impact resistant Excellent vibration dampening	Flexible prototypes
PVA (polyvinyl alcohol)	Soluble support material Dissolves in water	Support material
HIPS (high impact polystyrene)	Soluble support material most commonly used with ABS Dissolves in chemical limonene	Support material
Composites (carbon fiber, kevlar, fiberglass)	Rigid, strong, or extremely tough Compatibility limited to some expensive industrial FDM 3D printers	Functional prototypes Jigs, fixtures, and tooling

SLA

SLA 3D printing is highly versatile, offering resin formulations with a wide range of optical, mechanical, and thermal properties to match those of standard, engineering, and industrial thermoplastics.

SLA materials can be soft or hard, heavily filled with secondary materials like glass and ceramic, or imbued with mechanical properties like high heat deflection temperature or impact resistance.

Material range from industry-specific, like dentures, to those that closely match final materials for prototyping, formulated to withstand extensive testing and perform under stress.

FORMLABS MATERIALS	FEATURES	APPLICATIONS
Standard Resins	High resolution Smooth, matte surface finish	Concept models Looks-like prototypes
Clear Resin	The only truly clear material for plastic 3D printing Polishes to near optical transparency	Parts requiring optical transparency Millifluidics
Draft Resin	One of the fastest materials for 3D printing 4x faster than standard resins, up to 10x faster than FDM	Initial Prototypes Rapid Iterations
Tough and Durable Resins	Strong, robust, functional, and dynamic materials Can handle compression, stretching, bending, and impacts without breaking Various materials with properties similar to ABS or PE	Housings and enclosures Jigs and fixtures Connectors Wear-and-tear prototypes
Rigid Resins	Highly filled, strong and stiff materials that resist bending Thermally and chemically resistant Dimensionally stable under load	Jigs, fixtures, and tooling Turbines and fan blades Fluid and airflow components Electrical casings and automotive housings
High Temp Resin	High temperature resistance High precision	Hot air, gas, and fluid flow Heat resistant mounts, housings, and fixtures Molds and inserts
Flexible and Elastic Resins	Flexibility of rubber, TPU, or silicone Can withstand bending, flexing, and compression Holds up to repeated cycles without tearing	Consumer goods prototyping Compliant features for robotics Medical devices and anatomical models Special effects props and models
Medical and dental resins	A wide range of biocompatible resins for producing medical and dental appliances	Dental and medical appliances, including surgical guides, dentures, and prosthetics
Ceramic resin	Stone-like finish Can be fired to create a fully ceramic piece	Engineering research Art and design pieces

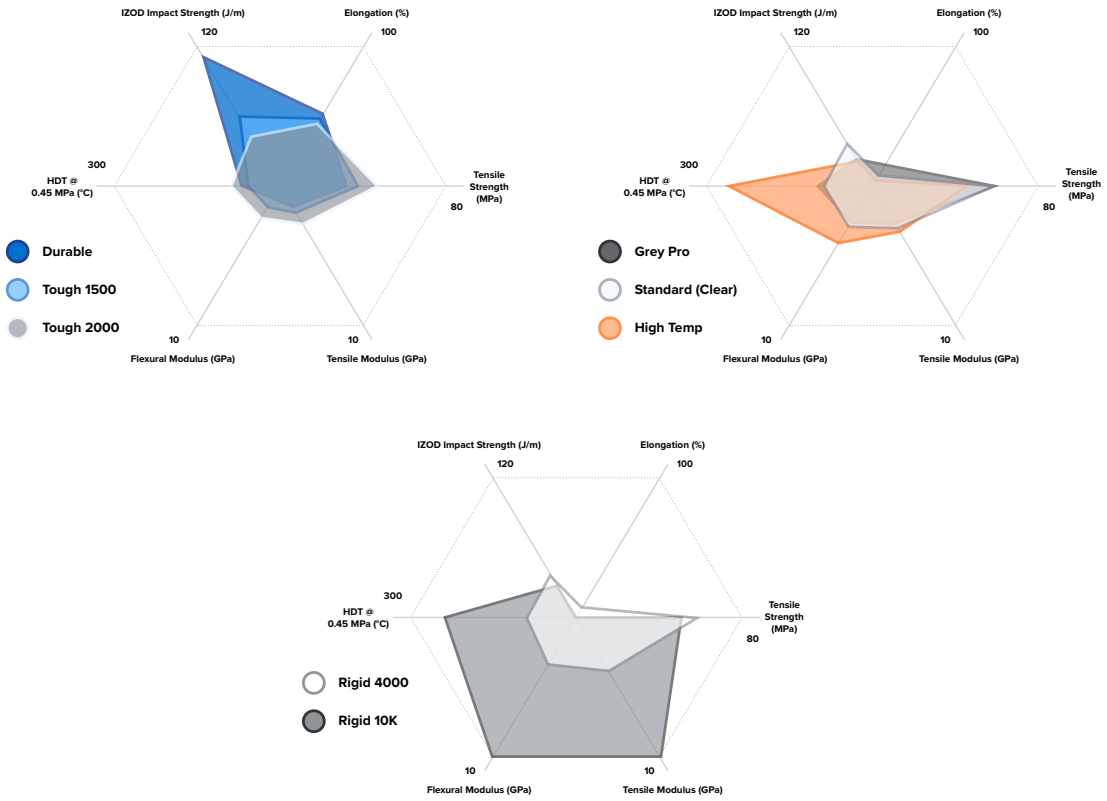


Image: Comparison of material properties of Formlabs SLA resins. For an interactive comparison of Formlabs resins, please visit the Formlabs materials comparison page.

For a materials selection guide, please visit our interactive material selector.

For a more detailed guide on each Formlabs resin, their printer compatibility, material properties, and print settings, please review the Formlabs guide to choosing the right material.

SLS

The material selection for SLS is limited compared to FDM and SLA, but the available materials have excellent mechanical characteristics, with strength resembling injection-molded parts. The most common material for selective laser sintering is nylon, a popular engineering thermoplastic with excellent mechanical properties. Nylon is lightweight, strong, and flexible, as well as stable against impact, chemicals, heat, UV light, water, and dirt.

3D printed nylon parts can also be biocompatible and not sensitizing, which means that they are ready to wear and safe to use in many contexts.

MATERIAL	DESCRIPTION	APPLICATIONS
Nylon 12	Strong, stiff, sturdy, and durable Impact-resistant and can endure repeated wear and tear Resistant to UV, light, heat, moisture, solvents, temperature, and water	Functional prototyping End-use parts Medical devices
Nylon 11	Similar properties to Nylon 12, but with a higher elasticity, elongation at break, and impact resistance, but lower stiffness	Functional prototyping End-use parts Medical devices
TPU	Flexible, elastic, and rubbery Resilient to deformation High UV stability Great shock absorption	Functional prototyping Flexible, rubber-like end-use parts Medical devices
Nylon composites	Nylon materials reinforced with glass, aluminum, or carbon fiber for added strength and rigidity	Functional prototyping Structural end-use parts

Metal

SLM and DMLS can produce parts from an extensive range of metals, some of the most popular being:

- **Titanium:** lightweight and has excellent mechanical characteristics. It is strong, hard, and highly resistant to heat, oxidation, and acid.
- **Stainless steel:** high strength, high ductility, and is resistant to corrosion.
- **Aluminum:** lightweight, durable, strong, and has good thermal properties.
- **Tool steel:** hard, scratch-resistant material that you can use to print end-use tools and other high-strength parts.
- **Nickel alloys:** high tensile, creep, and rupture strengths and are heat and corrosion-resistant.

These materials can be used for many industrial applications spanning a variety of industries. Precious metals can also be 3D printed, but their applications are mainly limited to jewelry making (Source: Hubs).

A key strength of metal 3D printing is its compatibility with high-strength materials, such as nickel or cobalt-chrome superalloys that are very difficult to process with traditional manufacturing methods. Using metal 3D printing lets one create a near-net-shape part that can be later post-processed to a very high surface finish (Source: Hubs).

For more information on specific material properties for metal 3D printing, please refer to the Hubs Introduction to metal 3D printing.

4. Evaluate 3D Printer and Material Manufacturers

MATERIAL BIOCOMPATIBILITY

Biocompatibility information is required for 510(k) and premarket approval (PMA) submissions in the United States and other regulatory submissions worldwide. It proves whether the device will be compatible with the biological system in which it is intended. Missing or inadequate information can lead to significant delays in bringing the device to market.

Biocompatibility testing requirements should be determined based on the intended use of the device (type, area, and duration of exposure). Determining testing requirements early in the development process will allow ample time to complete testing before submission to regulatory bodies. It should stem from the expected contact between the device and the human body. Three different categories typically define contact:

1. Direct Contact: Comes into physical contact with the patient.
2. Indirect Contact: Comes into physical contact with a fluid, gas, or other material that has direct contact with the patient.
3. No Contact: Does not have direct or indirect contact with the patient and is therefore exempt from biocompatibility requirements.

Formlabs conducts biocompatibility testing based on ISO 10993, ISO 18562, and ISO 7405 standards and publishes the information on relevant resins. As the testing is conducted on standardized printed samples, manufacturers with complex design geometries and other modifications must independently validate the biocompatibility of the finished devices for their intended use. The below table contains information on types of biocompatibility testing based on bodily contact and duration of contact.

DEVICE CATEGORIES			BIOLOGICAL EFFECTS							
Device Type	**Body Contact**	**Contact Duration** **Limited** ≤ 24 Hr **Prolonged** 24 Hr–30 Days **Permanent** ≥ 30 Days	Cytotoxicity	Sensitization	Irriation or Intractuaneous	Reactivity System (Acute) Toxicity	Subchronic Toxicity	Genotoxicity	Implantation	Hemocompatability
SURFACE DEVICES	Skin	Limited	X	X	X	-	-	-	-	-
		Prolonged	X	X	X	-	-	-	-	-
		Permanent	X	X	X	-	-	-	-	-
	Mucosal Membrane	Limited	X	X	X	-	-	-	-	-
		Prolonged	X	X	X	0	0	-	0	-
		Permanent	X	X	X	0	X	X	0	-
	Breached or Compromised Surfaces	Limited	X	X	X	0	-	-	-	-
		Prolonged	X	X	X	0	0	-	0	-
		Permanent	X	X	X	0	X	X	0	-
EXTERNAL COMMUNICATING DEVICES	Blood Path, Indirect	Limited	X	X	X	X	-	-	-	X
		Prolonged	X	X	X	X	0	-	-	X
		Permanent	X	X	0	X	X	X	0	X
	Tissue/Bone/Dentin Communicating†	Limited	X	X	X	0	-	-	-	-
		Prolonged	X	X	0	0	0	X	X	-
		Permanent	X	X	0	0	0	X	X	-
	Circulating Blood	Limited	X	X	X	X	-	0‡	-	X
		Prolonged	X	X	X	X	0	X	0	X
		Permanent	X	X	X	X	X	X	0	X
IMPLANT DEVICES	Tissue/Bone	Limited	X	X	X	0	-	-	-	-
		Prolonged	X	X	0	0	0	X	X	-
		Permanent	X	X	0	0	0	X	X	-
	Blood	Limited	X	X	X	X	-	-	X	X
		Prolonged	X	X	X	X	0	X	X	X
		Permanent	X	X	X	X	X	X	X	X

X = ISO 10993-1 tests 0 = Additional tests that may be applicable † = Tissue includes tissue fluids and subcutaneous spaces ‡ = For all devices used in extracorporeal circuits

Image: Information on types of testing based on bodily contact and duration

FORMLABS CERTIFICATIONS AND STANDARDS

Formlabs printers, materials, and associated products comply with various safety and quality standards in different jurisdictions. For statements and documentation related to medical device standards, QMS, environmental standards, HIPAA compliance, FDA Master Files, TSCA, electrical safety, and more, please visit the Formlabs certifications and standards article here.

Product manufacturers using 3D printers for production must ensure that medical devices are accurate, reliable, and safe. This is only facilitated through rigorous workflow validation, testing, and control. Further, recent changes in global regulatory requirements for medical device production brings controlled workflows to the forefront for future-proofing manufacturer capabilities. If you are evaluating printer manufacturers and are curious about open-mode platforms (i.e., bring your own resin) and controlled-mode systems, please visit this page for more information.

SUPPLIER SELECTION AND MANAGEMENT

The reliability of a supplier can impact the supply chain operations for your medical device and, frankly, your bottom line. For a closer look at how the supplier process works in the medical device industry and the steps manufacturers need to follow when selecting a supplier, please review the "Choosing and Managing Your Medical Device Suppliers" article from Greenlight Guru, which includes details for purchasing processes from FDA 21 CFR §820.50 and ISO 13485:2016, Section 7.4.1. Supplier selection criteria should include a review of the supplier's corrective and preventive action (CAPA) procedures, training, testing and validation, cleanliness or sterilization procedures in their facility, labor practices, and standards of current good manufacturing practices.

The supplier and the manufacturer should have a formal agreement outlining the relationship's expectations and requirements (e.g., quality agreement, supply agreement specification, and material or component specification). At a minimum, this should include preferred test methods, properties required, and any critical process controls for ensuring the production of safe, effective products that are of a consistent standard. Your supplier agreement should also contain some requirements around communication, especially in the event of deviations or nonconformances. There should also be easily accessible CAPA procedures in place that can be followed to rectify quality events as needed.

Once you select a supplier, your organization will need a robust quality system for managing and storing all of your supplier management records. It's something you will be audited for; supplier management has always been a frequent source of audit findings and continues to be closely looked at by auditors and inspectors. Greenlight Guru allows you to keep your approved supplier list, your documented procedures, and evidence of your evaluations easily accessible and always up-to-date to ensure the most optimal supplier management.

Please visit these links for an approved supplier list and a checklist for selecting suppliers and contract manufacturers, provided by Greenlight Guru.

5. Consider QA/RA Requirements And Constraints

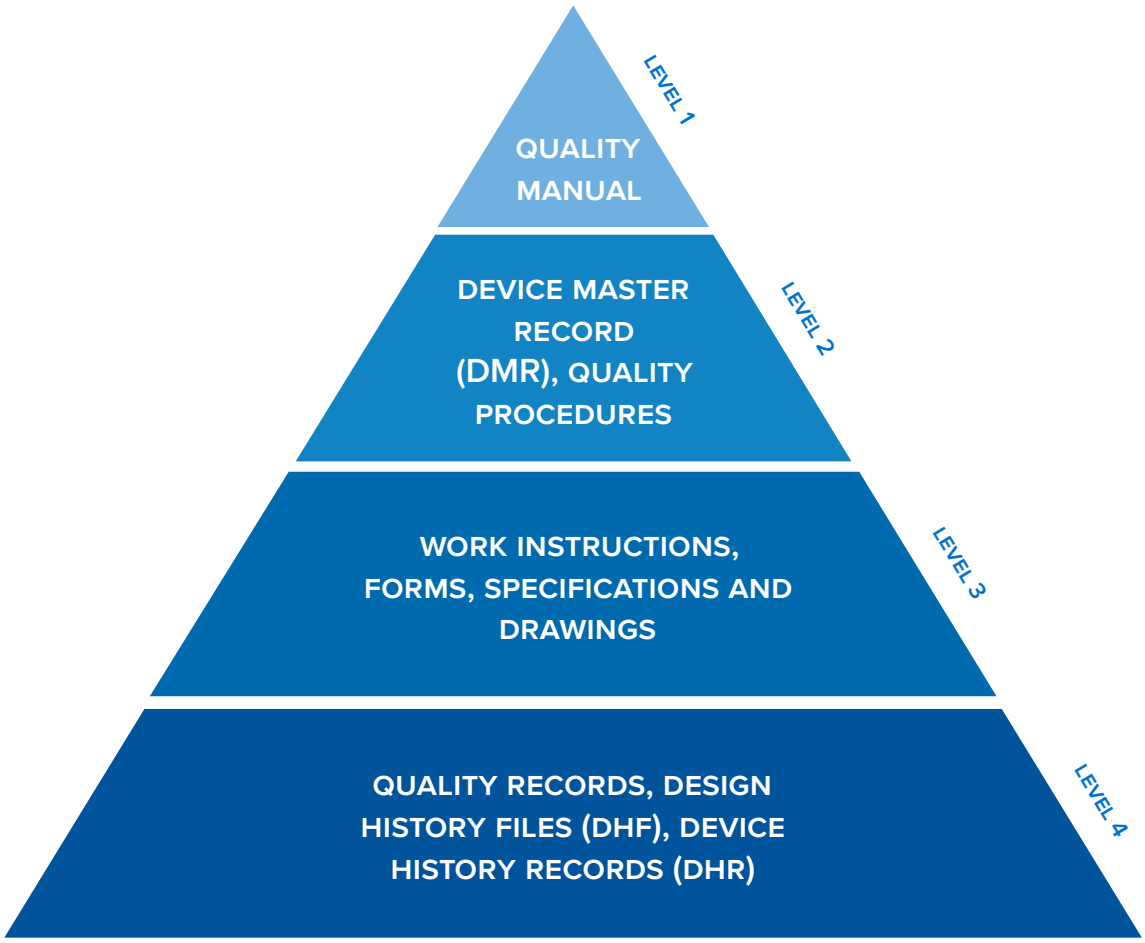
TAKEAWAYS FROM REGULATORY AND STANDARDS BODIES

This section will include perspectives and recommendations related to ISO 13485, ISO 10993, ISO 14971, and FDA and MDR considerations.

ISO 13485

According to the American Society for Quality (ASQ), a quality management system (QMS) is defined as: "A formal system that documents the structure, processes, roles, responsibilities, and procedures required to achieve effective quality management."

A QMS is comprised of the core set of business policies, procedures, forms, and work instructions, along with their sequence, interactions, and resources required to conduct business within a medical device company. Quality records are documentation that demonstrate the QMS is being executed and followed.



Example of QMS Hierarchy

> *"To align with ISO 13485:2016, contents of your QMS should address the specific, applicable requirements of the international standard, as well as the specific, applicable regulatory requirements of the markets where you plan to manufacture and market medical devices."*
>
> **Greenlight Guru**

If you are like the majority of the medical device industry, chances are you have a QMS that is a combination of paper-based processes and general-purpose tools, loosely held together by a group of people within your company – usually document control. Greenlight Guru has an industry-specific software platform architected to support the requirements of ISO 13485:2016 (and other regulatory requirements), where the requirements are addressed automatically with no configuration required. Please review the Ultimate Guide to ISO 13485 QMS for Medical Devices that will, in large part, follow the major sections and headings of ISO 13485:2016, and provide you specific, actionable steps and best practices you can apply in your medical device company.

Note: Even if you choose to outsource any process(es) that impacts requirements of the standard (for example, contract manufacturing), it is your responsibility to monitor and ensure controls over the outsourced processes. This includes defining roles and responsibilities in documented quality agreements with any outsourcing resources.

ISO 14971

Risk Management, per ISO 14971, is defined as the combination of the probability of occurrence of harm and the severity of that harm. The intent behind Risk Management is to identify, evaluate, analyze, assess, and mitigate potential product issues. Risk Management is a total product life cycle process.

The topic of Risk Management can be daunting and, at times, confusing. Thankfully, ISO 14971 exists and helps provide guidance and direction. ISO 14971 provides a thorough explanation of relevant terms and definitions and defines a risk management process. Greenlight Guru has written the Ultimate Guide to ISO 14971 to align with the latest version of ISO 14971 and provide you additional tips and insights for medical device risk management. Note that the focus of the ultimate guide is strictly medical device product risk management.

Nearly every medical device regulatory agency has placed the topic of Risk Management front and center. In fact, regulatory agencies, including the FDA, are now using risk-based processes throughout their internal processes when reviewing device submissions and conducting inspections and audits. The U.S. FDA, Health Canada, EU Competent Authority, Australia TGA, and Japan MHLW require you to have a Risk Management process defined and Risk Management documentation for your products. These regulatory agencies also recognize ISO 14971 - Medical devices – Application of Risk Management to Medical Devices.

The current version of ISO 14971 was released in December 2019. This version replaced the previous two versions of the standard utilized by many of you worldwide: ISO 14971:2007 and EN ISO 14971:2012. The EN version was applicable if you were selling medical devices in Europe. While there is still an EN version of ISO 14971:2019, it is now identical to the regular version of ISO 14971:2019. When selling in Europe, it is essential to know that additional risk requirements apply, outlined in the EU MDR (more on the MDR later in this guide).

For a visual overview of risk management for medical devices, see the charts below:

RISK MANAGEMENT FOR MEDICAL DEVICES

AS DEFINED BY ISO 14971

The purpose of this infographic and the ISO 14971 standard is to help med device manufacturers establish a risk management process that they can use to:
Identify Hazards
Estimate and evaluate Risks
Develop, Implement and Monitor the Effectiveness of Risk Control Measure

1 ESTABLISH A RISK MANAGEMENT FRAMEWORK

- Define your risk management process
- Establish management roles and responsibilities
- Document your risk management plan
- Establish a living risk management file

2 SPECIFY INTENDED USE

Understand and define the scope of your device and document intended to use

3 IDENTIFY HAZARDS

Identify the potential sources of harm associated with your product. These are known as Hazards

4 DEFINE HAZARDOUS SITUATIONS AND FORESEEABLE SEQUENCE OF EVENTS

Estimate risk of each hazardous situation

5 ESTIMATE RISK

Risk is the combination of severity of potential harm and probability of that harm occuring.

6 EVALUATE THE RISKS IDENTIFIED

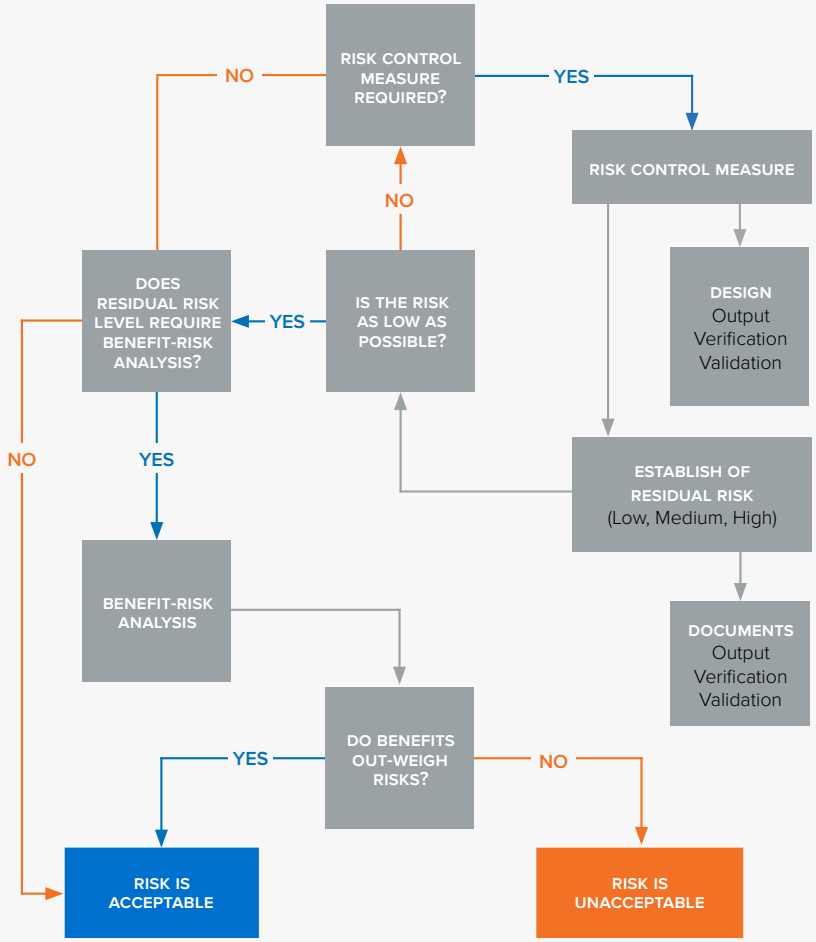
- Are these risk levels acceptable?
- Is risk required?

Probability	NEGLIGIBLE No or negligible risk to patient	MINOR Slight customer inconvenience; little to no effect on product performance, non- vital fault	SERIOUS Short-term injury or impairment requiring additional medical intervention to correct (e.g. reoperation)	MAJOR Severe, long-term injury; potential diability	CRITICAL Loss of limb; life-threatening injury.
FREQUENT 1 in 100		REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis
PROBABLE 1 in 1,000		REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis
OCCASIONAL 1 in 10,000			REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis
REMOTE 1 in 100,000				REQUIRES Benefit-Risk Analysis	REQUIRES Benefit-Risk Analysis
IMPROBABLE 1 in 1,000,000					REQUIRES Benefit-Risk Analysis

Severity

7 RISK CONTROL

Use Risk Controls to reduce risks to acceptable levels



8 EVALUATION OF OVERALL RISK ACCEPTABILITY

- Evaluate rish of the product in it's entirety
- Is this risk level acceptable?
- Do the benefits outweigh the potential risks?

9 RISK MANAGEMENT REIVIEW

Carry out a risk management review and prepare a risk management report before sending your device to commercial production.

10 PRODUCTION AND POST-PRODUCTION INFORMATION

Internal audits, CAPAs, complaints, customer feedback and non-conforming materials all 'feed' into the risk management process.
Risk management is a total product lifecycle process.

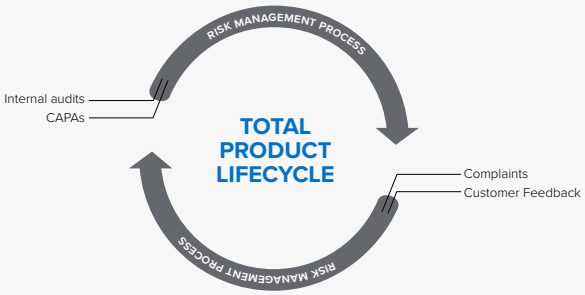


Image: A visual overview of risk management for medical devices, as outlined in ISO 14971

ISO 10993

ISO 10993-1 is the medical device industry's globally recognized standard for the biological evaluation of medical devices, and the protection of humans is its primary goal.

Conducting a biological risk assessment is an essential first step of demonstrating the biocompatibility of your medical device and should be done within the framework of a risk management process.

A biological evaluation should involve a comprehensive risk assessment of your:

- medical device,
- material components of the device,
- manufacturing processes, and
- clinical use of the device, including anatomical location as well as frequency and duration of exposure.

Following the first phase of the biological evaluation process, knowledge gaps and other significant findings will need to be compiled into a biological evaluation plan (BEP). Your BEP will serve as your initial risk assessment and guide you in addressing known risks. This is typically done by way of biocompatibility testing and further evaluation.

After you've identified and documented all known risks in your BEP, the next step is to address those risks by following the requirements from ISO 10993-1 for biological testing.

Biological testing and evaluation are most commonly carried out via:

- Written evaluation based on scientific literature and any clinical use of the materials.
- In vivo or in vitro biological tests.
- Chemistry tests along with toxicological risk assessment.

As mentioned when we discussed medical-grade materials in Chapter 3, biological testing isn't something to leave until the last minute; it should be considered right from the onset of the product lifecycle and undoubtedly well before you are ready to send in your product submission for regulatory review.

The third step you'll want to follow when applying the requirements from ISO 10993-1 is to create a biological evaluation report. This final report summarizes the overall biological risk evaluation and assessment, substantiated by data and objective evidence. You also need to include a formal statement confirming the biological risk analysis and risk controls that have been completed.

Formlabs has tested multiple materials for biocompatibility and sterilization compatibility, including medical, dental, and engineering resins, as well as our nylon powders. As of this writing, the list of testing on commercially available resins can be seen below. Reports can be downloaded from this page.

		Contact Type	Skin	Mucosal Membrane	Mucosal Membrane	Breathing Gas Pathways	Pharmaceutical Containers, Drug Delivery, and Medical Device Components	
		Duration of Contact	> 30 days	<24 hr	>30 days	> 30 days	> 30 days	
		ISO Standard	EN ISO 10993-1 EN ISO 10993-3 EN ISO 10993-5	EN ISO 10993-1 EN ISO 10993-3 EN ISO 10993-5	EN ISO 10993-1 EN ISO 10993-3 EN ISO 10993-5 EN ISO 10993-10 EN ISO 10993-11	EN ISO 18562-1 EN ISO 18562-2 EN ISO 18562-3 EN ISO 18562-4	USP <88> Class VI	Sterilization Compatibility
Medical (SLA) [1]	BioMed Clear Resin		✓	✓	✓	✓	✓	Steam, Gamma, EtO, E-Beam
	BioMed Amber Resin		✓	✓				Steam, Gamma, EtO, E-Beam
Dental (SLA) [1]	Dental LT Clear V2 Resin		✓	✓	✓			
	Surgical Guide Resin		✓	✓				Steam
	Custom Tray Resin		✓	✓				
	IBT Resin Resin		✓	✓				
	Temporary CB Resin		✓	✓	✓			
	Permanent Crown Resin		✓	✓	✓			
	Denture Base Resin		✓	✓	✓			
	Denture Teeth Resin		✓	✓	✓			
	Dental LT Clear V1 Resin		✓	✓	✓			
Engineering (SLA)	Tough 1500 Resin		✓					Steam, Gamma, EtO, E-Beam
Fuse (SLS)	PA 12 Powder		✓	✓				Steam, Gamma, EtO, E-Beam
	PA 11 Powder		✓					Steam, Gamma, EtO, E-Beam

[1] All Medical and Dental Resins listed above are ISO 13485 and ISO 14971 compliant

Image: Biocompatibility and sterilization compatibility testing conducted on Formlabs resins. Source: Formlabs Standards and Certifications

Note: Specific sterility assurance levels may be impacted by variables such as manufacturing conditions, part geometries, packaging types, and sterilization modalities.

21 CFR 820

21 CFR Part 820 is a set of FDA quality system regulations (QSR) that outlines the current good manufacturing practice (CGMP) requirements that medical device manufacturers in the United States must follow regarding their quality system. These CGMP requirements ensure medical device companies establish a QMS that enables the delivery of safe, effective, and compliant products.

As stated by the FDA, 21 CFR Part 820 covers “the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use,” including the facilities and designs used for those processes.

In Section 820.3, you will see definitions for over 30 different terms used throughout the document that are meant to ensure manufacturers and regulators share a common understanding of the terminology in use. If you're confused about the meaning of a term, refer to Section 820.3 or lean on trusted, outside resources, such as the Greenlight Guru list of the top medical device terminology.

21 CFR Part 820, though a dense document, lays out medical device QSR in a digestible way for manufacturers to best interpret and apply to their own specific device. The QSR consists of 15 subparts and is structured by way of order, from big picture questions regarding scope to detailed rules about what manufacturers should do and when.

The FDA conducts regular inspections to ensure compliance with its QSR. The FDA uses the Quality System Inspection Technique (QSIT) to evaluate the alignment of internal quality system processes with regulatory requirements. The stakes of compliance are clear.

For more information on 21 CFR Part 820, use this in-depth, easy-to-understand guide from Greenlight Guru that paints a comprehensive picture of the document by explaining the regulations in a way that is easy to understand. Each subpart of the regulation is accompanied by specific advice on how you can comply and common mistakes manufacturers make, so you can make sure to avoid the pitfalls.

In 2018, the FDA announced plans to harmonize 21 CFR Part 820 with ISO 13485:2016, though not much progress has been made on this front. The main difference between the two regulations is that ISO 13485:2016 is a voluntary standard that defines quality system requirements. 21 CFR Part 820 comes from the FDA, a federal agency, meaning that non-compliance can incur punitive measures that range from citations to recalls to fines and, in rare cases, to litigation. While the FDA is local to the United States, much of the world recognizes and follows ISO standards.

FDA: TECHNICAL CONSIDERATIONS FOR AM MEDICAL DEVICES

In December 2017, the Center for Devices and Radiological Health within the US FDA issued a guidance document specific to devices using additive manufacturing (AM) titled Technical Considerations for Additive Manufactured Medical Devices. Per the FDA: "The purpose of this guidance is to outline technical considerations associated with AM processes, and recommendations for testing and characterization for devices that include at least one additively manufactured component or additively fabricated step." Please review the table below for an overview of the various requirements, regulatory considerations, and links to relevant resources from Formlabs or Greenlight Guru.

		CONSIDERATIONS [COMMERCIAL MED DEVICE FIRMS OR POINT-OF-CARE (POC) MANUFACTURERS]	FORMLABS RECOMMENDATIONS, STATEMENTS, AND SUPPORTING RESOURCES

OVERALL DEVICE DESIGN	GENERAL	[Market segment: medical device and POC]
		• Compare desired feature sizes of the final finished device to the minimum possible feature size of your AM technique and the manufacturing tolerances of the individual machine.
		  ◦ This helps you compare build parameters and conditions under which the final device is expected to be made to your design.
		  ◦ The purpose of this comparison is to determine the reliability of the print.
		• Pixelation of features (when smooth surfaces become stepped) can lead to rougher surface finishes.
		  ◦ Some devices require smooth surface finishes for patient safety.
		  ◦ Surface finish requirements should be documented in specifications.
			***Formlabs is not involved in this step of the process. Device design should be performed prior to loading a file in PreForm to ensure desired device specifications. Model smoothing and any other surface alterations performed before printing should be completed before loading a file in PreForm to ensure the desired surface finish.**
			• MeshMixer is a useful tool for smoothing, meshing, sculpting, and modifying/preparing structures for printing. For a Meshmixer tutorial, click here.
			• The Formlabs ecosystem integrates smoothly with Rhino, SolidWorks, OnShape, 3Shape (dental focused), Fusion 360, and Netfabb CAD systems to streamline the print process.

PATIENT-MATCHED DEVICE (PMD) DESIGN	INTRO	[Market segment: POC]
		• PMDs may be produced within a defined design or performance envelope
		  ◦ This envelope is determined before patient matching can be initiated.
		  ◦ The envelope describes the minimum and maximum dimensions, mechanical performance limits, and other clinically relevant factors.
		• PMDs are NOT customized devices meeting the FD&C Act custom device requirements.
		  ◦ Most PMDs fall under the requirements for their respective device type.
		• Modifications of design may have direct consequences for the patient.
		  ◦ You should identify clinically relevant design parameters, the predetermined range for these parameters, and which of the parameters can be modified for patient-matching before the device can be used by any patient.
			***Formlabs is not involved in this step of the process. Design and performance envelopes should be determined and analyzed before uploading to PreForm. The use of Formlabs printers may be part of your prototyping process to refine your design or performance envelope, but Formlabs is not involved in the actual designing of devices.**

	EFFECTS OF IMAGING	[Market segment: POC] • Factors that may affect the fit and performance of AM image-based PMDs include: minimum image feature quality and resolution; smoothing or image processing algorithms that may alter dimensions when compared to reference anatomy; rigidity of anatomic structures being imaged; and clarity of anatomic landmarks used to match the device to the patient's anatomy. • Small changes in size or geometry may be difficult to identify during visual inspection of the device and may only be detected once in use by a patient. It is also important to note the range of changes (e.g., deformation) that may be experienced by soft tissue at a target location when comparing true anatomy to a reference image. This should be considered when designing and testing your device. • Anatomy can change over time (e.g., disease progression), even between the time the patient is imaged and the device used. This allowable time should be noted as an expiration date of the device. *You should employ a risk-based approach, taking into consideration the intended use of your device as well as your design methodologies to assess worst-case scenarios.	***Formlabs is not involved in this step of the process. Imaging and design should be completed before loading a file in PreForm to ensure the correct specifications of the part.** • Formlabs does not convert image files to 3D-printable files, but we recommend overlaying created 3D models on the images to ensure that the model accurately represents the target anatomy's dimensions and form. • The changes in anatomy over time should be considered when determining the required lead time for the PMD manufacture. • Visit the Formlabs Clinical Innovator Web Series to hear directly from clinicians about imaging, segmentation, sterilization, and other workflow requirements. • Consider clinical literature, including Methods for verification of 3D printed anatomic model accuracy using cardiac models as an example, when verifying anatomical model accuracy.
	INTERACTING...*	[Market segment: POC] • PMDs are often made by altering features of standard-sized devices. This is typically done through device manipulation software. • Feature alterations can also be done by manual methods using key anatomic landmarks or specific measurements on radiographs. • Any software or procedure used to make modifications to device design based on clinical input should include internal checks that prevent the operator from exceeding determined pre-established device specifications	***Formlabs is not involved in this step of the process. Design interaction and manipulation should be completed before loading a file in PreForm to ensure the correct specifications of the part.** If any part is altered using any CAD software, Formlabs recommends including internal checks that prevent the user from over-modifying the part before printing.
	COMPLEX DESIGN FILES	[Market segment: POC] • PMDs that follow patient anatomy closely are especially vulnerable to errors in file conversion. For example, anatomic curves are typically geometrically or mathematically complex, increasing the likelihood of error. • For PMDs, all file conversion steps are typically performed every time a device is built instead of once during the design phase of a standard-sized device. This means you should perform internal checks for each model to prevent inaccurate devices. ◦ See Section V.C.I.A(1) on data integrity in the FDA guide for more information.	***Formlabs is not involved in this step of the process. All design and model files should be converted and checked against the anatomical reference to ensure accurate models.** Formlabs recommends converting files to OBJ or STL files before uploading to PreForm for each patient-specific device created to ensure quality printed devices. A single conversion during the design of a standard-sized device could lead to design errors and unmet specifications during file conversion. Files can be adapted, repaired, and finalized before printing • Dedicated tools available for both automatic and manual STL repair functions: Meshmixer, Meshlab, Magics, Blender, Netfabb • See the "repaired" hyperlink for tutorials on each resource and details on STL repairs

*Interacting with Design Models

PATIENT-MATCHED DEVICE (PMD) DESIGN

CYBERSECURITY AND PII

[Market segment: Medical device and POC]

- Proper management and care of PII and PHI are essential to maintain patient privacy throughout the device design and manufacturing process.
  - See HHS Guidance on Significant Aspects of the Privacy Rule for more information on patient privacy.

- The Formlabs website and optional Dashboard service use HTTPS URLs and are encrypted using industry-standard 256-bit RSA encryption.
  - Formlabs stores data using Amazon Web Services, whose infrastructure and controls are subject to annual SAS-70 Type II audits and AWS information security management processes and whose controls have achieved ISO 27001 certification.
- Formlabs hardware encrypts all outside traffic via SSL, firmware updates are signed and encrypted, hardware uses only a single port (35) to handle all print upload and device communication with PreForm, and hardware uses industry-standard multicast DNS for device discovery.
- All remote print jobs are stored on the private Formlabs AWS account. During transit, information is encrypted through HTTPS SSL before reaching the private account. Uploads and downloads are secured through signed, temporary, and single-use upload URLs.

For more information on Formlabs security, please visit our Connectivity and Security page.

*While Formlabs has security measures in place, it is recommended to avoid using PII and PHI in any file names to comply with HIPAA.

SOFTWARE WORKFLOW

FILE FORMAT CONVERSIONS

[Market segment: Medical device and POC]

- Medical device design and manufacture typically involve interaction between several software packages, often from different manufacturers. This requires files to be compatible across the different software applications used to maintain design and file integrity.
- Errors in file conversion can negatively impact your final device and component properties, including dimensions and geometry.
  - Because of this, you should verify critical attributes and performance criteria of your final product as part of your software workflow validation.
- When possible, final device files for printing should be maintained and archived or referenced in robust, standardized formats that can store AM-specific information (i.e., AMF format).

***All file format conversions should be completed before uploading to PreForm to ensure the file's highest quality print and compatibility with the Formlabs ecosystem.**

Formlabs software (PreForm) is compatible with OBJ and STL files. Regardless of where the file is created, the file must be uploaded to PreForm in either of these two forms.

- Files/designs can often be exported from CAD software as OBJ or STL files that can then be uploaded to PreForm for printing preparation.

DIGITAL DEVICE DESIGN TO PHYSICAL DEVICE

[Market segment: Medical device and POC]

- **Build volume placement**: The distance between each device or component in the build volume and whether they are identical or different designs can affect material properties, surface finish, and ease of post-processing. Build orientation of each device can also impact functional performance by affecting anisotropic properties. Many machines have areas of the build volume where they function optimally and areas where they do not. This affected region may be different for every machine.
  - Your operational qualification (OQ) should include challenging the build volume placement to establish control limits resulting in products that meet all requirements.
- **Addition of support material:** The location, type, and the number of supports in your print can affect a final finished device's geometric accuracy and mechanical properties. Each AM machine and technology have different support needs to produce a quality device. Most supports from any machine can be removed physically or by chemical means.
  - Automated algorithms can be used to choose the location and number of supports, but geometric complexities or printing limits often require manual intervention when adding supports to a print file.
  - Common structures that may need support include overhangs, high aspect ratio features that protrude from the main body of the device, internal features, and thin features prone to warping.
  - All manufacturing material removal processes should ensure that material residues are removed to the level where they do not impact the safety or effectiveness of the device.
- **Slicing:** Nominal layer thickness is determined by machine specifications and software capabilities. However, the machine's technical characteristics and the material' may further influence achievable layer thickness.
  - Choice of layer thickness should be documented and reflect a balance between the achievable and desired surface texture, bonding between and curing of each layer, sensitivity to power fluctuations, accuracy, quality, and printing speed.
- **Build Paths:** The path traced by the energy or material delivery system can impact the quality of your final device. The space between each line of the build path and the path speed change the amount of melting and remelting that the boundaries of each line of material will experience. Further, certain build path selections may result in an orientation or anisotropy in the device.

Build Volume Placement

- PreForm has a function that auto-orients a part in the build volume of your selected printer. Please read below for further considerations on manual orientation practices.
- SLA: Formlabs suggests model orientation best practices, including tilting flat surfaces to 10-20°, preserving integrity at intersections, preserving fine details on your models, preventing suction cups, and reducing minima. Some Formlabs considerations on SLA build plate placement include:
  - It is recommended to place parts close to the center of the build platform.
  - A crowded build platform can harm print quality.
  - To reduce print time on a Form 2, you can place the longer supports closer to the wiper side. On a Form 3, you can orient your parts to be parallel to the mixer side.
- SLS: Formlabs suggests positioning parts as close to the center of the build volume as possible, orienting parts at an angle to avoid warping, distributing parts uniformly within the build volume, and positioning parts for assembly parallel to each other or with mating surfaces facing upward.

Support Material

- Support structures reinforce overhangs and other delicate features. Because of this reinforcement, supports increase the likelihood of print success but also increase the amount of post-processing work. However, if a model is entirely self-supporting, it can be printed directly on the build platform without the need for supports.
- In PreForm, supports can be auto-generated to ensure print success or added manually. Auto-generated supports can also be edited after being applied to the model. Be sure to keep in mind that even if the model is supported, adding too few supports can cause warping of thin prints. To avoid this issue, Formlabs recommends using PreForm's auto-generated supports.
- Supports can sometimes be removed by hand but may require clipping with needle-nose pliers or Exacto knives. It is recommended to clip them as close to the part as possible to avoid further post-processing steps, as support material that cannot be removed with tools may need to be sanded.
- When selecting a printing method, one thing to keep in mind is that SLS printing does not require supports for any print.

SOFTWARE WORKFLOW	DIGITAL DEVICE DESIGN TO PHYSICAL DEVICE	Before printing, you should assess whether differences in the build path have the potential to significantly affect the performance of your device (if so, it is essential to maintain consistency). If a non-solid fill density is used, you should identify whether internal voids are externally accessible or sealed. If they are not sealed, you should assess the risk associated with patient exposure. Machine Parameters and Environmental Conditions: Proper calibration and preventative maintenance are critical factors in achieving low rejection rates. To maintain the desired and acceptable calibration, machine parameters can be modified. Environmental conditions in the build volume can also affect final device quality; for those without a self-contained build volume, ambient temperature, atmospheric composition, and flow patterns can impact solidification, layer bonding, and mechanical properties. Finally, optimal settings and parameters for a single model of a machine can vary when printing different devices or for multiple models of a machine printing the same device. Because of its effect on device quality, it is critical to establish and maintain procedures to control environmental conditions. Parameters that may have a significant impact on the final device may include instantaneous power of the energy delivery system, build speed or beam speed, build path, total energy density, and focal point or nozzle diameter.	**Slicing** PreForm's Slicer tool allows you to see inside a model by displaying the model in layers in the order they will be printed. If you do not use auto-generated supports, this can be a good method for determining whether or not supports are needed for your model and where they may be needed. The layer size for your print can be adjusted in PreForm, depending on the material selected. Formlabs layer sizes range from 25 to 200 µm. When selecting your layer size, something to keep in mind is that larger layers will print faster but have lower quality. **Build Paths** • As each layer is formed in Formlabs printers, chemical bonds hold the layers together, creating isotropy throughout the part. • If your printed parts appear stretched or compressed, you can change the X or Y Scale values in the printer's settings to adjust the laser's path and compensate for the distortion. For more information on settings manipulation for the Form 2, please visit the Formlabs Fine Tuning guide. If you are operating on the Form 3 or later, please contact Formlabs Support. **Machine Parameters and Environmental Conditions** • The operating temperature for all Formlabs printing, washing, and curing machines is 18-28 °C. • Formlabs printers all operate within a self-contained build volume. • Ventilation is highly recommended for safety when working with IPA during post-processing and cleaning. • Formlabs SLA printers automatically heat resin to a set temperature (~35 °C) before starting a print. You can start the print before the automatic start temperature once it reaches the minimum start temperature (20-30°C), but this may cause adherence issues. ◦ The temperature control for all Formlabs SLA printers is an air-heated print chamber. • The Fuse operating internal temperature is up to 200 °C. Temperature control of the Fuse machine consists of quartz tube heating elements and positive temperature coefficient (PTC) cartridges. ◦ For user safety and printed part development, a 75-minute cool-down period is calculated within the print time. An additional cool-down time is recommended before touching the print to fully develop material properties and avoid warping. This may take up to half the print time. **Power requirements:** • Form 2: 100-240 V, 1.5A, 50/60 Hz, 65 W • Form 3/3B: 100-240 V, 2.5 A, 50/60 Hz, 220 W • Form 3/3BL: 100-240 V, 8.5 A MAX, 50/60 Hz, 650 W • Fuse 1: EU: 230 V, 7.5 A • US: 120 V, 15 A
	VALIDATING AND AUTOMATING SOFTWARE PROCESSES	[Market segment: Medical device and POC] * Refer to FDA Guidance on "General Principles of Software Validation" if you use a workflow that automates one or more software steps.	• Formlabs's Dashboard tool remotely monitors print progress and printer availability and allows users to: ◦ Manage material usage, including resin manufacture date, date last used, and cartridge ID, ◦ Review and download a record of previous print jobs, and ◦ Share and access print data. ◦ For more information, visit the Formlabs Dashboard overview page. • Formlabs's PreForm software uses advanced calculations to generate supports and optimize print settings to ensure successful, quality prints. ◦ PreForm's primary functions are scale, orient, support, and layout. All of these features can combine into one workflow with a one-click print. ◦ For more information and links to more specific resources, please visit the Formlabs PreForm FAQ page. • When Formlabs firmware or software displays "Beta," it means the firmware or software is not yet validated. • For a complete list of Formlabs PreForm software revisions and release notes, please visit the PreForm downloads and release notes page. • Please visit the Firmware downloads and release notes page for a complete list of Formlabs firmware release notes. For more information on Formlabs software/firmware validation and revalidation, please refer to the "Managing Updates" section of Chapter 7.

MATERIAL CONTROLS	STARTING MATERIAL	[Market segment: Medical device and POC] • Throughout the printing process, the material may undergo significant physical and/or chemical changes. This can significantly impact the success of the build cycle and properties of a final device. • The following aspects of your starting material should be documented prior to printing: the identity of the material/chemical by common name, chemical name, trade names, Chemical Abstracts Service (CAS) number, recognized consensus material standard, material supplier, incoming material specifications, and material certificates of analysis (COAs) with any test methods used. • Specifications for incoming materials or test methods should be based on the AM technology you use, the intended use of the final device, and the information available about the material or test methods. Specification examples include: particle size/distribution/ relevant rheological performance for powders or filament diameter and diametric tolerances for filaments; viscosity or viscoelasticity and pot life for fluids; composition, purity, water content, molecular formula, chemical structure, molecular weight, molecular weight distribution, glass transition temperatures, melting/crystallization point temperatures, purity information for polymers; chemical composition and purity for metals/metal alloys/ceramics; mix ratio with specifications provided for each component for composite materials. • When any material spec changes affect the build process, the effect on the final device should be understood and documented.	The Form 2 and Form 3B are only compatible with Formlabs resins. For a complete list of Formlabs resins, click here. • Navigate this site to see technical datasheets, sterilization information, certifications, and instructions for printing with each resin. • Formlabs resin families include standard, engineering, flexible/ elastic, tough and durable, dental, jewelry, specialty, medical. Please visit the link above for a list of resins in each family. Formlabs medical resins are biocompatible materials manufactured in an ISO 13485 certified facility. Our technology has been validated in FDA-cleared workflows. Formlabs Healthcare resins include: • BioMed Clear, used suited for medical device and device components, jigs and fixtures, surgical planning and implant sizing tools, research and development • Suitable for long-term bodily contact • BioMed Amber, best used for medical device and device components, surgical planning and implant sizing tools, research and development ◦ Suitable for short-term bodily contact • Elastic 50A, best used for vascular system models, simulating soft tissue such as skin, medical device prototyping, and testing • Tough 1500, best used for prototypes that repeatedly bend and quickly return to shape, jigs, and fixtures requiring repeated deflection, simulating the strength and stiffness of polypropylene • Clear, best used for models requiring color contrast via painting or injecting, prototyping tubular or microfluid devices Visit this page to help you determine the best resin for your application.
	MATERIAL REUSE	[Market segment: Medical device and POC] Unused material could be exposed to conditions that alter it from its virgin state. To account for this, the FDA recommends documenting any evidence that material reuse doesn't adversely affect the final device by describing the reuse process. This may include a description of processes like filtering, a limit on the percent of reused material, and monitoring for changes in chemistry, oxygen, or water content.	For SLA materials: • Formlabs resins require proper storage to maximize the usable lifetime. Two factors known to affect shelf life significantly are light exposure and room temperature. ◦ Used resins can be stored in their respective resin tanks as long as the tank lid covers the tank. • For quality prints, you should use a different resin tank for each type of Formlabs resin. Merely cleaning the resin tank to change resins may lead to contamination and print failures. • Do not pour resin from a tank or other holding vessel back into any cartridge to avoid contamination. Contamination can significantly affect print quality and success. For more information on resin care, please visit the Formlabs Resin Care page. For SLS materials: • The Sift powder recovery machine will automatically recycle used Nylon powder and mix it with new powder. It does this by filtering out particles to be remixed with new powder and reused in future prints. • The Fuse allows you to print with up to 70% recycled powder
POST-PROCESSING	GENERAL	[Market segment: Medical device and POC] • All post-processing steps should be documented and include a discussion of their effects on materials used and the final device. It is important to identify any potentially detrimental effects of post-processing and describe any mitigations implemented. • Care should be taken to ensure the printing and post-processing processes maintain the required device performance. • Following printing, the desired surface roughness of the device can be achieved through post-processing steps like mechanical polishing, but hard-to-reach spaces may remain in the as-built state. These spaces should be assessed for their effects on the mechanical performance of the device or component.	Formlabs post-processing solutions simplify and automate 3D printing post-processing. SLA prints require post-processing in the Form Wash and Form Cure (curing is optional for Standard resins) to ensure quality results and desired material properties. Following these processes, further post-processing steps can be taken to achieve the desired surface finish. • The Form Wash automatically cleans the part in IPA to get rid of excess resin on the part. The wash time depends on the material used. • Form Cure is a UV light chamber that brings washed parts to their maximum mechanical properties. Non-standard resins have unique recommended settings, which are listed on the Formlabs website. ◦ Other methods for post-curing exist, including natural sunlight, UV nail salons, DIY cure boxes, etc. If you choose to use one of these alternative methods, Formlabs recommends using a setup that utilizes both light and heat. • Sanding SLA parts is often the best method for smoothing edges, removing blemishes, and getting rid of leftover support marks. • SLA prints can be dyed, painted with acrylic, spray painted, and coated to achieve desired colors and surface finishes. If you use a standard resin, the Color Kit is another way to achieve the desired color without painting your parts. SLS prints require minimal time and labor for post-processing compared to other 3D printing processes. The required steps include removing parts from the build chamber, separating them, and cleaning them of excess powder (typically completed using compressed air or a media blaster). • Any excess powder can be filtered and recycled using the Sift. • Formlabs recommends media blasting or media tumbling SLS parts for a smoother surface finish. Parts may be spray painted, lacquered, electroplated, and coated to achieve different colors, finishes, and properties of cleaned parts.

PROCESS VALIDATION AND ACCEPTANCE ACTIVITIES	PROCESS VALIDATION	[Market segment: Medical device and POC] • Device quality is impacted by the AM process, and quality may vary for an identical device or component when built using different AM machines, even if the devices are the same model with the same print parameters. For this reason, knowledge of how variability affects the final device is critical to ensuring part quality. • Process validation must be performed where the results of a process cannot be fully verified by subsequent inspection and test to ensure and maintain quality for all devices and components built in a single build cycle, between build cycles, and between machines. • Criteria for acceptance must be established before testing. • For validated processes, all monitoring and control methods and data must be documented. ◦ Test methods used for process monitoring and control must also be validated. • Types of factors to consider when performing process validation include in-process monitoring of process parameters, temperature melt pool data, build space environmental conditions, etc.), manual and automated visual inspection with defined acceptance criteria, non-destructive evaluation, and test coupon evaluation.	**It is a manufacturer's responsibility to ensure their final device, including validation of the design, materials, and post-processing is safe and effective for use.** • Process validation should consist of qualifying your machine's capability to reproduce parts identical to the design specifications. Factors that could affect the outcome of a print, such as machine setup and environment, design of the build platform, etc. and control of these factors should be considered. • Formlabs recommends choosing a method and frequency for inspection of completed parts to ensure the parts are acceptable for use. We also recommend making plans to allow an appropriate response to unexpected machine function in order to protect patients from potentially unsafe products. This may include batch records, a reaction plan, etc. * Refer to Greenlight Guru for QMS considerations.
	REVALIDATION	[Market segment: Medical device and POC] • All process deviations and changes to your device or manufacturing process should be identified and analyzed for potential risks. Some changes and deviations may trigger the need for revalidation of the process. ◦ Some triggers for revalidation include software changes, changes in material or material handling, changes in spacing or orientation of devices or components in the build volume, changes to software workflow, physical relocation of a machine, and changes to post-processing steps or parameters. • When considering a change to a previously cleared or approved device that uses AM, rely on existing FDA guidance for their regulatory pathway.	• Formlabs provides a list of revisions and releases for both our firmware and our PreForm software updates. • Formlabs also regularly reviews and signs quality agreements according to customer needs. These agreements typically include change notice requirements. For more information on revalidation, please visit the "Managing Updates" section of Chapter 7.

	ACCEPTANCE ACTIVITIES	[Market segment: Medical device and POC]
		• Some acceptance activities for individual devices can be performed through non-destructive evaluation (geometry, morphology, some performance characteristics). Non-destructive techniques include calipers, ultrasound, computed tomography (CT) or micro-CT, x-ray, dye penetration, confocal microscopy, and hyperspectral imaging.
		  ◦ If a non-destructive evaluation technique is used in your process validation/acceptance activities, your choice of technique should be discussed and documented.
			• Just because a 3D printer has "high resolution" in the printer specifications does not mean your 3D printed parts will be accurate or precise.
			  ◦ You define the tolerance in your accepted parts. Generally, tighter tolerances means higher manufacturing costs and quality assurance.
			  ◦ The importance of accuracy level depends on your application (e.g., in medical applications, accuracy is crucial).
			* The best way to evaluate a 3D printer is to inspect real parts.
			* Post-curing and model post-processing can cause shrinkage in some parts. Because of this, analysis and acceptance activities are crucial to the printing and validation processes.
			Relevant literature on accuracy:
			• Evaluation of Medical 3D Printing Accuracy in Surgical Planning Models
			• Methods for Verification of 3D Printed Model Accuracy
			• Anatomic Model Accuracy with Formlabs Printers

	TEST COUPONS	[Market segment: Medical device and POC] • It is recommended that test coupons be used to help with process validation and identify the print process's worst-case conditions. They can also be used for in-process monitoring. ◦ Test coupons may not be needed if the process is validated and coupon testing is not a process-monitoring activity defined in the QMS. • Test coupons suitable for destructive mechanical testing can be simple shapes, or they may contain one or more structural features representative of the component/device that can be assessed using destructive techniques. • When used, the coupons should be validated to accurately and reproducibly represent the one or more printed parts within a specific build volume.	Formlabs has developed a test print called the Formtest to aid in validating the reliability of our printers. Other test prints exist, or you can create your own that uses positive and negative features to ensure the reliability and precision of the printer. To request a Formtest file for your own use, please contact Formlabs.
QUALITY DATA	GENERAL	[Market segment: Medical device and POC] • Analysis of sources of quality data to identify existing and potential causes of a nonconforming product or other quality problems is essential to maintaining a quality process. • It is important to consider whether it's necessary to keep track of the location of parts in the build volume. The answer to this question depends on the information you obtain during your process validation activities as well as design specifications. • Level of specificity is important in identifying possible causes of failure when multiple different components are made in the same build volume at the same time. Quality data must be able to be analyzed to enable proper identification of quality problems and investigation of the cause of nonconformities.	Formlabs has conducted studies on best practices for successful printing, but we recommend conducting your own tests and analyzing the resulting data to ensure the quality of your unique parts. • Understanding how the printer functions and best practices for successful prints is crucial in identifying possible causes of failure If you need to generate a nonconformance report, please see Greenlight Guru's resource on writing a nonconformance report.

21 CFR 11

21 CFR Part 11 is the FDA's regulations for electronic documentation and electronic signatures. While our focus is on medical device companies and the compliance of their quality systems with this regulation, the rules of 21 CFR Part 11 also apply to companies in pharma, biotech, biologics developers, and other FDA-regulated industries.

21 CFR Part 11 is divided into three sub-parts:

- The General Provisions section discusses the scope of the regulations and when and how they should be implemented. It also defines some of the key terms used in the regulations.
- The Electronic Records section sets forth the requirements for the administration of closed and open electronic record-keeping systems, then discusses signature manifestations and requirements for establishing a link between signatures and records.
- Finally, the Electronic Signatures section is split into three parts: general requirements for electronic signatures, electronic signature components and controls, and controls for identification codes/passwords.

21 CFR Part 11 provides an opportunity for medical device companies to reap the organizational benefits of paperless record-keeping systems. It also helps the FDA ensure that document security and authenticity are adequately maintained when medical device companies use electronic record-keeping systems. While some may argue that requirements of 21 CFR Part 11 place an additional regulatory burden on these companies, it's important to note that significant benefits can be derived from implementing these electronic systems. Medical device companies will benefit from embracing the regulations of 21 CFR Part 11 because using an eQMS will catalyze protecting the integrity and confidentiality of their proprietary data.

Since its original publication, 21 CFR Part 11 has generated significant confusion among medical device makers and other industry professionals who may use electronic records. The FDA published a guidance document in August 2003 to clarify the scope and implications of various parts of the regulations. This document also served to further elucidate the requirements for software validation, audit trails, management of legacy systems, maintenance of copies of records, and record retention. This document provides helpful information about what companies need to comply with its 21 CFR Part 11 requirements. It is important to remember these kinds of guidance documents themselves are not the law, and medical device companies should always refer directly to 21 CFR Part 11 when assessing their compliance status with FDA regulations.

In this comprehensive guide, Greenlight Guru will take you through each section of 21 CFR Part 11, explaining what the requirements mean and expounding the most critical points for you to know as a medical device company. Use this checklist to ensure you comply with 21 CFR 11.

MDR

The European Medical Devices Regulation (EU MDR) is a legal document that establishes quality regulations with which medical device manufacturers must comply to sell their devices in Europe. On May 25th, 2016, the EU MDR was enacted to govern the quality requirements of medical devices for sale in the European Economic Area (EEA). The EU MDR replaces both the Medical Devices Directive (93/42/EEC) and the Active Implantable Medical Devices Directive

(90/385/EEC) and allows medical device manufacturers a three-year transition period to establish compliance with the new requirements (ending in 2020 for medical devices and 2022 for in-vitro medical devices. One of the objectives for revising the EU MDR was to expand post-market surveillance of medical devices in Europe. To add an additional layer of safety for consumers, the EU MDR also mandates unique device identification (UDI) for all medical devices sold in the continent, ensuring that authorities can efficiently trace devices through the supply chains and initiate prompt and targeted recalls when required.

The EU MDR has also formalized the expectations that your QMS, documents, records, product information, risk, etc., are interconnected. Said another way, all of the documentation and records of your QMS and products need to be a seamless system of data and information.

One of the first things to know about the MDR is that the regulation is four times longer than the old MDD. There is an increased emphasis on risk and safety and a considerably expanded scope for "regulated devices." Medical purpose devices and active implantable medical devices (AIMD) are now included in the MDR. Previously, certain devices and accessories were not within the scope of the regulation. We highly recommend that you begin working with your Notified Body now to figure out what applies to you and how your devices will be impacted. It is up to you to know the timelines for your devices and what you will need to do to ensure they are compliant with the MDR.

The EU model wants to move more toward a whole lifecycle focus, so there is an emphasis on continuously updating your risk, your technical file, and ongoing evaluation of your devices. This expectation is fundamental for medical device companies to properly manage their devices throughout the entire product lifecycle–from design and development, through design transfer, through post-market surveillance, through product and process changes. How are you going to ensure all of these aspects are connected and tied together? Greenlight Guru's eQMS is built to do just this.

Resource Management/Supply Chain

MDR identifies distributors, importers, and EU-authorized representatives as Economic Operators, each with specific responsibilities regarding verification of compliance, cooperation in complaint handling and field safety corrective actions, and cooperating with manufacturers and Competent Authorities in device traceability. Some distributors and importers may never have had a quality system before. Under this regulation, they will need to develop one.

UDI and Labeling

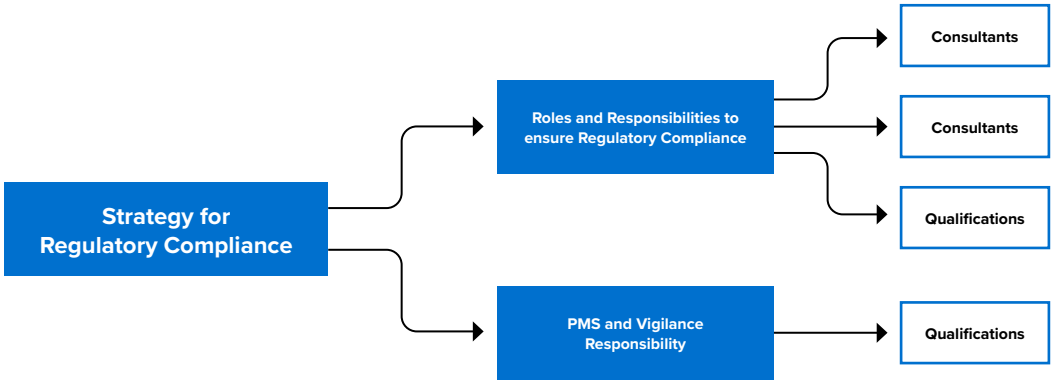
Those registered under the FDA will be familiar with UDI codes, but this is a new requirement under the MDR and is addressed in Article 27. You need to develop an SOP for UDI and labeling that:

- Defines storage of the UDI at each level (electronically is preferred)
- Details the process for importing UDI information into EUDAMED. You also need to include monitoring of EUDAMED. The process goes live in May 2022.

You are also required to keep an up-to-date list of all UDIs.

MDR: Regulatory Compliance

All companies should have within their quality system a defined strategy for regulatory compliance. Doing so might result in defining a new SOP. The EU MDR outlines the requirements of the "person responsible for regulatory compliance." They must have a relevant degree or sufficient work experience to understand and meet the requirements of the standard. It also outlines that if you are a small company, you don't have to have this person on staff, but you should consult with a company that has regulatory compliance expertise.



MDR: GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

See below for some of the critical requirements of the MDR that the manufacturer must fulfill:

Risk management

There is a broadening of the scope of risk analysis, even though you may have met this under ISO 13485:2016 and ISO 14971:2019. You need a risk management plan for each device, tighter risk analysis, risk controls, post-market risk procedures, and training on device safety as needed.

Labeling

There are additional requirements for labeling, such as the need to provide a GSPR checklist. You are also required to provide information on warnings, precautions, or contraindications on the labeling. For class III devices and implantables, a summary of safety and clinical performance is required on the labeling.

MDR: QMS Preparation

While QMS considerations are detailed in Chapter 7, here are a few summarized points to help you prepare your QMS for the EU MDR:

- Understand the key changes in the MDR and conduct a GAP analysis to understand where you are now and where you need to be to comply.
- Compliance with ISO 13485:2016 QMS requirements will help you to comply with MDR, as they are similar. "Guidance on the relationship between EN ISO 13485: 2016 (Medical devices - Quality management systems - Requirements for regulatory purposes) and European Medical Devices Regulation and In Vitro Diagnostic Medical Devices Regulation" is a helpful document to compare ISO 13485:2016 with the MDR.
- You need a very practical system for risk management, and it needs to be focused across the entire lifecycle of the device. Risk is a key focus in the changes.

- Ensure that everyone considered an “economic operator” for your device (suppliers, distributors, importers, etc.) understands the changes and has a plan for compliance.
- You need a robust system for documenting your QMS. An eQMS is preferable, allowing you to keep it updated and transparent easily. Greenlight Guru’s software platform is an excellent solution for this, including a built-in system for the technical documentation requirements.

For an MDR + IVDR gap analysis toolkit, please try these tools intended to help manufacturers begin the transition to Europe’s Medical Device Regulation (MDR) and In Vitro Diagnostic Regulation (IVDR) by understanding and assessing which changes must be made to comply with Chapter I requirements.

As you assess and prepare for the EU MDR (and all of the other global medical device regulation changes), more and more emphasis will be placed on your QMS. Greenlight Guru’s eQMS Software is exclusively focused on the medical device industry, and my top responsibility to you is to ensure that this solution keeps you ahead of these changes.

Formlabs certifies that its Class I medical devices manufactured before May 25th, 2021, and expiring no later than May 25th, 2023, can be used and sold in accordance with the EU MDR. Formlabs also certifies that its Class IIa medical devices can be used and sold in accordance with the EU MDR. For information on Formlabs compliance with the MDR, visit the Formlabs MDR FAQ page.

MHRA

If you intend to place a medical device on the United Kingdom (UK) marketplace, then changes in the regulatory landscape resulting from Brexit are relevant to you. The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive authority in the UK responsible for governing its healthcare products, such as medicines, medical devices, and blood components for transfusion.

MHRA has recently published new guidance on rules that will govern the regulation of medical devices. There is a grace period for some changes, but others are in effect immediately.

Note that the new MDR and IVDR are exclusive to the EU marketplace and do not automatically apply in the UK. One exception is Northern Ireland, which maintains a special status. Medical devices entering Northern Ireland must register with MHRA UK but follow the EU market requirements of either MDR and IVDR. A CE Mark will remain a requirement for market entry in this region.

The UKCA mark will only be recognized in Great Britain. Existing UK Notified Bodies have become “Approved Bodies” and can conduct the UKCA mark process, and they can no longer issue the CE Mark. Additionally, the UKCA mark is not recognized in the EU, EEA, or Northern Ireland markets.

Click here for more information on how the MHRA is regulating medical devices in the UK post-Brexit.

6. Establish A QMS

A QMS is comprised of the core set of business policies, procedures, forms, and work instructions, along with their sequence, interactions, and resources required to conduct business within a medical device company. Quality records are documentation that demonstrate the QMS is being executed and followed and describe how your company addresses medical device regulations. The FDA defines the rules in 21 CFR Part 820. And if you plan to go to market in the U.S., these regulations are required. Outside the U.S., Europe requires a quality system to be established to meet the medical device regulations (and/or IVD regulations). Many medical device companies implement a quality system certified to ISO 13485:2016 to satisfy EU needs.

Greenlight Guru encourages "bootstrapping a QMS" for early-stage startups. Early on, you don't need to spend too much time implementing a robust quality system. You need to be focused on product development. And as you get closer and closer to going to market, there are software tools, like Greenlight Guru and others, you can use to gradually implement more and more of a QMS.

IMPLEMENTING YOUR QMS

If you are going through medical device product development, there are at least four parts of a quality system that you need to put in place:

- Design Controls
- Risk Management
- Document Control & Records Management
- Supplier Management

Refer to regulatory requirements and resources in Chapter 5 for information on bullets 2-4. Read below for more information on Design Controls and additional QMS considerations. For more information on CAPA processes and requirements, please refer to Greenlight Guru's Ultimate Guide to Corrective and Preventive Action for Medical Devices.

Visit Greenlight Guru's website for design control, document management, risk management, and other regulatory solutions.

Design Controls

You must design and develop a safe medical device. The FDA, European Commission, Health Canada, and all other regulatory bodies worldwide will want some assurance that your medical device is safe before you bring the product to market. And this is the essence of Design Controls: proof that you have designed a safe product that meets user needs and requirements.

Technically speaking, "Design Controls" is an FDA term and defined in 21 CFR §820.30. In ISO 13485 speak, the terminology and intent are similar and covered in section 7.3 Design and Development.

The table below compares the FDA clauses for Design Controls to ISO 13485:2016 clauses regarding Design & Development.

DESIGN CONTROLS FDA 820.30	DESIGN & DEVELOPMENT ISO 13485:2016
(a) General	7.3.1 General
(b) Design and development planning	7.3.2 Design and development planning
(c) Design input	7.3.3 Design and development inputs
(d) Design output	7.3.4 Design and development outputs
(e) Design review	7.3.5 Design and development review
(f) Design verifications	7.3.6 Design and development verification
(g) Design validation	7.3.7 Design and development validation
(h) Design transfer	7.3.8 Design and development transfer
(i) Design changes	7.3.9 Control of design and development changes
(j) Design history file	7.3.10 Design and development files

Both FDA Design Controls regulations and ISO 13485 Design & Development requirements expect you to keep documentation and records throughout the product development process.

The Design History File (DHF) is a great place to keep all of your Design Control's "evidence."

For more information on design controls, visit Greenlight Guru's Ultimate Guide to Design Controls.

SOPs

It is essential to consider SOPs in virtually all aspects of your QMS. An SOP is a set of mid-to-high level written instructions that documents how an organization or department should achieve specific tasks. SOPs may be developed for routine and regular procedures, such as document control, and should also be developed for essential tasks that aren't so regular, like CAPAs. As a medical device company, your SOPs form an integral part of an effective quality management system.

All SOPs should do the following:

- Document how activities are to be performed to maintain consistency and to support quality practices.
- Describe the analytical process validation and qualification processes and processes for maintaining, calibrating, and using the equipment.
- Maintain quality control and assurance processes, ensuring compliance with regulations.

Medical device companies must adhere to many requirements to maintain regulatory compliance, and those must be clearly documented. To name just a few, separate SOPs are required for each of the following:

- Document controls
- Manufacturing
- Transporting and storing products
- Supplier management
- Reporting problems or failures
- Initiating and conducting CAPA
- Risk management
- Design controls
- Training
- Clinical evaluation

For more information on SOPs, visit this guide from Greenlight Guru.

7. Prepare For Process Validation

VERIFICATION AND VALIDATION

For verification and validation, it may be most helpful to start with definitions and regulatory requirements. According to an FDA Quality System Regulation Process Validation document:

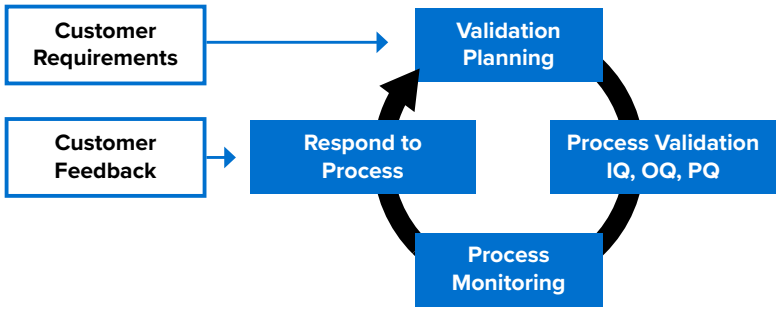
- Per 21 CFR §820.3 (aa): **Verification** means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.
- Per 21 CFR §820.3 (z), **Validation** means confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.
- Per 21 CFR §820.3 (z)(1), **Process Validation** means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

To further distinguish validation from verification, the first sentence of 21 CFR §820.75 states:

> *"Where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedures."*

As part of quality system process validation, manufacturers should consider personnel, equipment location, maintenance, and other variables.

Customer Requirements and PV
Risk Management



PROCESS VALIDATION APPLIED TO ADDITIVE MANUFACTURING

According to ASME, which published Process Verification & Validation for Medical Devices Using Additive Manufacturing, process verification and validation are two important and commonly misunderstood activities in developing medical devices. The ASME document explains the differences between these two activities and how they apply to additive manufacturing (AM) for medical devices.

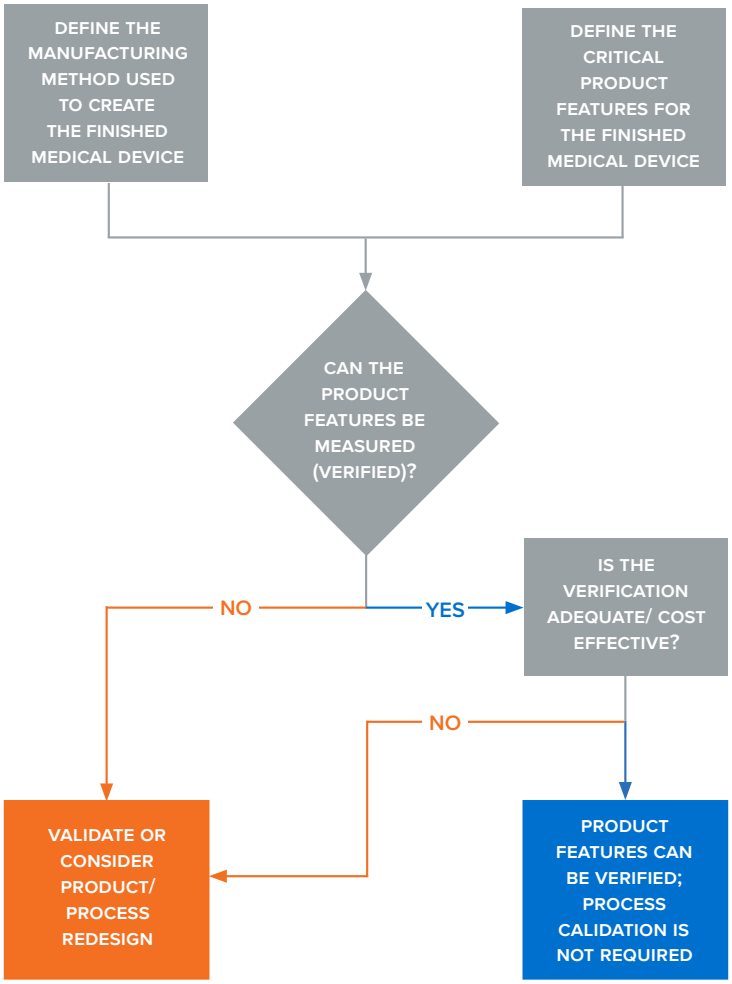
In virtually all medical devices, there are certain features or characteristics of the device, called CTQs (critical-to-quality), that are important for the device to function correctly; these features are often used to create the product specifications. Some common examples of CTQs are:

- Dimensions and tolerances
- Clearance or interference fit between mating parts
- Raw material mechanical properties such as tensile strength, hardness, density
- Raw material chemical composition
- Part weight
- Strength of a packaging seal

To demonstrate that the manufactured medical device meets the design specifications, documented proof must exist to demonstrate that the CTQs have been met. Typically, there are two ways to do this: process verification or process validation.

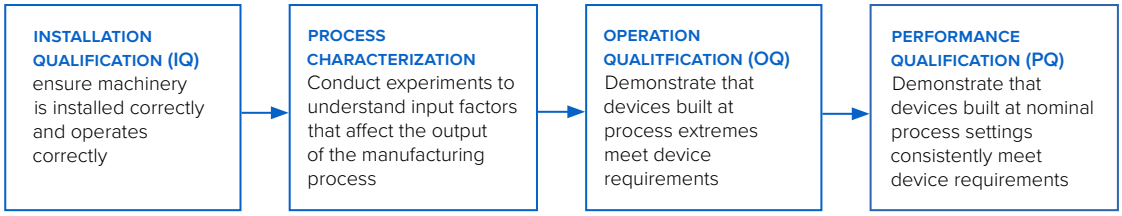
If a CTQ can be measured, it is said that the CTQ can be **verified**. For example, the length of a bone screw can be verified by measuring it with calipers, and the weight of an instrument can be verified by weighing it on a scale.

On the other hand, validation is used when the test method to check the CTQ would alter or destroy the device. For example, validation would be considered for chemical composition, static tensile properties, macroscopic density, and porosity. Regulation also states that all automated systems must be validated for their intended use even if you verify.



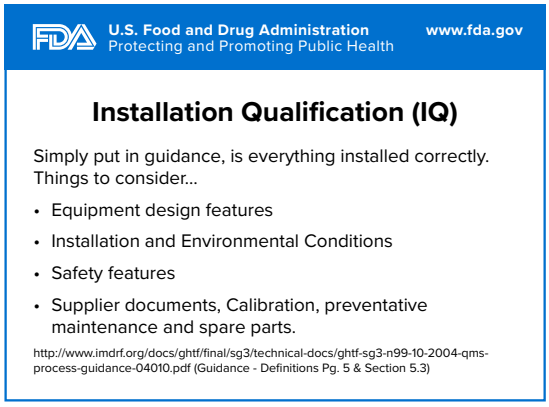
When thinking about **validation** for AM, it's easy to become focused on the printing step. However, several activities usually happen upstream of the printing process and several activities happen downstream from the printing process. All of these steps should be defined to understand the entire manufacturing process fully. Additionally, the inputs to and the outputs from each step in the manufacturing process should be identified.

IQ/OQ/PQ



Installation Qualification (IQ)

According to the American Society of Mechanical Engineers (ASME), IQ is a formal activity to demonstrate that all manufacturing equipment used to produce a medical device has been installed correctly and operates per the manufacturer's specifications. Before installing the equipment, an IQ protocol is written to describe the equipment to be installed, the method of installation, and the acceptance criteria used to demonstrate that the installation was successful. An IQ report must also be generated to document the successful installation of the equipment. Things to consider include equipment design features, installation and environmental conditions, safety features, supplier documents, calibration, preventative maintenance, and spare parts (FDA).



SECTION	REQUIREMENT/CONTENT
Purpose	State the equipment needs to be qualified
Scope	State whether the installation is for new equipment or modifying previous qualified equipment
Equipment/ System Description	Describe what the equipment does, how it is used, what process/products use it, and its basic design features
Supplier	Vendor certification and safety feature verification
Equipment Components	Identify and briefly describes each major component of the subject equipment Define the system/equipment boundaries with other systems or equipment Ancillary equipment used in conjunction with the equipment being qualified should be identified as appropriate
Utilities	Utilities required to operate the equipment should be identified
Construction, Installation, and Requirements	Specify the cleaning procedures that must be executed after the equipment is installed Document that the cleaning procedures have been successfully executed and completed

SECTION	REQUIREMENT/CONTENT
Supporting Documentation	List supporting documentation that may be used to identify or operate the equipment such as Engineering Turnover Packages, Purchase Orders, or Equipment Manuals
Maintenance Programs	Establish maintenance procedure. Include a listing of any preventive maintenance activities
Spare/Change Parts	Provide a list of spare parts and change parts, if applicable, required for system operation, including a description of the part and part number of reference
Drawings	List and include in the qualification protocol for the system drawings used to support the IQ
Testing and Acceptance Criteria	Acceptance criteria must be approved by the site designate review board or project team prior to executing any IQ Define the test procedure; IQ testing must be designed to confirm that the equipment is installed in accordance with manufacturers recommendation or document justification for exceptions Define the acceptance criteria; for an IQ this is usually a Pass/Fail result
Discrepancies	Discuss and justifies events per required deviation or exception procedure
Summary and Conclusion	Summarize IQ test results, which demonstrate that the equipment was installed correctly Provide a conclusion on whether the equipment installation is acceptable

Sections and Requirements. Source and ©: IVT Network

Process Characterization

During process characterization, the variables listed in the table below should be tested with test coupons to determine a "worst-case" build file used in OQ and PQ. For example, during process characterization, it may be found that smaller coupons are weaker than larger coupons or that coupons printed in a horizontal orientation are weaker than coupons printed in a vertical orientation.

PROCESS VARIABLE	ADDITIVE MANUFACTURING	TRADITIONAL SPECIAL PROCESSES
Type of Part	Variable	Fixed
Part Orientation in Space (i, j, k)	Variable	Fixed
Part Location in Space (x, y, z)	Variable	Fixed
Variety of Parts / Range of Sizes	Variable	Fixed
Number of Parts per Build	Variable	Fixed

Once the process window has been defined and the worst-case build file has been established, the OQ and PQ can be executed.

Operational Qualification (OQ)

The purpose of an OQ is to prove that parts made to the limits of the processing window will meet the design requirements. The first step of OQ is to develop the production processing window based on the Process Characterization step results. The next step is to write an OQ protocol that describes the parts to be tested, the processing window extremes

FDA U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

Performance Qualification (PQ)

Demonstrate the process will consistently produce acceptable product under normal operating conditions. Things to consider...

- Approved procedures and limits from OQ
- Acceptable product
- Simulate actual manufacturing conditions
- Is the process repeatable and stable long term

http://www.imdrf.org/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n99-10-2004-qms-process-guidance-04010.pdf (Guidance - Definitions Pg. 5 & Section 5.5)

to be challenged, the number of parts to be produced at each processing window extreme, the test method used to evaluate the parts, and the acceptance criteria for the devices created by the process. The protocol is then executed, and the results are documented in an OQ report.

SECTION	REQUIREMENT/CONTENT
Purpose	State the equipment needs to be qualified
Scope	State whether the installation is for new equipment or modifying previous qualified equipment
Equipment/System Description	Describe what the equipment does, how it is used, what process/products use it, and its basic design features
If above fully described in the IQ, then a reference to the IQ is acceptable	
Operational Qualification Pre-requisites	Verify all IQ tests have been completed prior to execution of operational qualification or that any IQ testing not yet completed has been identified in a protocol exception report as non-critical for OQ testing to begin
Test Equipment Calibration Verification	A completed record of qualified test equipment and approved materials that is used during protocol execution List calibration date and next due date
Standard Operating Procedures	Establish operating, maintenance, setup and/or cleaning procedures for the equipment Procedure(s) shall be approved and effected before or by end of OQ is completed
Alarm/Control Challenges	Identify and challenge critical alarms associated equipment/system. Note: In some cases, the alarm studies may be deferred to an overriding operating system, such as Building Management System or equivalent Challenge the equipment/system operator controls and indicators such as controllers not challenged as part of a separate software validation package and buttons, lamps, switches, etc. that are used for control or monitoring of the equipment
Operating Parameters	Verify the key and critical process parameters (some equipment may not have critical process parameters) Verify the operating ranges and acceptance criteria for each parameter Notes: Software parameters must also be considered; separate computer validation protocol can be used to address this
Rationale and Sampling Locations	Provide rationale for: • Qualification approach taken • Sample size rationale • Selected test conditions • Critical parameters
Testing and Acceptance Criteria	Define the test range for each critical process parameter for verification The testing range typically "brackets" the operating range to ensure equipment is qualified with extra security; e.g., if temperature operating range is 50°C to 100°C, then the test range should be 40°C to 110°C. The process will be challenged at the extremes of the critical process parameters wherever possible. The number of test runs needs to be statistically justified and it may be depending on the complexity of the equipment
Test Result Documentation	Summarize test results and confirms the acceptance criteria

Figure: OQ sections and requirements. Source: IVT Network

Performance Qualification (PQ)

The PQ demonstrates that the manufacturing process can produce a consistent result using the nominal process setting every time the process is run. The idea is to demonstrate that the

process can produce the same result consistently when considering the various sources of common-cause variation, such as manufacturing shut-downs for maintenance, change-overs from one job to the next, raw material lot changes, etc. The first step is to establish the nominal processing settings. Typically, these settings are midway between the extremes established in the OQ. The next step is to write a protocol that describes the parts to be tested, the nominal processing window, the number of simulated production runs, the number of parts to be produced per run, the test method used to evaluate the parts, and the pass/fail criteria. The protocol is then executed, and the results are documented in a PQ report.

MANAGING UPDATES

How medical device companies manage changes and updates will undoubtedly have a considerable impact on their business, including their internal processes and the products that they design, develop, manufacture, and distribute into the market. Ultimately, how companies handle and manage changes will impact patient lives.

As needs for changes arise, you'll need to properly manage any changes made to ensure everything is accounted for in your quality management system and the resulting documentation and records.

New products, processes, or controlled documents all require change management practices to be put in place. Changes can involve modifications to records and procedures in your design controls or your device master record (DMR). You might find yourself needing to do additional validation on a device, or maybe you are changing suppliers, which requires changes to associated documents and procedures.

Revalidation may be required when there is a change in a process, especially when it is a change that would require the requalification of the IQ, OQ, or PQ. Activities that can trigger the need for revalidation include:

- Design change that creates a new worst-case condition
- Addition of a new part size in a part family where the new part size represents a new worst case
- Relocation of the validated manufacturing equipment
- Addition of new manufacturing equipment
- Negative trend(s) in quality indicators (FDA QSR Process Validation)

Software and firmware changes and updates can also lead to the need for revalidation. For this reason, it is essential to track process updates and understand the purpose of each update, as well as the necessity of it, even if it doesn't require you to revalidate your process. Formlabs provides release notes for all PreForm firmware updates to make changes easier to track and understand. Some of these updates may require revalidation (i.e., those that change the process itself), while others may not.

As with product development in general, change management requires a high degree of traceability within your quality management system (QMS). That means transparent, traceable relationships between the different stages of the change management process documented in your QMS. If this is done correctly, you will see how each decision you make in change management leads into the next, carefully documenting each step of the process in chronological order.

Some different standards and regulations outline the QMS requirements that will dictate your change management procedures. Design change management is covered under 21 CFR §820.30(i), and 21 CFR §820.40(b) covers document control changes. Changes should be verified or, where appropriate, validated, according to 21 CFR §820.75 before implementation. In terms of international standards, document and design change management is discussed in ISO 13485 (see section 4.1.4 for change management requirements specific to QMS processes).

Please visit the Greenlight Guru Definitive Guide to Change Management for Medical Devices for more information on change management.

FORMLABS RESOURCES FOR VERIFICATION AND VALIDATION

In addition to the resources referenced in the Takeaways from Regulatory Bodies: FDA section of Chapter 5, medical device manufacturers can also consider these resources from Formlabs:

Formtest: Measuring 3D Printer Reliability

In the context of additive manufacturing, reliability has multiple meanings. Each speaks to a different situation, but all pertain to one underlying question: "If I print something, will it meet my expectations?" We can break down this question further into four categories: If I print something, will it:

- Print the same as last time? **Print-to-print reliability.**
- Print the same on all of my printers? **Printer-to-printer reliability.**
- Print the same the first time and the 100th time I print it? **Ongoing reliability.**
- Complete successfully? **Field reliability.**

The Formtest is a model that can evaluate the performance and reliability of a 3D printer. The part's features help us assign quantitative scores related to printer performance. In designing the Formtest, we identified four aspects as most likely to vary between printers and multiple prints within printer:

- Positive features (wires, walls, etc.).
- Negative features (holes, slots, etc.).
- Structural features (bridges, overhangs, etc.).
- Dimensional accuracy (small dimensions, larger dimensions).

The Formtest contains features for all four categories mentioned before, as well as a fifth "functional" category to relate the results to real-world applications:

- Positive features: wires and two sets of walls.
- Negative features: holes and two sets of slots.
- Structural features: two sets each of bridges and overhangs.
- Dimensional features: base and octagonal-base cylinder with known dimensions.
- Functional features: M3 nut hole, M4 bolt, M4 threaded hole.

For more detailed information on Formlabs dimensional accuracy tests, please read below. For a free STL, OBJ, or .Form version of the Formtest, contact Formlabs.

Understanding Accuracy and Precision in 3D Printing

The quality of end-use parts in additive manufacturing can be evaluated with several metrics, one of which is dimensional accuracy. For some applications, such as surgical guides or jigs and fixtures for medical devices, dimensional accuracy is paramount to whether the part is usable.

What impacts dimensional accuracy?

1. The 3D printer used to create the part. In some cases, there may be accuracy variations between printers.
2. The materials selected for the part.
3. Support placement on and removal from the part.
4. The post-curing steps taken after the parts are cleaned.

Formlabs created an internal test called the Formtest to determine the dimensional accuracy of Form 3 and Form 3B. We tested two models, one with features under 50mm and one with features over 50mm. Notably, we printed multiple parts per printer across several printers to highlight Form 3's ability to repeatedly accurate parts.

TEST PRINT SETUP

Printers Used	Four Form 3s
Model Printed	Test models (photos below)
Layer Height	50 microns
Post Processing	Form Wash + Form Cure
Material Used	Grey V4 Resin
Software	Preform 3.9
Measurement Tool	Hexagon CMM with CMM Manager (Nikon Metrology)

The image below shows the test print in PreForm. Each test contains two features for each 1 mm, 4 mm, 9 mm, 27 mm, and 50 mm dimension, measured in the XY direction.

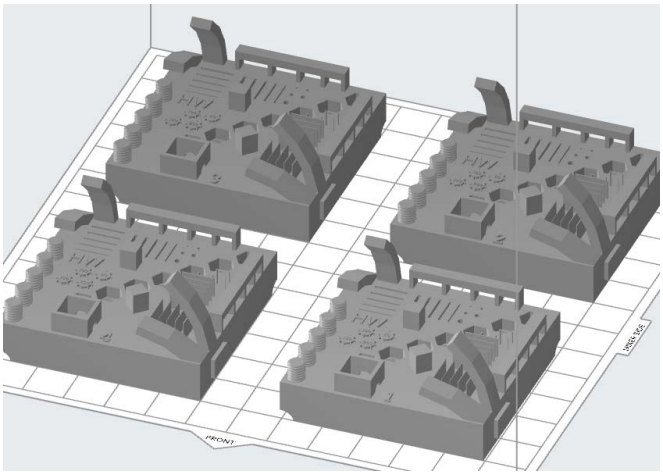


Figure 1

The topline results are as follows: The average deviations from the ideal, or exact, print size are small, ranging from 0 to 100 microns. Form 3, printing in Grey Resin, demonstrates consistent accuracy across multiple prints and sizes, meeting the requirements for various manufacturing applications. The table below details the average deviation from the ideal or perfect print for each intended feature size.

INTENDED FEATURE SIZE	AVERAGE DEVIATION FROM IDEAL (MM)	STANDARD DEVIATION (MM)
1mm	-0.02	0.03
4mm	-0.01	0.03
9mm	-0.01	0.03
27mm	-0.04	0.04
50mm	0	0.07

Table 1: Average size deviation and standard deviation results binned by intended feature size (n = 160 for 1 mm, 9 mm, 27 mm, and 50 mm features, n = 320 for 4 mm). This table shows how Form 3 meets the accuracy requirements required for 3D printing applications. These results represent data accumulated over 160 test prints, meaning the printers are reliably accurate over a range of prints.

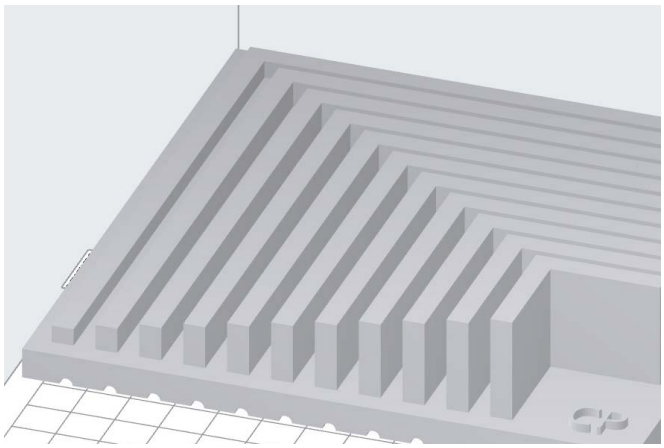


Figure 2

Figure 2 offers a look at a range of larger sizes, from 60mm to 130mm, increasing in increments of 10mm. Our results are similar to those obtained by the smaller test print size in Figure 1: the Form 3, printing in Grey Resin, shows little to no variation in size tolerance across a range of sizes. When these results are grouped by size, the data shows that the average deviations from the ideal are small, ranging from 0 to 100 microns.

INTENDED FEATURE SIZE	AVERAGE DEVIATION FROM IDEAL (MM)	STANDARD DEVIATION (MM)
60 mm	0.03	0.04
70 mm	0.00	0.04
80 mm	-0.01	0.06
90 mm	-0.01	0.07
100 mm	-0.05	0.09
110 mm	-0.1	0.1
120 mm	-0.1	0.1
130 mm	-0.1	0.1

The data presented in the tables above (full report here) is only for the printed parts as shown in Figure 1 and Figure 2. It is not possible to extrapolate from this data that all prints of the same size will perform exactly the same. Still, Formlabs is confident in the accuracy of its printers across all available Formlabs resins. As noted, all prints in this report were created in Grey Resin.

All Formlabs resins undergo a rigorous testing process before being released, and we would expect to see similar results across our material portfolio. However, variations may occur, especially depending on part geometry. Not all printers or resins will output exactly the same results. Some printers, by the nature of mass production, will skew larger or smaller on average. This phenomenon can be observed in our dataset, with some printers creating parts slightly

larger than average, and others slightly below average. This is a normal print variance present in 3D printing.

Additionally, degrees of freedom that cause distortions and anisotropic shrinking can contribute significantly to dimensional inaccuracies. Formlabs calibrates all 3D printers before shipping, resulting in a much tighter distribution of variations. Calibration reduces, but does not completely eliminate, these inaccuracies. If you have additional questions about the accuracy of our printers, please contact a sales expert.

Additional Formlabs Resources for V&V

- Model orientation best practices for SLA printing
- Model orientation best practices for SLS printing
- Schedule of maintenance (Form 3/Form 3B SLA)
- Schedule of maintenance (Fuse 1 SLS)
- Manuals and Safety Guides (SLA)
- Manuals and Safety Guides (SLS)

8. Commercialization Considerations

For a detailed guide on bringing medical devices to market, please review this resource from GG. A summary can be found below.

EU

For information on how devices are classified under the EU MDR, visit this page.

SELF-CERTIFIED DEVICES

As part of your regulatory plan, you have already determined which EU directives apply to your device and determined the classification of your device. Implementing a quality management system that is compliant with ISO 13485 is a crucial piece that should already be done at this point. You will also need to identify a notified body and have them audit you to ISO 13485 so you can receive your Certification. Class I devices can be self-certified, so your notified body will not need to review technical file documentation.

CERTIFIED DEVICES

The technical files for Class IIa and IIb devices or design dossiers for Class III devices will need to be reviewed by your notified body to obtain a CE certificate. The technical file/design dossier is very similar to the DHF, but there are some differences. One is that your notified body often expects a specific format for the documentation. Oftentimes you can take information directly from the DHF and rearrange the format to please your notified body. One crucial step that is sometimes overlooked is establishing a physical location in Europe or appoint a European representative for your company. You then need to prepare a Declaration of Conformity (DoC), stating that your device complies with the appropriate directives.

At this point, you can contact your notified body to schedule the technical file audit. Assuming all goes well, they will submit a CE certificate for your product that is valid for three years.

UNITED STATES

PRE-MARKET SUBMISSIONS

As we discussed previously, your device classification will dictate the type of submission to the FDA:

- Class II: Devices in this class pose a moderate level of risk to the user, and all of them require a premarket notification (510(k) submission) before they can be legally marketed. Items like pregnancy testing kits, intravenous kits, sutures, and powered wheelchairs could fall into this category. These devices are important for health care, but a malfunction would be unlikely to cause critical harm to a patient.
- Class III: Class three devices are typically either implanted medical devices or those that sustain life, like an implantable pacemaker, blood vessel stents, or other implanted devices. Devices in this class are seen as the highest risk for patients, as any problems with the device could lead to significant adverse outcomes for the patients. Class III devices require pre-market approval (PMA) submission before being marketed in the USA.

The purpose of a **510(k) submission** is to provide the FDA with documented evidence that proves that your medical device is substantially equivalent to a predicate device, one already approved for marketing by the FDA.

Proving substantial equivalency means that you'll need to compare and contrast your device with the predicate device. While laboratory testing is a typical requirement, human testing is usually not needed for 510(k) submissions.

Information from your documented Design Controls process, such as intended use, indications for use, design inputs, and design verification are all valuable inputs for your 510(k) submission. The FDA processes 510(k) applications in 30-90 days. There can be an extended period of back and forth discussions in some cases, delaying the time to actual clearance. You should consider this when you build your project timeline.

A PMA, on the other hand, is more in-depth than a 510(k); it is used to prove that a new device is safe and effective for the end-user and typically requires clinical trials with human participants, along with laboratory testing. The standards here are much higher than for 510(k) submissions, and the FDA has just 180 days to accept or reject the application.

Another less commonly used option, the **De Novo pathway**, is a classification process that uses a risk-based methodology for the approval of new and novel devices to be sold in the market.

Generally speaking, companies using the De Novo pathway do not qualify for 510(k) clearance because there is not an existing predicate device substantially equivalent already on the market. Since they are not showing equivalence to a predicate, companies must be prepared to argue their robust risk mitigation strategy when submitting a De Novo request.

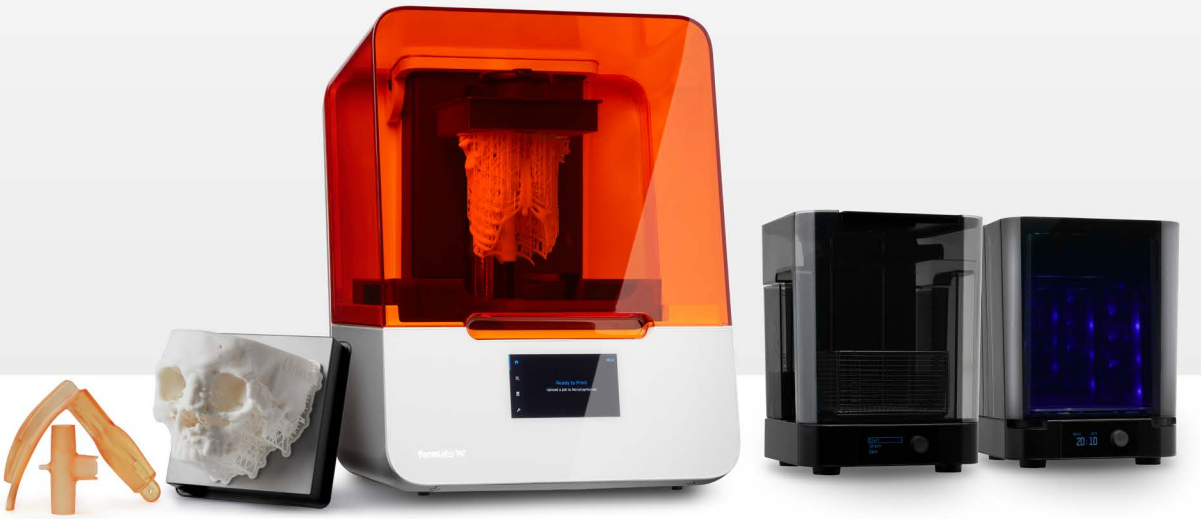
Class I Devices

Class I: These devices are simple, with minimal risk to the user. They are subject to the general regulatory controls of medical devices and typically do not require any premarket submissions.

Appendix

Below you will find a shortlist of relevant resources that do not fit into the main body of this guide:

- FL Regulatory Workflow Support
- 21 Resources for Quality & Regulatory Teams to Advance the Quality of your Medical Devices and Control Risk
- 17 Free Resources for Product Developers to Accelerate Bringing a Device to Market
- Special 510(k) vs. Abbreviated 510(k) vs. Traditional 510(k): Which FDA Program Applies to my Device?
- FDA 510(k) Submission Checklist
- How to Demonstrate Substantial Equivalence in 5 Steps
- Ultimate Guide to Training Management for Medical Device Companies
- Beginner's Guide to Design Verification and Design Validation for Medical Devices
- Approved Supplier List Form Template
- Library of Tools and Templates from Greenlight Guru



Ready To Invest in Formlabs Medical 3D Printing?

For medical device firms, in-house 3D printing allows quick iteration cycles, shortening the product development cycle and creating more time for creative solutions.

Every medical facility should have access to the latest tools to improve care and provide the best patient experience. Get started now or expand your in-house production with Formlabs, a proven, cutting-edge partner in medical 3D printing.

Reach out to our medical experts to learn more about how in-house 3D printing can supplement your current medical device design and manufacturing workflow.

Contact the Formlabs Medical Team

BioMed Clear Resin is a clear high-impact resistant resin for biocompatible applications requiring long-term skin or mucosal membrane contact. Order a free sample part manufactured in our ISO 13485 facility and printed on Form 3B.

Request a Free Sample Part

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