Guideline for creating
medical devices with

Somos® BioClear

stratasys

Solution Guide

Summary

Somos® BioClear has passed cytotoxicity, irritation, sensitization, and USP VI.
A toxicological profiling of the components has been performed. A Device Master File to support this material is accessible through the FDA. Ask a sales representative for more information.

Steps in the production process of 3D printed parts can influence the final part safety. This document gives guidance on areas to pay attention to when using Somos® BioClear.

Machine preparation & cleaning	Printing	Cleaning	UV-postcure	Cleaning 2	Sterilization
Contamination prevention: Cleaning procedures: vat, recoater, lens	**Mechanical properties:** Software for build preparation (support, slicing, laser settings)	**Removal of uncured residue:** Volume of part & cleaning bath	**Complete conversion:** UV curing length, curing durationw	**Removal of unwanted substances:** Cleaning solution, volume, temperature, duration	**Chemical modification due to interaction in the process:** Changing mechanical properties, color, and toxicity of surface
Build failure prevention: Machine maintenance, laser, moving parts	**Build accuracy:** Machine settings (waiting time)	**No cross contamination:** Refreshing of cleaning media	**Controlled process:** On time replacement of lights	**No cross contamination:** Refreshing of cleaning media	**Part geometry:** Are all areas of your part cleaned?
		Transparency: Duration	**Is the complete surface exposed:** Part geometry (need to reach complete surface)		**Temperature:** High temperature >Tg makes part deformable, internal unwanted substances can come to the surface
			Temperature: Increased temperature can speed up conversion process		**Moisture:** Parts can take up water, it takes some time to come back to original state

Figure 1: Factors that can influence cytotoxicity result

Introduction

Patient safety and product efficacy is critical in developing a medical product. Material selection is a key part of the development of a new product. To give confidence of the fit for medical applications, Stratasys performed an extensive study developing a processing procedure enabling the final printedpart to pass

1. Cytotoxicity <24hr (ISO 10993-5)
2. Irritation & Sensitization (ISO 10993-10)
3. USP VI (ISO 10993-11).

This paper gives users insight into the important factors critical for safety.

Complexities in the 3D printing process can cause changes in the chemical composition of the material before and after processing the resin (production process, software, printer, UV-curing, and sterilization). Testing the resin alone cannot sufficiently show safety for final product chemistry. Understanding how production processes can affect safety of the final part is therefore key in developing 3D printed medical parts with a resin (see Figure 2).

This document can be used as a reference for setting up production of a Somos® BioClear medical products for <24hr contact. Geometry plays a critical role and process parameters may need adaption to reach the optimized process settings. Final validation of the device is the responsibility of the device manufacturer. This paper does not guarantee the safety of the final devices.

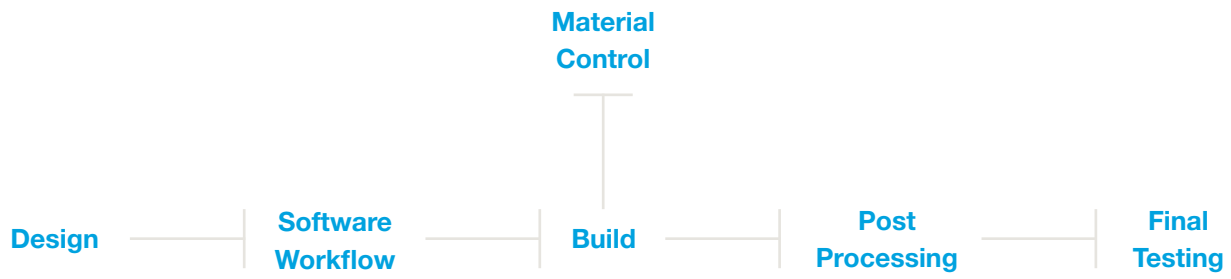


Figure 2: Material in the product development flow

Goal

This white paper shares Stratasys research findings on the safety of Somos® BioClear and the effect of processing parameters on the safety of the final chemistry of the part. This information should guide the development of optimal post-processing conditions for a final medical device. According to ISO 10993-1, framework for a structured program of assessment for evaluation of biological safety characteristics and properties of the material include: chemical, toxicological, physical, electrical, morphological, and mechanical properties prior to biological evaluation. The compositional characteristics are under the control of Stratasys. Processing of materials can affect the chemistry and is under the medical device manufacturers responsibility. To support different processing options, Stratasys tested settings to identify critical parameters in the processes and effects on the chemistry. Due to the wide range of parameters and processes, not all can be fully tested. In collaborative projects, new options can be investigated.

Medical Device Risk Classifications

The risk classification is determined by factors like invasiveness, duration of contact, impact on life, technology, intended use(r), effect on treatment decision making, and active vs passive. Based on the classification, type of contact, and duration, a certain type of testing is required – seen in Annex I. The notified body depends on the country where the material is sold, in which they can apply their own classification system and requirements. Based on the hazard and harms and risk analysis of product and process, quality controls have been implemented in production of Somos® BioClear.

Resin Handling

Exposure to ultraviolet can affect the life of the material. Storage temperature should be between 15–30°C. Cytotoxicity has been done using a year-old batch and did not show changes in the outcome. When the resin is in the machine, the room should be clean, well ventilated, and contain no direct sunlight. Humidity should be between 10–20%. When the resin viscosity is changed >30%, it may impact the mechanical properties. Always use protective clothing and gloves when working with the resin.

Cleaning Somos® BioClear

Stratasys has developed a cleaning method for medical applications with <24 hr patient contact produced using Somos® BioClear. Somos® BioClear printed parts are tested in external certified companies with certificates filed in the Device Master File at the FDA. Parts of different surface area (cm^2) to mass (g) ratios ranging from 1 to 26 have passed cytotoxicity tests.[1] Cleaning duration, temperature, cleaning medium, and sonification have been evaluated to identify optimal settings. Although all parts cleaned with the patented cleaning solution passed cytotoxicity testing in this experiment, we have taken the best scoring parameters for our advised cleaning process.

1. IPA wash 10 mins – Clean IPA must be used for every project

   Optional: For highly detailed parts – IPA ultrasonic wash 10 min, make sure to confirm your ultrasonic part cleaner is compatible with IPA since the fumes are a fire hazard
2. Second IPA wash – 10 min
3. Blow excess IPA off part with compressed air
4. Allow to air dry for 1 hour
5. UV post cure – 30 min/side
6. Base solution wash 5 min with gentle agitation

   Base solution:

   a. 20% IPA

   b. 80% DI water (distilled water)

   c. 30 grams NaHCO3 per liter of solution (NaHCO3 is baking soda)
7. Clean DI water (distilled water) wash – 5 min with gentle agitation
8. Blow dry with compressed air

Residuals of unreacted materials or photo initiator components in 3D printed parts can be partially removed using a validated cleaning process after the UV-curing step. To pass cytotoxicity with our selected worst-case sample parts, an initial cleaning of five minutes at 37°C and a second cleaning with the cleaning agent was sufficient. The extraction studies showed that higher temperatures and longer durations can extract more components from printed parts. At a higher temperature, the chemical network becomes more mobile and particles can move more freely.

The highest temperature tested in the cleaning validation was 70°C and during sterilization, 137°C. A temperature above 39–47°C Tg (glass transition temperature) can bring the part into a plastic state in which deformation can occur when force is placed on the parts. In about four hours, 80% of the mechanical strength returned to the part. When no force is applied to the part during cooling, geometry is kept intact (depending on the geometry of the initial part, since increased weight of a part that is not supported can still cause deformation).

[1] These cytotoxicity tests were performed within one month of washing. If longer times between washing and use are expected, then appropriate storage conditions should be simulated and tested.

Sterilization

Autoclave sterilization gamma radiation was positive in our test. More information on the cycles used can be found in Annex II. Sterilization can have effects on mechanical properties and color as can be seen in Figure 3, 4, and 5. Figure 3 & 5 show the changes of Gamma Sterilization.

Packaging

Ensure that the fabricated and post-processed part is packaged to protect it from humidity and light during transport.

Figure 3: Color change due to Gamma radiation

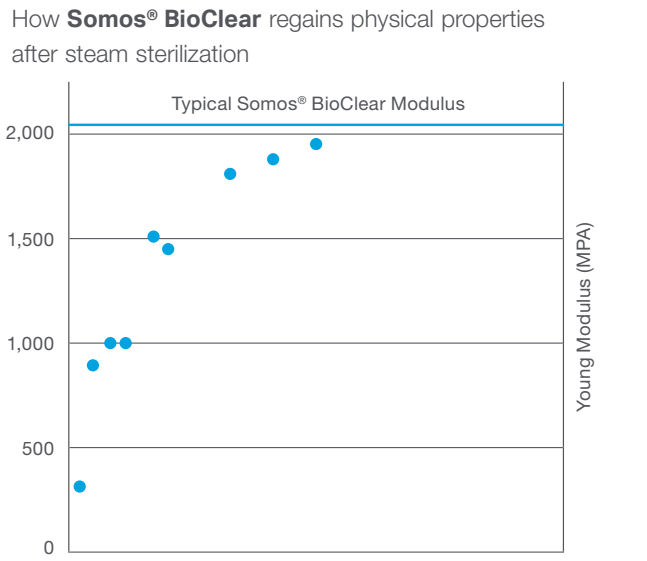
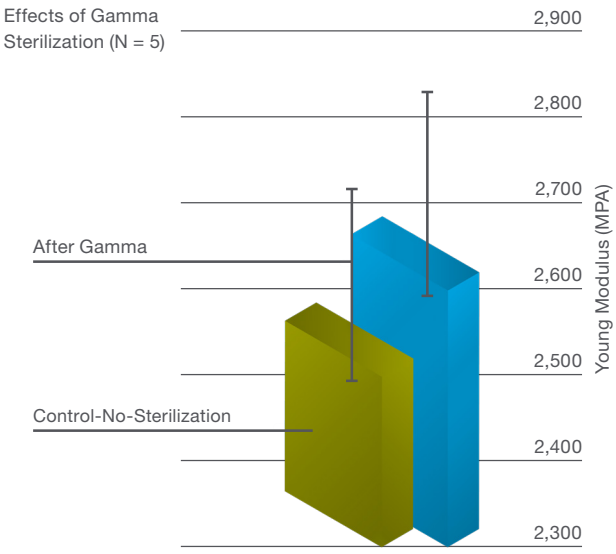


Figure 4: Property change over time after steam sterilization (long version)



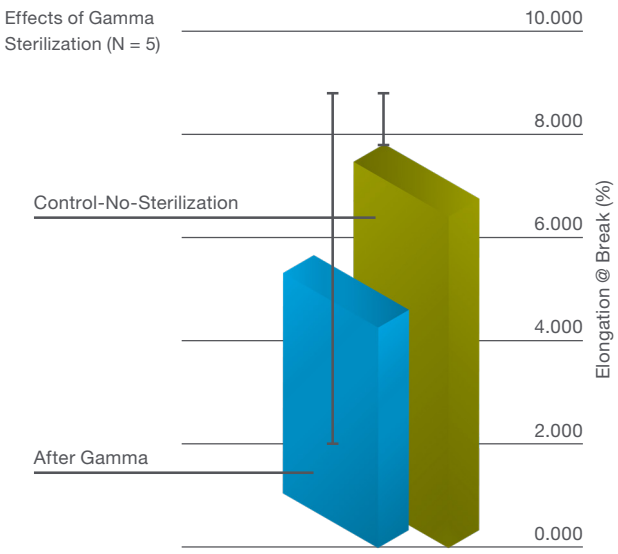
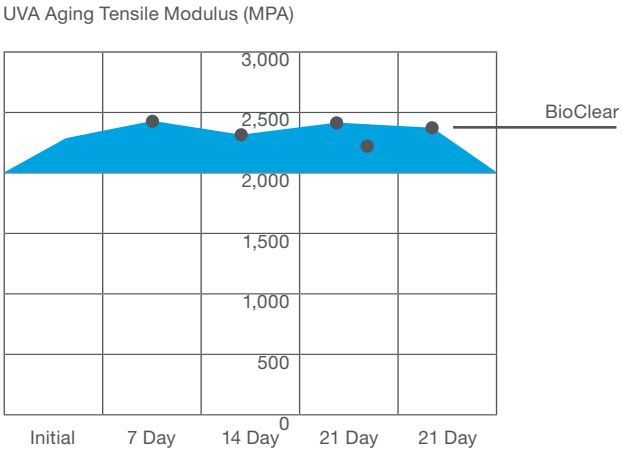
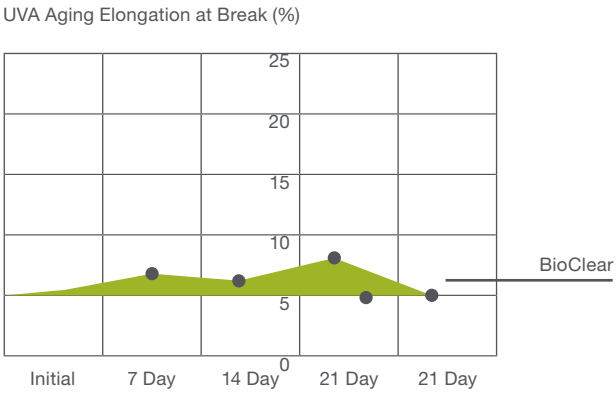


Figure 5: Effects of Gamma Sterilization on mechanical properties

Mechanical Changes

The measurements in Figure 6 show the change in mechanical properties over time as indication for change in the part during storage. As can be seen, the material shows only small changes over time.





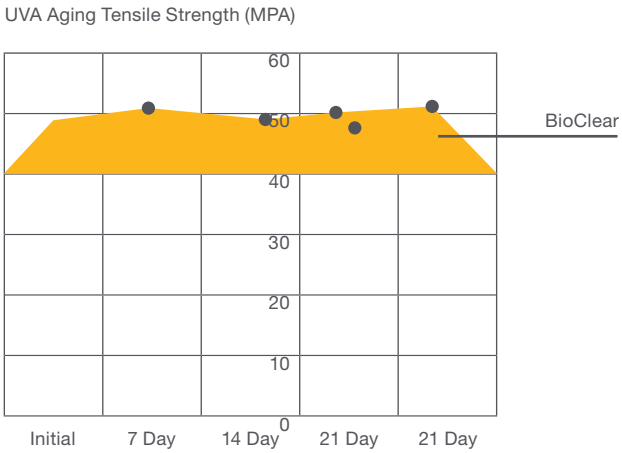
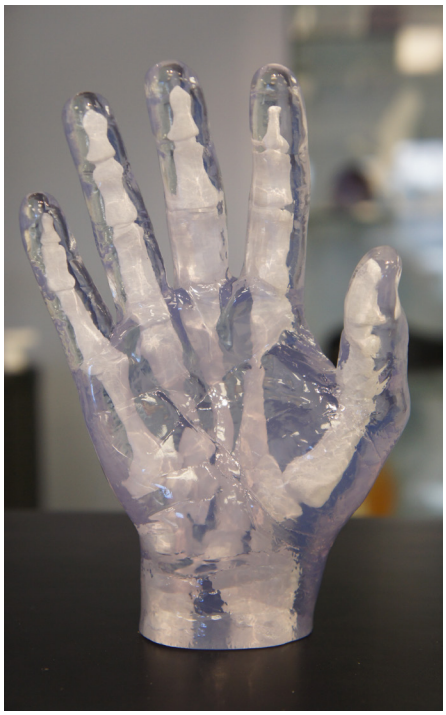


Figure 6: Mechanical measurements over time

Conclusion

Somos® BioClear is a material that has been understood and investigated in detail. Stratasys provides advice and support when developing new applications with this material. A Device Master File containing all confidential information and test certificates that customers can refer to is available by the FDA.

Access can be granted via request with your sales contact. Many parameters play a role in the safety of a final product. This study can help mitigate some of the risk and give a solid base and understanding of **Somos® BioClear**.



User Recommendations

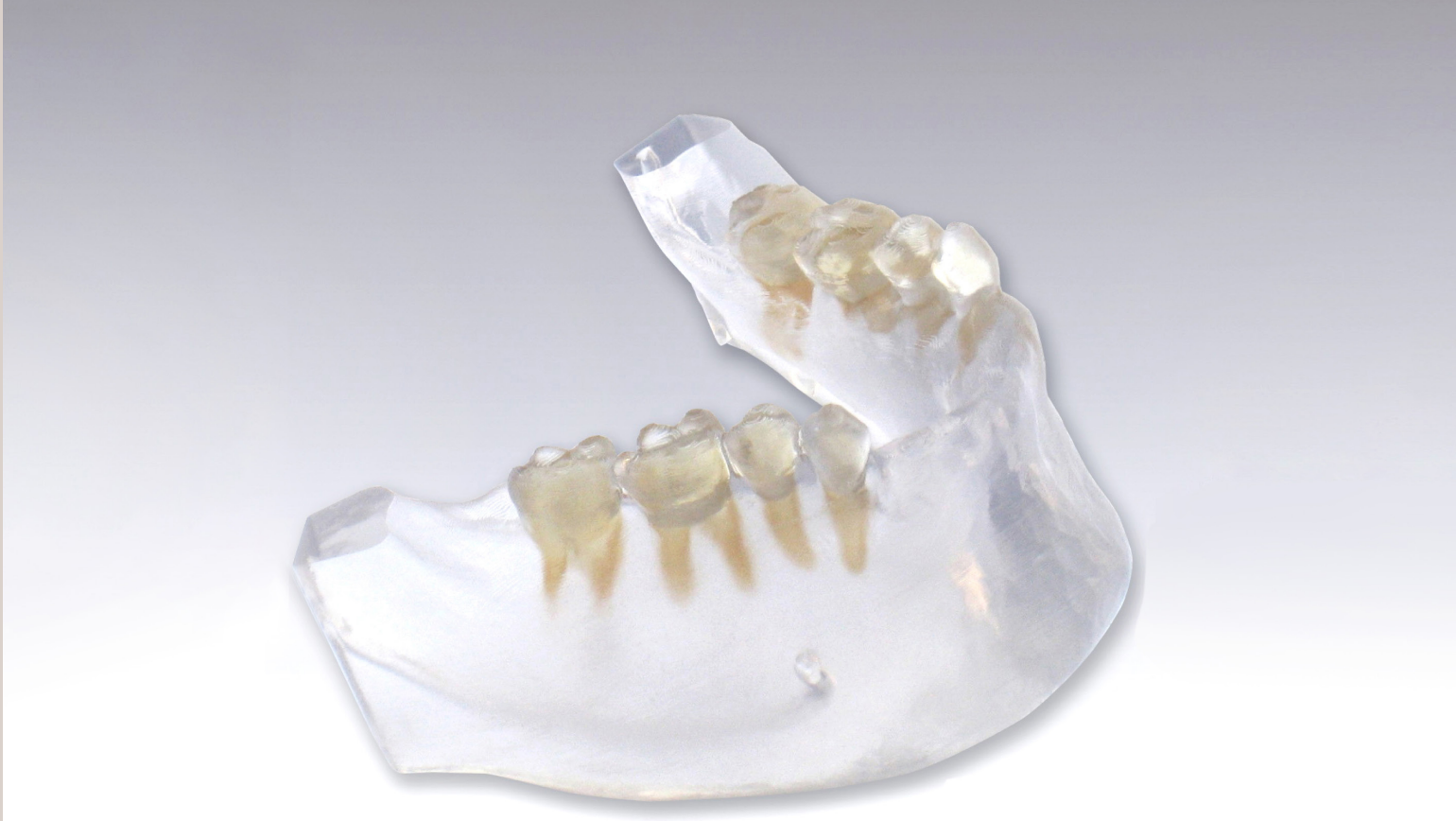
- Do not use in applications requiring >24hrs patient contact without further validation of safety according to standards (see Annex I & II).
- Implement 2nd cleaning advised by Stratasys.
- Perform process validation after you have optimized your complete process. All steps in your production processes can influence final part safety. Select the worst-case samples and optimize cleaning based on design geometry. ISO 10993-5 cytotoxicity is a sensitive, relatively fast, inexpensive test that can indicate safety of the product and process and provide confidence to proceed with further tests for biocompatibility if so required.
- Limit stock time and exposure to high temperatures and/or perform validation of stock and exposure times.

Annex I
Table A1 of ISO 10993-1:2018

Medical Device Categorization by Contact			End points of Biological Effect															
Nature of Body Contact		Contact Duration A = Limited (≤24hr) B = Prolonged (24hr–30 days) C = Permanent (30 days)	Physical and/or chemical information	Cytotoxicity	Sentitization	Irritation of intracutaneous reactivity	Material mediated pyrogenicity	Acute systemic toxicity	Subacute toxicity	Subchronic toxicity	Chronic toxicity	Implantation effects	Hemocompatibility	Genotoxicity	Carcinogenicity	Reproductive/Developmental toxicity	Degradation
Category	Contact																	
Surface Devices	Skin	A	X	E	E	E												
		B	X	E	E	E												
		C	X	E	E	E												
	Mucosal Membrane	A	X	E	E	E												
		B	X	E	E	E		E	E			E						
		C	X	E	E	E		E	E	E	E	E		E				
	Breached or Comprimised Surfaces	A	X	E	E	E	E	E										
		B	X	E	E	E	E	E	E			E						
		C	X	E	E	E	E	E	E	E	E	E		E	E			
Externally Communicating Devices	Blood Path Indirect	A	X	E	E	E	E	E					E					
		B	X	E	E	E	E	E	E			E	E					
		C	X	E	E	E	E	E	E	E	E	E	E	E	E			
	Tissue/Bone/Dentin Communicating	A	X	E	E	E	E	E										
		B	X	E	E	E	E	E	E			E						
		C	X	E	E	E	E	E	E	E	E	E		E	E			
	Circulating Blood	A	X	E	E	E	E	E					E					
		B	X	E	E	E	E	E	E			E	E					
		C	X	E	E	E	E	E	E	E	E	E	E	E	E			
Implant Devices	Tissue/Bone	A	X	E	E	E	E	E										
		B	X	E	E	E	E	E	E			E						
		C	X	E	E	E	E	E	E	E	E	E		E	E			
	Blood	A	X	E	E	E	E	E				E	E	E				
		B	X	E	E	E	E	E	E			E	E	E				
		C	X	E	E	E	E	E	E	E	E	E	E	E	E			

X = Prerequisite information available in Material Masterfile needed for risk assessment.

E = End point to be evaluated in the risk assessment (either through the use of existing data, additional endpoint-specific testing or a rational for why assessment of the endpoint does not require an additional dataset).

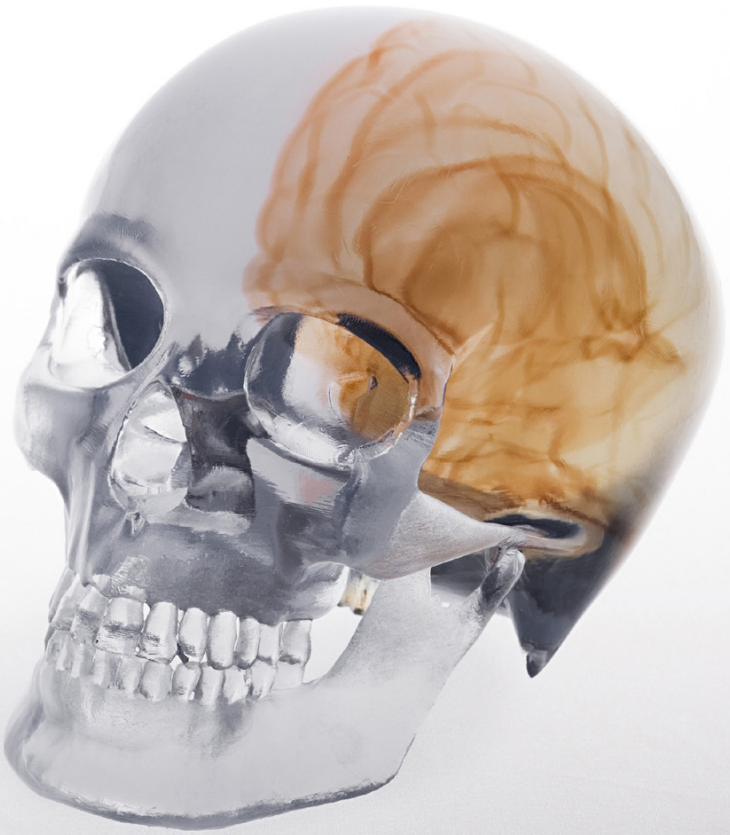


Annex II
Sterilization Testing

Method	Hydrogen Peroxide Gas Plasma	Irradiation	Ethylene Oxide	Steam Autoclave	
Equipment	Sterrad 200	Gamma	Thermally post-cured 2 hrs, 80°C	All American Electric Pressure Steam Sterilizer	Flash sterilization
Dosage	Six-Injection Cycles (most-aggressive)	Min 30.6 kGy, Max 33.0 kGy	59% to 62% RH	Pressure: 17–21 psi	
Temperature			Preconditioning: min 12 hrs, 40°C – 52°C	124°C – 127°C	134°C
Duration		224 minutes	Dwell Time: 4 hrs. Aeration Time: 6 hrs.	35 minutes	4 minutes
Results	Fail	Pass	Fail	Pass	Pass
Changes		Color changes to green opaque		High temperature can cause deformation up to 6 hours after sterilization.	High temperature can cause deformation up to 6 hours after sterilization.

Disclaimer

All materials offered by Stratasys are supplied under a contract containing detailed product specifications, and the user shall be exclusively responsible for, and shall bear full responsibility for the consequences i) whether or not the product is suitable for use in the devices (or for any other (authorized) use that customer may wish to make of the product), and (ii) whether the product specifications are sufficient and sufficiently well defined in order for the product to be fit and suitable for use by user. User undertakes to keep itself actively informed as to developments in the relevant fields of its applications.



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