CYROLITE® Medical Polymers for Blood-Contacting Applications

Introduction

Polymers used for medical devices which contact circulating blood must not only meet biocompatibility requirements, but must also be, transparent, structurally resilient for the application, and easy to incorporate into high-volume manufacturing. CYROLITE® materials, including the Med 2 and G-20 HIFLO® compounds are well suited to these applications with an established performance history. CYROLITE® compounds have passed ISO10993 and USP class VI testing, exhibit easy weldability, high toughness and clarity. To highlight some of these performance capabilities, additional testing was conducted on gamma-radiation-sterilized CYROLITE® injection-molded components which focus on the blood compatibility of the device, suitability for ISO-594 Luer lock connectors, and suitability for tubing bonding, using DEHP-free medical tubing.

Test Devices and Conditioning

To assess the biocompatibility, Luer performance, and tubing bond performance of the material, two different molded components were used. Flat plaques were molded for platelet testing, since a flat surface was ideal for microscopic examination. Second, a y-site was designed and molded for all other testing which included standard ISO-594-2 male Luer lock (§3.2.2 Figure 1), a ISO 594-2 female Luer lock (§3.2.2 Variant a), and a tubing pocket for 5/32" medical tubing. These molded components allowed evaluation of relevant characteristics established with as-molded components, rather than using resin pellets or machined samples for evaluation.

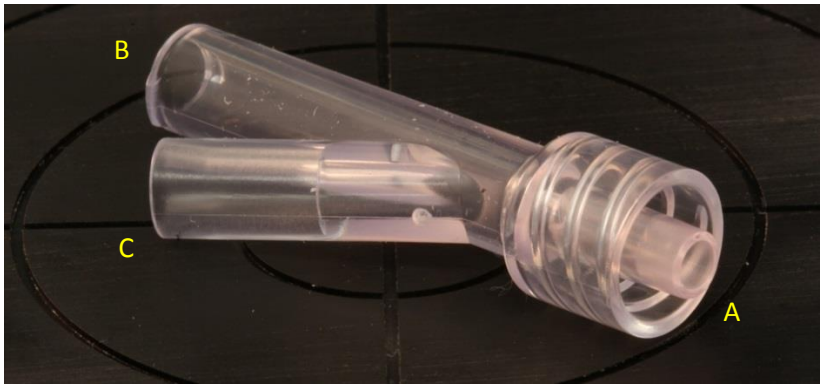

Figure 1: Injection Molded y-site with Male Luer lock (A), Female Luer lock (B), and 5/32" tubing pocket (C)

Plaques and y-site devices were both gamma radiation sterilized to >50kGy. This level of radiation exposure exceeded typical maximum-dose sterilization levels seen with most polymeric medical devices.

Quantitative Hemocompatibility

Sterile CYROLITE® Med 2 and G-20 HIFLO® y-site samples were provided to Toxikon Corporation (Bedford, MA) for testing with human blood. Citrated human blood was directly

exposed to the components at a ratio of $3cm^2/mL$[1], and a complete blood count calculated concurrent with negative and untreated samples. Results are shown in Figure 2.

CYROLITE® Med 2 and G-20 HiFlo®: Hemocompatibility results								
Comparison	**White Blood Cell**	**Red Blood Cell**	**Hemoglobin**	**Hematocrit**	**Mean Corpuscular Volume**	**Mean Corpuscular Hemoglobin**	**Mean Corpuscular Hemoglobin Concentration**	**Platelet**
Sample vs. Negative Control	No decrease	No decrease	No decrease	No difference	No difference	No difference	No difference	No Decrease
Sample vs. Untreated	No decrease	No decrease	No decrease	No difference	No difference	No difference	No difference	No Decrease

Figure 2: Hemocompatibility Results

Both materials showed no decreases in cell count and no change in other parameters, indicating that the materials did not produce a deleterious effect on human blood.

Platelet Analysis

Sterile plaque samples of multiple materials, including CYROLITE® Med 2 and G-20 HIFLO® were provided to the North Carolina State University Center for Electron Microscopy (Raleigh, NC). After samples were immersed in human blood, and cells dehydrated and fixated, sample images were examined and platelets were enumerated by categorizing as non-activated, partially-activated, and fully-activated depending upon their morphological state[2]. Figure 3 provides the results of the analysis.

Platelets (per sq.mm)	**CYROLITE® Med 2**	**CYROLITE® G-20 HIFLO®**	**Medical grade polycarbonate**	**Co-polyester**	**Impact modified SMMA**	**Transparent ABS**
Total Adhered	824	1422	2276	1722	1677	1003
Fully Activated	0	0	75	30	225	60

Figure 3: Total adhered platelets and activated platelets per material type

CYROLITE® Med 2, G-20 HIFLO®, and transparent ABS resins had the three lowest quantities of adhered platelets, with the Med 2 and G-20 HIFLO® both showing no activated platelets – platelets in their final contributing stage to the coagulation cascade. This study showed that the CYROLITE® materials may have reduced numbers of adhered and activated platelets when compared to materials used for similar medical applications.

Luer Testing

Sterile CYROLITE® Med 2 and G-20 HIFLO® resin y-sites were evaluated in accordance with testing and gauging procedures specified in ISO 594-2[3] at EG-Gilero (Durham, NC). To better simulate clinical usage of tapered Luer connections, female and male Luers were attached to like-material mating Luers rather than stainless steel reference fixtures as specified in the standard. Ten of each female and male Luer end of the y-sites were evaluated with

application torques and forces as specified in the standard. A summary of the results is presented in the table below.

Material	Table 1 Dimensions and Tolerancing	§4.1 Gauging	§5.2 Liquid Leakage Under Pressure	§5.3 Air Ingress Under Vacuum	§5.4 Separation Force	§5.5 Unscrewing Torque	§5.6 Ease of Assembly	§5.7 Resistance to Overriding	§5.8 Stress Cracking
Med 2	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	9/10 Pass	None
G-20 HIFLO®	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	10/10 Pass	None

Figure 4: Summary of Female and Male Luer Testing

With the exception of one female Luer CYROLITE® Med 2 y-site during Resistance to Overriding testing, all samples passed all elements of the ISO 594 testing. Extra component flexing associated with attaching polymer Luers to other polymer Luers, rather than steel reference Luers likely allowed the extra flexibility of the system to allow the thread to skip for this one sample. However Evonik generally recommends designing female Luer lock connectors with the more common, full thread female Luer, rather than the minimalist ISO 594-2 §3.2.2 a-variant, minimalist tab design.

Medical Tubing Bonding

5/32" OD Tygon® ND 100-65 DEHP-free Medical tubing was solvent bonded into the tubing pockets of y-sites molded from CYROLITE® Med 2, G-20 HIFLO®, and four other medical grade materials. Bonds were created using two solvents: 100% Cyclohexanone, and a 50/50 blend of Cyclohexanone and MEK. All tubing was bonded to the samples prior to sterilization. Bonded tubing was pulled out of the tubing pockets, in-line with the pocket, using a tensile testing device. The peak force values at failure were recorded and averaged for samples of the same material. A summary of the test results is shown below, with all break forces in pounds-force.

Solvent Type	CYROLITE® Med 2	CYROLITE® G-20 HIFLO®	Co-polyester	Medical grade polycarbonate	Impact modified SMMA	Transparent ABS
Cyclohexanone	11.38	11.29	15.75	10.32	5.65	9.15
Cyclohexanone/MEK	12.66	11.89	12.65	10.88	6.04	9.73

Figure 5: Tubing bond test results

The CYROLITE® materials exhibited higher bond strengths than all other resins other than the co-polyester material bonded using cyclohexanone.

Discussion

CYROLITE® compounds have a history of biocompatibility, processability, and toughness which make them excellent candidates for blood-contacting applications. Superb hemocompatibility – including the potential to not cause platelet aggregation or activation to

the same extent of other materials – shows that the resins are ideally suited for direct contact with human blood. Additionally, their material toughness (5 times the impact resistance of unmodified acrylics), make them well suited to appropriate compressive fluid connectors and loaded regions of a device. Finally, the easy bondability of the materials streamlines manufacturing when attaching to tubing – which otherwise might require time intensive, multi-step adhesive joining.

References

1. ISO (2007). ISO 10993-12:2007 Biological evaluation of medical devices – Part 12: Sample preparation and reference materials. Geneva, Switzerland: ISO
2. Evonik Industries. (2016) *Examination of platelet adhesion and activation on gamma-sterilized medical polymers*.
3. ISO (1998). ISO 594-2:1998(E) Conical fittings with 6% (Luer) taper for syringes, needles and certain other medical equipment – Part 2: Lock fittings. Geneva, Switzerland: ISO

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