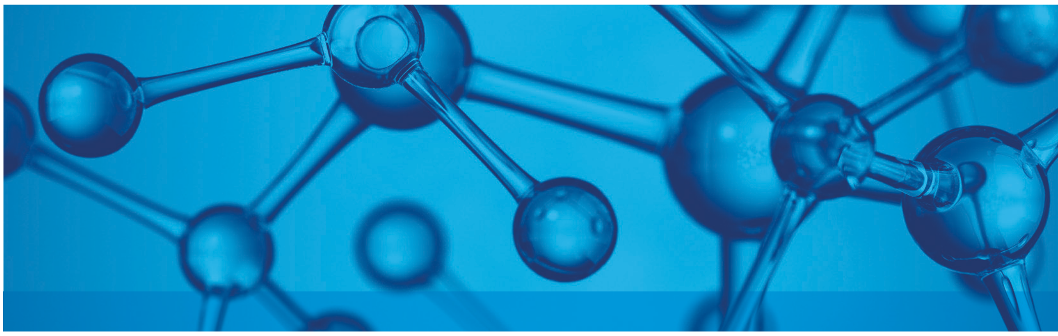


Shelf Life and Sterilization Study

Ixef® PARA HC-1022 and GS-1022

Ixef® polyarylamide (PARA) HC-1022 and GS-1022 are high-performance, medical-grade polymers offered for use in medical devices that are in contact with bodily tissue or fluids for less than 24 hours.

These materials are often used for single-use devices. To support this, Solvay has tested their compatibility with relevant sterilization techniques and multi-year storage. Testing was conducted in Solvay's laboratories in Alpharetta, GA, which have ISO 9001 certification and ISO 17025 accreditation. Results presented in this document are for the following:

- Exposure of all medical-grades listed in Table 1 to a 100 kGy dose of gamma radiation
- Multi-year aging of Ixef® GS-1022 WH01 at 23 °C (73 °F) before and after a 100 kGy dose of gamma radiation
- Multi-year accelerated aging of Ixef® GS-1022 WH01 at 60 °C (140 °F) before and after a 100 kGy dose of gamma radiation
- Exposure of Ixef® GS-1022 WH01 to five cycles of flash steam sterilization
- Exposure of Ixef® GS-1022 WH01 to two cycles of standard steam sterilization
- Packaging recommendations for extended storage

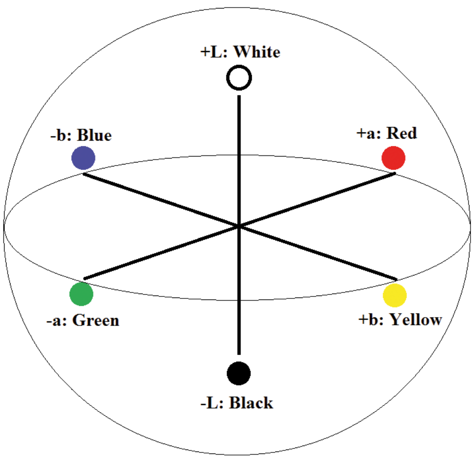
Test Methods

Color and Color Change

Table 2 lists the medical-grade variants of Ixef® 1022 included in the study. There are seven colored gamma-stabilized (GS) grades and two non-stabilized grades.

L*a*b color space was used to evaluate color change. Color space is tracked using three values: L (brightness), a (red/green), and b (blue/yellow). A three-dimensional representation of this color space is shown in Figure 1.

Figure 1: CIE color space



A single numerical value, ΔE, can be used to estimate the degree of overall color change by using the equation shown below. Table 1 presents the significance of ΔE values to the naked eye.

$$\Delta E = \sqrt{(L_2 - L_1)^2 + (a_2 - a_1)^2 + (b_2 - b)^2}$$

Table 1: Typical ΔE significance to the naked eye

ΔE Value	Color change as seen by the naked eye
ΔE < 1	Unable to distinguish
1 ≤ ΔE < 2	Noticeable by some upon close inspection
2 ≤ ΔE < 3	Noticeable upon close inspection
ΔE ≥ 3	Clear change in color

Tensile Properties

Tensile properties were collected in accordance with ASTM D638 Standard Test Method for Tensile Properties of Plastics. Test samples were injection molded ASTM Type 1 tensile bars with a nominal thickness of 3.2 mm. Samples were tested at 5.1 mm/min until break. Outputs included strength at break, elongation at break, and modulus.

Flexural Properties

Flexural properties were collected in accordance with ASTM D790 Standard Test Methods for Flexural Properties of Unreinforced and Reinforced Plastics. Test samples were injection molded ASTM flexural bars with a nominal thickness of 3.2 mm. Outputs included strength at break and modulus.

Gamma Radiation Sterilization

Medical-grade variants of Ixef® 1022 are commonly used for single-use instrumentation, and they are often sterilized using a gamma radiation dosage of ≤ 100 kGy. Tensile and flexural properties as well as color change were evaluated before and after a 100 kGy dose of gamma radiation.

Gamma Sterilization Procedure

Samples for gamma sterilization were submitted to the Sterigenics Facility in Charlotte, NC. All samples were exposed to a minimum of 100 kGy of gamma radiation. After exposure, samples were returned to Solvay for property evaluations and inclusion in a shelf-life and accelerated aging study. Until testing was completed, all samples were kept in a metal-based, moisture-barrier packaging.

Color Change

Table 3 summarizes the color change (ΔE) of Ixef® 1022 medical grades after exposure to a 100 kGy dose of gamma radiation. The majority of single-use applications typically require no more than 50 kGy; therefore, color changes shown here are believed to be a worst case scenario.

Table 2: Color change resulting from a 100 kGy dose of gamma radiation

Ixef® Grade	Gamma Stabilized	Color Change, ΔE	As-Molded	After Gamma Radiation, 100 kGy
HC-1022 NT000	No	45.0		
HC-1022 BK000	Yes	0.2		
GS-1022 WH01	Yes	6.3		
GS-1022 GY51	Yes	0.8		
GS-1022 GY01	Yes	0.5		
GS-1022 GY02	Yes	4.3		
GS-1022 BU01	Yes	2.2		
GS-1022 BN01	Yes	1.3		
GS-1022 GN01	Yes	0.2		

Ixef® HC-1022 NT000, the only grade which is not gamma stabilized, observed significant yellowing. The white and lighter shade of gray had a minimal color shift. The remaining colors were not significantly affected.

Tensile and Flexural Properties

Table 3 presents the relative change in tensile and flexural properties after exposure to a 100 kGy dose of gamma radiation.

Based on an appropriate assumption of +/–5 % testing error, the change in tensile strength, flexural strength, and flexural modulus are not significant. Tensile elongation properties dropped slightly, averaging –4.2 %. Tensile modulus properties increased slightly, averaging +4.2 %. The small changes in tensile properties are thought to be the result of minor cross-linking of split polymer chains. While this should not significantly impact polymer performance, it should be accounted for during design.

Table 3: Relative change in properties after 100 kGy dose of gamma radiation

	Tensile Properties (ASTM D638)			Flexural Properties (ASTM D790)	
Grade	**Strength**	**Elongation**	**Modulus**	**Strength**	**Modulus**
HC-1022 NT000	−0.3%	0.0%	+7.2%	−2.4%	0.0%
HC-1022 BK000	−1.8%	−8.7%	+1.5%	−1.4%	−0.7%
GS-1022 WH01	−2.8%	−9.5%	+5.7%	−0.7%	+2.3%
GS-1022 GY51	−0.3%	−4.8%	+6.3%	+2.3%	+2.1%
GS-1022 GY01	−0.3%	−5.0%	+7.9%	−2.7%	0.0%
GS-1022 GY02	+0.8%	−5.0%	+6.7%	−0.9%	0.0%
GS-1022 BU01	−0.5%	0.0%	+4.5%	−2.7%	−0.3%
GS-1022 BN01	−0.5%	0.0%	+5.0%	+0.2%	+1.7%
GS-1022 GN01	−1.3%	−5.0%	+5.1%	−3.0%	−0.7%

Shelf Life and Aging

Standard Aging Procedures

As-molded and gamma sterilized samples of Ixef® GS-1022 WH01 were stored in a climate controlled area maintained at 23°C and 50% relative humidity. Like other polyamide-based polymers, it is important to protect Ixef® PARA from high moisture environments that require parts to be sealed in moisture-barrier packaging. To demonstrate the importance of packaging, both packaged and un-packaged samples were evaluated. Packaged samples were sealed in a combination metal foil / PET film packaging which was highly moisture resistant and gamma stable.

Standard Aging Results

Table 4 presents color change, tensile, flexural, and thermal properties of Ixef® GS-1022 WH01 with and without packaging. Table 5 shows similar data after the samples were exposed to a 100 kGy dose of gamma radiation.

Table 4: Property changes in unsterilized samples aged at 23°C, 50% RH

	No Gamma Radiation						
		1 year		3 years		5 years	
Property	**As-Molded Control**	**Ambient**	**Sealed**	**Ambient**	**Sealed**	**Ambient**	**Sealed**
Color – CIE L*a*b							
Color Change, ΔE	0.0	0.3	0.5	1.4	0.1	Test data available January 2019	
Characteristic Temperatures – DSC – ASTM D3418							
Glass Transition, T_g	78.7	81.2	77.3	74.3	76.1		
Recrystallization, T_c	204.9	204.6	203.5	202.7	202.4		
Melt, T_m	233.6	232.2	231.6	233.4	233.6		
Tensile Properties – ASTM D638							
Strength at Break, MPa	269	257	277	242	277		
Elongation at Break, %	2.1	2.1	2.1	2.0	2.0		
Modulus of Elasticity, MPa	20,408	21,098	20,960	21,925	21,994		
Flexural Properties – ASTM D790							
Strength at Break, MPa	385	381	405	375	401		
Modulus of Elasticity, MPa	20,891	22,063	21,925	21,512	21,718		
Biocompatibility							
Cytotoxicity, ISO 10993:5	Pass	Pass	Pass	Pass	Pass		
Physiochemical Testing, ISO 10993:18	Pass	Pass	Pass	Pass	Pass		

Table 5: Property changes in gamma sterilized samples aged at 23°C, 50% RH

Property	Exposed Control	After Gamma Radiation, 100 kGy					
		1 year		3 years		5 years	
		Ambient	Sealed	Ambient	Sealed	Ambient	Sealed
Color – CIE L*a*b							
Color Change, ΔE	6.3	2.9	2.7	2.2	2.0	Test data available January 2019	
Characteristic Temperatures – DSC – ASTM D3418							
Glass Transition, T_g	80.6	80.5	80.8	71.4	74.6		
Recrystallization, T_c	201.6	203.4	202.8	200.4	200.7		
Melt, T_m	233.1	231.3	231.9	232.2	232.5		
Tensile Properties – ASTM D638							
Strength at Break, MPa	261	255	259	241	277		
Elongation at Break, %	1.9	2.0	2.0	2.0	2.0		
Modulus of Elasticity, MPa	21,581	21,374	21,236	22,132	21,236		
Flexural Properties – ASTM D790							
Strength at Break, MPa	352	376	381	365	409		
Modulus of Elasticity, MPa	21,374	22,132	22,201	21,580	21,650		
Biocompatibility							
Cytotoxicity, ISO 10993:5	Pass	Pass	Pass	Pass	Pass		
Physiochemical Testing, ISO 10993:18	Pass	Pass	Pass	Pass	Pass		

Observations on Ambient Condition Aging

Unpackaged and gamma sterilized samples showed a small drop in tensile and flexural strength but no significant change in modulus. A small drop in the glass transition temperature was observed, which is expected due to moisture absorption. Gamma sterilization also resulted in a color shift that slowly stabilized over the course of three years. Overall, no detrimental change in properties was observed.

Accelerated Aging Results

Testing was repeated at an elevated temperature (60 °C) to accelerate the effective aging of samples. A common assumption for plastics is that every 10 °C increase in temperature doubles the rate of aging. Based on this, the following equation can be used to estimate the accelerated aging factor (f) resulting from a temperature increase from T_1 to T_2.

$$f = 10^{T_2-T_1}$$

Using this equation, it was calculated that increasing the temperature from 23 °C to 60 °C resulted in an accelerated aging factor (f) of approximately 5,000. This means that one year at 60 °C is believed to be approximately equivalent to 5,000 years at 23 °C. This estimation may be high as the higher temperature of 60 °C significantly decreases the presence of moisture, which can significantly expedite the aging of Ixef® PARA. This can be avoided by using moisture-barrier packaging.

Due to 5,000 years being excessive compared to likely requirements, a conservative estimate for aging is that one year of accelerated aging at 60 °C demonstrates that Ixef® 1022 medical grades, when properly packaged, have a shelf-life of approximately 10 years at 23 °C.

Table 5 presents color change as well as the tensile, flexural and thermal properties of Ixef® GS-1022 WH01 with and without packaging. Table 6 presents similar data after the samples were exposed to a 100 kGy dose of gamma radiation.

Table 6: Property changes in unsterilized samples after one year at 60°C, ambient RH

Property	As-Molded Control	No Gamma Radiation: 1 year Ambient	1 year Sealed	3 years Ambient	3 years Sealed	5 years Ambient	5 years Sealed
Color – CIE L*a*b							
Color Change, ΔE	0.0	3.2	2.5	6.9	4.5	Test data available January 2019	
Characteristic Temperatures – DSC – ASTM D3418							
Glass Transition, T_g	78.7	76.4	78.2	76.1	77.7		
Recrystallization, T_c	204.9	202.8	202.9	203.1	202.5		
Melt, T_m	233.6	233	232.8	233.4	234.4		
Tensile Properties – ASTM D638							
Strength at Break, MPa	269	280	280	281	281		
Elongation at Break, %	2.1	2.1	2.1	1.9	1.9		
Modulus of Elasticity, MPa	20,408	21,305	21,305	22,339	22,270		
Flexural Properties – ASTM D790							
Strength at Break, MPa	385	403	398	390	395		
Modulus of Elasticity, MPa	20,891	22,201	22,201	22,063	21,856		
Biocompatibility							
Cytotoxicity, ISO 10993:5	Pass	Pass	Pass	Pass	Pass		
Physiochemical Testing, ISO 10993:18	Pass	Pass	Pass	Pass	Pass		

Table 7: Property changes in gamma sterilized samples after one year at 60°C, ambient RH

Property	Exposed Control	After Gamma Radiation, 100 kGy: 1 year Ambient	1 year Sealed	3 years Ambient	3 years Sealed	5 years Ambient	5 years Sealed
Color – CIE L*a*b							
Color Change, ΔE	6.3	4.2	3.4	8.3	2.5	Test data available January 2019	
Characteristic Temperatures – DSC – ASTM D3418							
Glass Transition, T_g	80.6	76.1	80.0	71.8	73.4		
Recrystallization, T_c	201.6	202.4	202.9	201.4	201.8		
Melt, T_m	233.1	231.1	231.6	231.7	231.8		
Tensile Properties – ASTM D638							
Strength at Break, MPa	261	279	275	268	278		
Elongation at Break, %	1.9	2.0	2.0	1.7	1.9		
Modulus of Elasticity, MPa	21,581	22,270	21,512	22,132	22,201		
Flexural Properties – ASTM D790							
Strength at Break, MPa	382	393	392	365	395		
Modulus of Elasticity, MPa	21,374	22,270	22,270	21,994	21,856		
Biocompatibility							
Cytotoxicity, ISO 10993:5	Pass	Pass	Pass	Pass	Pass		
Physiochemical Testing, ISO 10993:18	Pass	Pass	Pass	Pass	Pass		

Observations on Accelerated Condition Aging

Maintaining plastics at elevated temperatures can result in annealing. This happens when polymer chains are squeezed closer together (chain segmental relaxation), which increases strength and stiffness at the cost of elongation. Annealing was observed to a slight degree with the Ixef® GS-1022 WH01 samples held at 60 °C for one year. Strength and stiffness increased slightly, but elongation remained unchanged.

Gamma radiation resulted in a decrease of strength and elongation. Over the course of one year at 60 °C, however, the strength and stiffness of the polymer recovered slightly. Because moisture is significantly reduced at elevated temperatures, unpackaged and packaged test results were very similar.

There is a little more variability in the glass transition temperature (T_g) of the material after gamma sterilization and accelerated aging; however, it is still within a few degrees of nominal. Overall, properties are holding at the three year mark with signs of annealing effects due to the elevated temperature. The most stable retention was observed in packaged samples.

Biocompatibility Testing

Biocompatibility testing was conducted by NAMSA laboratories using appropriate protocols for ISO 10993:5 and 10993:18. The ISO 10993:18 tests were conducted using two extracts: sodium chloride and hexane. The values presented in Table 8 are considered passing.

Table 8: Acceptance criteria for shelf life and gamma sterilization biocompatibility testing

Biocompatibility Test	Acceptance Criteria
Cytotoxicity	
Cell reactivity	Grade 0: no cell lysis
Physiochemical testing (Aqueous NaCl)	
Non-volatile residue	≤47 mg
Residue on ignition	≤40 mg
Heavy metals	≤1 ppm
Buffering capacity	≤1.0 ml
Physiochemical testing (Hexane)	
Non-volatile residue	≤8 mg
Residue on ignition	≤1 mg
Turbidity	≤0.4 NTU

Steam Sterilization

Due to Ixef® PARA being a modified nylon, it is prone to absorbing large quantities of moisture which can greatly affect its properties. Furthermore, Ixef® PARA is designed for optimal operation at or below 75 °C. Due to the very high temperatures and moisture concentration in a steam sterilizer, it is not recommended for this polymer. However, it has been acknowledged that it may be required for single-use instrumentation to undergo short-cycle steam sterilization in the operating theatre. If an instrument composed of a medical grade of Ixef® 1022 is specified for any form of steam sterilization, it is important to understand the impact such a process would have to mechanical properties.

Steam Sterilization Procedures

Ixef® GS-1022 WH01 samples were exposed continuously in a Pre-Vac sterilizer using the following parameters for steam sterilization.

- Unit: Amsco Century Sterilizer SV-136H
- Cycle: Pre-Vac
- Temperature: 134°C to 136°C
- Pressure: 35 psig to 37 psig
- Vacuum: 27 inHg
- Standard cycle times: 18 min steam, 10 min dry (36 min total)
- Flash cycle times: 4 min steam, 10 min dry (15 min total)

The Pre-Vac sterilizer uses a dedicated steam generator supplied by filtered, de-ionized water that is chemically balanced per the manufacturer's recommendations. Details of test methods used are provided in the equipment reference section at the end of this document. Test results for Ixef® GS-1022 WH01 are summarized in Table 9.

Table 9: Relative property changes after steam sterilization

		Flash Cycles		Standard Cycles	
Tensile Property	**As Molded**	**1 Cycle**	**5 Cycles**	**1 Cycle**	**2 Cycles**
Strength at Break	Nominal	–4.2 %	–13.2 %	–12.8 %	–17.9 %
Elongation at Break	Nominal	10.5 %	5.3 %	5.0 %	5.0 %
Modulus	Nominal	–0.6 %	–4.1 %	–8.6 %	–11.9 %

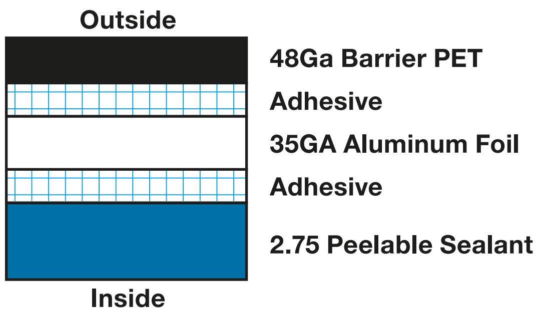
During steam sterilization, two things are happening to Ixef® 1022. First, moisture absorption causes a drop in strength and stiffness, and an increase in elongation. Second, high heat causes annealing, which has the opposite effect in that it increases strength and stiffness, and decreases elongation.

Because the effect of moisture absorption is more significant, these two effects do not cancel each other out. As the number of sterilization cycles increases, Ixef® 1022 will slowly lose strength and stiffness, but gain elongation. Due to the recurring absorption and evaporation of moisture on the surface of Ixef® PARA, the polymer will gradually lose its glossy surface appearance and become splotchy as color pigments and other additives are pulled towards the surface by the moisture. Because of this, it is highly recommended to avoid steam sterilization when using medical-grades of Ixef® 1022.

Packaging Recommendations

Proper packaging provides protection and prevents access to moisture, which Ixef® 1022 will readily absorb. Typically, this is multi-layer packaging that should have a least one layer of metal foil, plastic film and adhesive. The metal foil, commonly aluminum, provides strength and a moisture barrier. The plastic film, commonly a hydrophobic polymer such as PET, provides toughness, abrasion resistance, and an additional moisture barrier. Figure 2 shows a schematic of multi-layer packing produced by Mangar Industries Inc. Note that opposing layers can be used to create a pouch, or a single layer can be bonded directly to clamshell packaging. Breathable packaging, such as Tyvek®, is not recommended.

Figure 2: Example of recommended multi-layer packaging



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