Materials of Construction

Thermoplastic Piping Systems for Pharmaceutical Water Applications

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The use of thermoplastic plastics in pharmaceutical and biotech water and process systems is gaining greater acceptance. Water systems are often more efficiently operated when thermoplastics such as Polyvinylidene Fluoride (PVDF) and Polypropylene (PP) are employed as compared to ones constructed of stainless steel. It is important to consider the unique properties of thermoplastics when evaluating their merits for your system requirements. Issues such as thermal expansion, operating pressure and system temperature need to be taken into account. Should a water system’s criteria fall within the acceptable range of thermoplastics’ operating conditions, the choice of plastics over metals can easily result in years of trouble-free and low maintenance operation. This is demonstrated and proven by the many existing PVDF and Polypropylene Purified Water and WFI systems.

Why Consider Plastics?

Plastics offer numerous advantages over stainless steel systems. In particular to pharmaceutical and biotech systems, plastics should be considered for the following advantages:

- Corrosion & Passivation Free
- Simplified Welding Techniques
- Superior Surface Finish
- Purity of Material
- Reduced Operating Cost

Corrosion Resistance & Passivation

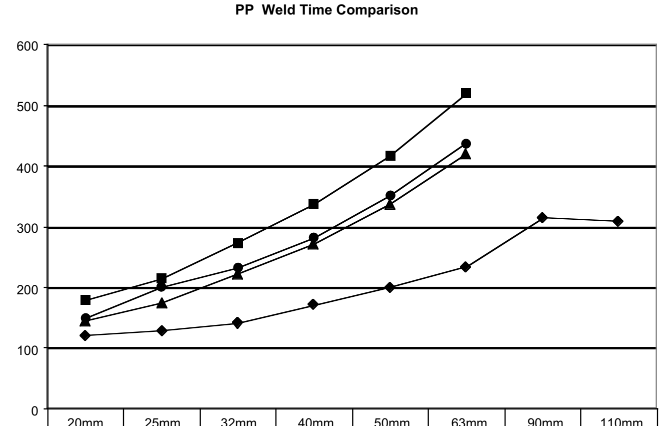
Plastics systems offer many advantages over stainless steel in pure water applications. Rouging, a common occurrence in metal systems is eliminated. Plastics simply do not corrode. By eliminating rouging, plastics also eliminate the many other timely and costly operations associated with it. Passivation, for example, ceases to be required.

Passivation is the process in which free ions are removed from the product surface of stainless steel systems. During welding or system cleaning the iron content is increased, disturbing the chromium/iron balance at the product surface. Systems become more susceptible to corrosion when this balance is disturbed.

ASTM 380 specifies how nitric acid, or other similar agents, is used to restore the desired equilibrium between chromium and iron. This process, when properly implemented, can restore the corrosion resistance of stainless steel systems. However, it is important to note even when properly conducted, passivation penetrates only 50 Å of the product surface (1). The remaining wall does not receive the restoration benefit of passivation. This becomes especially important with bioprocess applications, which may have suspended particles/cultures lending to system erosion. Small levels of erosion can quickly become major sources of ion contamination.

PVDF and PP Plastic systems are inherently superior to stainless steel in that they are manufactured from 100% pure resin. Unlike stainless steel compounds, there is virtually no difference in the chemical composition of manufactured lots of material. The welding process or chemical cleaning procedures does not degrade the corrosion resistance of thermal plastic systems. The cleanliness of material on the outside is the same as that on the product surface. Thus system downtime, chemical purchase and disposal, and corrosion are eliminated with thermoplastic systems. This results in enormous savings over the course of a water system’s life.

An additional benefit associated with pure plastics is that they do not contribute to ion contamination. In bioprocess applications, ion contamination is a serious source of concern for it directly decreases system yield. According Livingston, metal ion contamination can have a direct negative impact on yield (2)! Thermoplastic systems for bioprocess applications offer cleaner operation with increased production capacity.



	20mm	25mm	32mm	40mm	50mm	63mm	90mm	110mm
◆ A	120	127	140	170	198	232	313	308
■ B	178	213	272	337	416	519		
▲ C+	143	173	221	270	336	419		
● C+ PPn	148	199	231	281	350	437		

Figure 1: Comparison of different PP welding times for welding machines from two manufacturers using IR Fusion

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Simplified Welding Techniques
Thermoplastics offer simplified welding techniques. Both PVDF and PP are melt processable polymers. Systems are joined by a variety of thermal-fusion welding techniques. As mentioned, PVDF and PP resins are extremely pure and immensely consistent from lot to lot. This purity and consistency allows for dependable welding parameters, which translate into repeatable and reliable welding techniques. Stainless steel welding concerns such as sulfur concentration, chromium depletion, condition of tungsten electrode are not issues for thermoplastics. The result is simplified welding and installation practices with thermoplastic systems.

One of the most common welding methods for thermoplastics such as PVDF and PP is a non-contact method known as Infrared (IR) Fusion. IR Fusion is accomplished by bringing the pipe components into close proximity with a heating element. Direct contact with the heater is avoided in order to minimize the risk of material contamination. This simple procedure involves 4 basic steps.

Step One, Planing of Material: Both sections are planed simultaneously to produce a clean and level joining surface.

Step Two, Alignment: Material, prior to heating, is brought together to verify the alignment. This important step verifies the material has been planed properly and checks to ensure proper alignment. Improper alignment will cause weak welds subject to failure.

Quality welding machines will allow movement of the clamps to compensate for normal offsets in material alignment. Mis-aligned joints can and do cause system failures.

Step Three, Heating: The material is held near the heat source for a predetermined amount of time. The time and heater temperature varies between material, size and pressure rating.

Step Four, Material Joining: After heating, the heater is removed and the material is joined together with a set force or for a controlled distance. According to ASTM 2657, one should:

> *...bring the melted ends together immediately with sufficient force to form a uniform flash (bead)… This is the most critical part of the whole joining procedure. If the components are brought together with too much force, all molten material may be pushed out of the joint and cold material brought into contact forming a “cold” joint. If too little force is used, only the melt beads may be fused. (3)*

A cool down period is required as part of the joining process. The cooling period allows the weld area to strengthen. This period is affected not only by material, size and pressure rating, but also by manufacturers welding machine. Figure 1 compares different PP cooling periods for welding machines from two manufacturers utilizing IR Fusion. The cooling period, one of the longest steps in the entire welding process, should be evaluated for installation labor savings. In addition, it may be advantageous to use a single machine capable of welding your complete system size range.

An important factors in evaluating IR Welding technology (as stated in ASTM 2657) is the ability to monitor and control the force or speed in which molten material is joined. There are two commonly used and available methods to ensure proper system joining. One uses a mechanical stop, which seeks to control the absolute distance the joined materials are allowed to travel. The drawback to this method is the inability to directly monitor the force or speed in which the material is joined. Should the material be joined too quickly or with too much force, there is a small risk the molten material will be forced outside of the joining area. Additionally, small variances in the mechanical stop’s size or placement could result in insufficient or excessive applied force. Material joined together too slowly will cool down prior before an acceptable amount of material forms together. In either case, a cold joint would result.

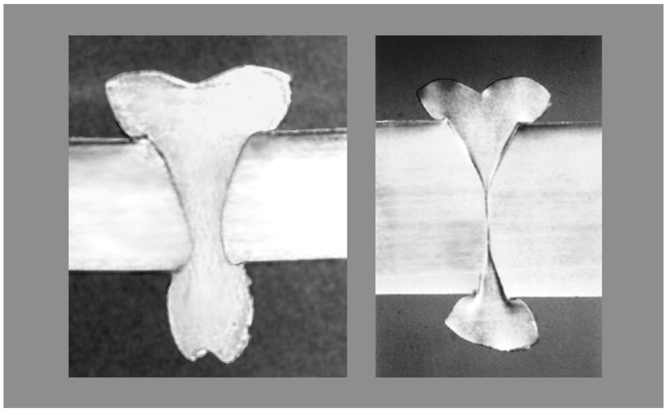


Figure 2: Cross section of an acceptable joint and cold joint

Figure 2 is a cross section of an acceptable joint and a cold joint. Although the exterior beads of both welds appear similar, the cold joint will likely fail once the system is pressurized. Cold joints are best prevented through proper training and experience. As with any installation, experienced weld technicians should be utilized.

The other available IR Fusion method controls the joining pressure by directly monitoring the force applied during the entire joining and cooling procedures. Various degrees of sophistication for force monitoring exist. From simple manual indication to complex computer controlled processes, the degree of sophistication required varies according to project requirements. Regardless of method, direct monitoring of joining force best prevents cold joints and guarantees high weld quality. Some systems are available with complete computer control of the key welding parameters of heat, time and joining force. Furthermore, many systems aid validation by electronically storing welding data for later review and QC.

Commonly available for ˚” (20mm) to 10” (250mm) pipe diameters, IR fusion does provide a small bead or seam 360° around the joint. While it could be perceived that the bead formation might lead to a stagnant zone or a location for bacteria growth, this is in fact not the case. The formation of the internal bead involves minimal roll back, eliminating pockets in the joint. Continuously operated systems provide for sufficient turbulence in the bead area to prevent biocolonization. Additionally, thermoplastic systems are not passivated and should not require shutdown when properly operated.

For systems where shutdown is preferred, beadless welding is available up to 2" to 3” (63mm to 90mm). These systems generally require an internal balloon to apply outward pressure as heat is applied. The balloon thus prevents the formation of an internal bead. The heating mechanism for these systems can vary. One common system uses a clamp with integral heating device. The clamp slowly heats the material to the melt point and then allows it to cool while holding weld area in place. Other systems use an external electric coupling (See Figure 3). Heat is generated as electricity is applied to the coupling.

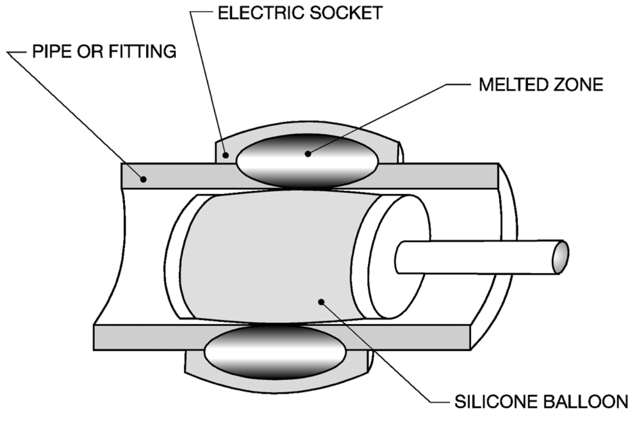


Figure 3: An external electric coupling weld

Although these systems provide excellent welds, they are time-consuming and are limited to 90mm (3") and smaller sizes. Since thermoplastic systems are inherently cleaner systems than stainless steel, these systems should be considered in applications were complete drainage is an absolutely necessity and labor costs not an issue. The effectiveness of non-beadless thermoplastic systems is evident in many successful semiconductor applications. In these systems, continuous operation is commonplace in spite of their extremely stringent purity requirements.

Superior Surface Finish

As with any water system, microbiologic growth and biofilm are factors, which need to be minimized; if not eliminated. Surface finish is often cited as critical factor in the proliferation of bacteria colonies. It is believed the rougher the surface finishes, the easier bacteria can adhere to and resist flushing. This is especially important in laminar flow conditions in which velocities along the system surface area are sufficiently slower than the interior. Absent of any beads our other turbulence causing phenomenon, systems with rough surfaces may experience biofilm difficulties.

Studies conducted by G. Husted of MicroTechno Research, Inc. have demonstrated thermoplastics such as PVDF and E-CTFE are more resistant than stainless steel to microbial fouling in Ultrapure Water (UPW) applications. (3)

The test was conducted to compare the amount of biocolonization between samples of stainless steel, Halar (E-CTFE) and PVDF

...by direct microscopic examination of 8mm diameter test coupons, presented to an E-1 quality UPW stream, in a Robbins Sampler (McCoy, et.al. 1981). This devise was designed by the Costerton biofilm group at the University of Calgary to provide replicate test surfaces for the study of microbial adhesion and biofilm formation. At weekly intervals 3 randomly selected discs of each test material are removed from the sampler, rinsed with a jet of double filtered UPW to remove non-firmly associated cells, stained with acridine orange, then viewed with epifluorescent illumination at 1,250X magnification. The surface of each test piece is directly examined for bacteria, adherent to the surface, and their number per unit area of the test piece determined.

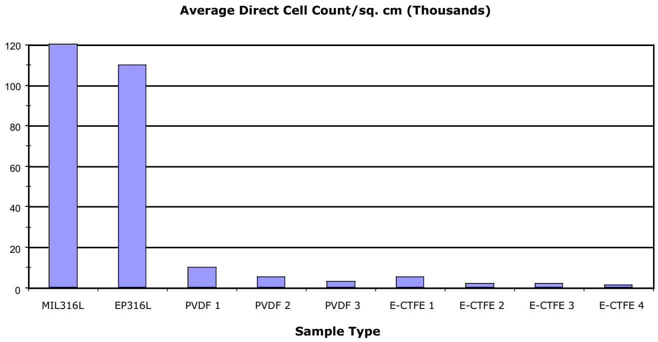


Figure 4: The results of comparing the avergae direct cell count per cubic centimenters of material

The study’s results clearly suggest PVDF and ECTFE systems are better suited than stainless steel to resist biofilm. Figure 5 depicts the results by comparing the average direct cell count per cm^2 material. Clearly, the thermoplastics are more resistant than stainless steels to the proliferation of bacteria colony formations. The studies results suggest surface finish is influential in resisting biocolonization.

Typically, high purity PVDF systems typically offer better surface finishes than stainless steel systems. Figure 6 compares the surface finishes of PVDF and PP to mechanically polished and mechanically/electro-mechanically polished 316 Stainless Steel. (5)

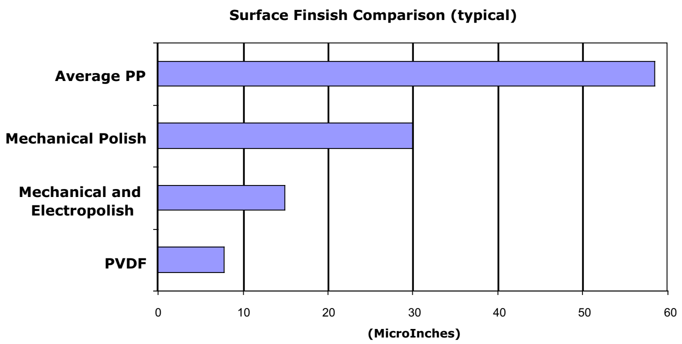


Figure 5: A comparison of the surface finishes of PVDF and PP to mechanically and mechanically/electropolished 316 stainless steel

Purity of Material

PVDF and PP unlike Stainless Steel do not rouge and provide superior purity as compared to stainless steel. The purity of resin provides additional advantages in overall system purity. For Polypropylene, these advantages warrant consideration even with rougher surface finishes than high grades of stainless. High purity grades of PVDF and PP have extremely low levels of extractable. The low extractable levels provide thermoplastic water systems with simplified operation. It is important to understand and evaluate the quality of resin being used for the various systems under consideration.

Not all PVDF or Polypropylene resin is the same. Various grades and production methods are available. Each production method has its unique merit for various applications. For UPW applications, it is essential only pure resins are used. PVDF resins with additives, for flame retardation for example, must be avoided for they have higher rates of leaching contaminants. Furthermore they do have different mechanical properties compared to pure PVDF material.

Polypropylene has been shown to be more stable and pure when produced as a copolymer. Products produced with random copolymer polypropylene (PPR) display better purity properties than those of hompolymer polypropylene (PPH). This fact is documented on in Table A and clearly shows the PPR material outperforming PPH. (6) When evaluating any purity data, it is important to also compare test methods. Only tests conducted to the same standard should be used for comparison of results. (See Table A)

Design Considerations

Both PVDF and PP piping systems are available with a wide assortment of zero dead leg vlaves, specialty fittings and high-purity flow meters. These components are available in molded and fabricated configurations and allow for complete thermoplastic construction of piping systems. Plastic design configuration can easily customized to meet specific requirements due to their inherently stable and repeatable nature. IR heating allows for immense flexibility in system fit-up.

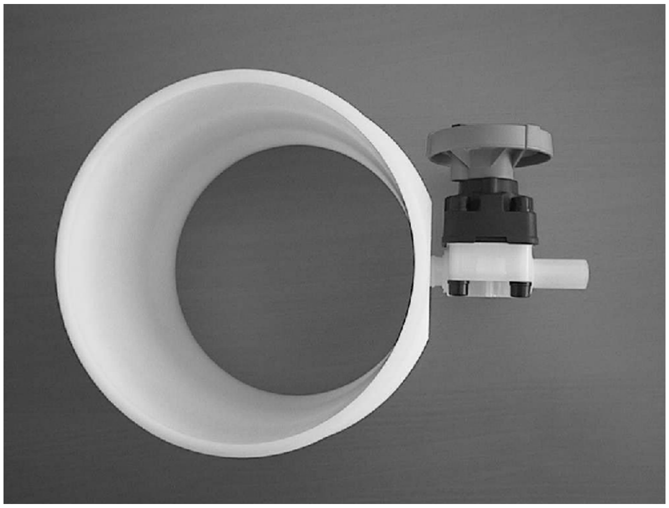


Figure 6: A large diameter, custom zero dead leg diaphragm valve

Before considering the specific design and fitting requirements of any thermal plastic systems, the water system qualification should be determined. Most pharmaceutical and biotech systems should have the majority, if not all, of their facility served with Purified Water systems as outlined by USP 24. Using plastics in a properly engineered Purified Water system will save installation, operation and maintenance costs. Cleaner operation and removal of passivation requirement result in sanitation cost savings and reduced need or elimination of system shutdowns.

Current USP24 guideline set bacteria levels at <50 and <10 colonies/ml for Purified Water and WFI respectively. Additionally, TOC should be less than 500ppb. When operating a thermal plastic water system, one should establish targets of significantly lower TOC levels. This is easily accomplished by proper system design and immensely helpful in reducing overall bacteria levels. Low TOC levels directly prohibit the proliferation of bacteria forming colonies.

As with any USP Water System, sanitation needs to be considered. Both ozone and UV light are acceptable and recommended means of providing continuos sanitation control. The small levels of required ozone do not harm plastic systems. Direct UV light used for sanitation, on the other hand, can degrade plastic systems. Degradation is avoided by means of simple light traps. Qualified system suppliers can provide assistance with system designs.

As always, heat is an excellent means to control bacteria.

PVDF Systems can be periodically steam cleaned (7) or elevated temperatures can be a viable option. Typically, 80°C has been the target temperature for heat sanitation. PVDF is recommended, but polypropylene should be avoided in such high temperature applications. However, recent guidelines have promoted lower temperatures as being just as affective. According to ISPE's "Baseline, Volume IV", 65°C is recommended and acceptable for validation. At this temperature, both PVDF and PP can be considered.

When designing USP Water Systems with elevated temperatures, operating pressures need to be examined. Plastics systems are limited in their operating pressure and design temperature. Most PVDF Systems 63mm (2") and below are rated for 230psi operations with the larger diameters either 230 or 150psi. Polypropylene, on the other hand, is generally limited to 150psi operation. Since most water systems operate well below these pressures, it is normally not an issue. However, regardless of nominal pressure rating, temperature affects plastic systems ability to handle pressures. Most thermoplastic manufacturers provide correction charts to determine the actual pressure rating at various temperatures.
(See Table B: Sample Temperature Correction Factors)

An additional engineering consideration with plastic systems is thermal expansion. Plastic systems expand at much greater rates than steel systems. Once this is understood, expansion is compensated for by one or two common means: anchoring or expansion loops.

Anchoring seeks to restrain a system from growing. This is accomplished by physically restraining the system at fixed points throughout the system. If temperature changes are not drastic, expansion forces can be absorbed by the system. It is important to anchor the points horizontal and vertical to prevent system buckling. Special restraint fittings as seen in Figure 7 are available from some manufactures. When properly clamped and secured, the integral ridges of the restraint fittings prevent horizontal expansion. The pipe is thus prevented from buckling and expanding. Known as Fixed Point Anchors, these fittings are essential to properly accounting for the forces of thermal expansion.

If a system requires being flexible due to thermal stress created by large temperature swings, loops, offsets and changes in directions can be designed to compensate for the growth. Mechanical devices such as bellows and expansion joints are discouraged due to the possibility of mechanical failure and reduced purity. Using an expansion loop, off sets or naturally occurring change in direction can compensate for thermal expansion. (See Figure 9) Allowing for expansion at change of directions will likely reduce or eliminate the need for loops. In all cases a thorough review of the system is required and use of

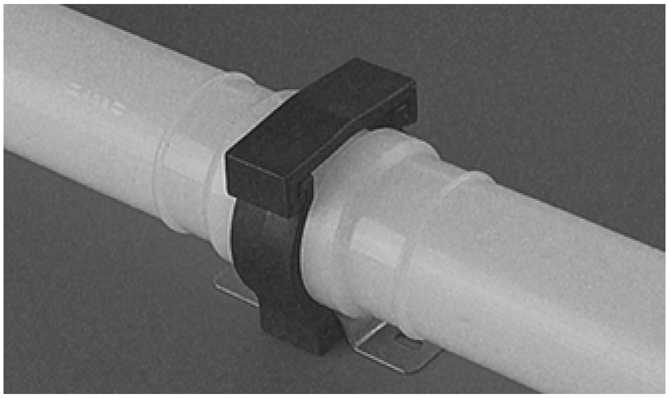
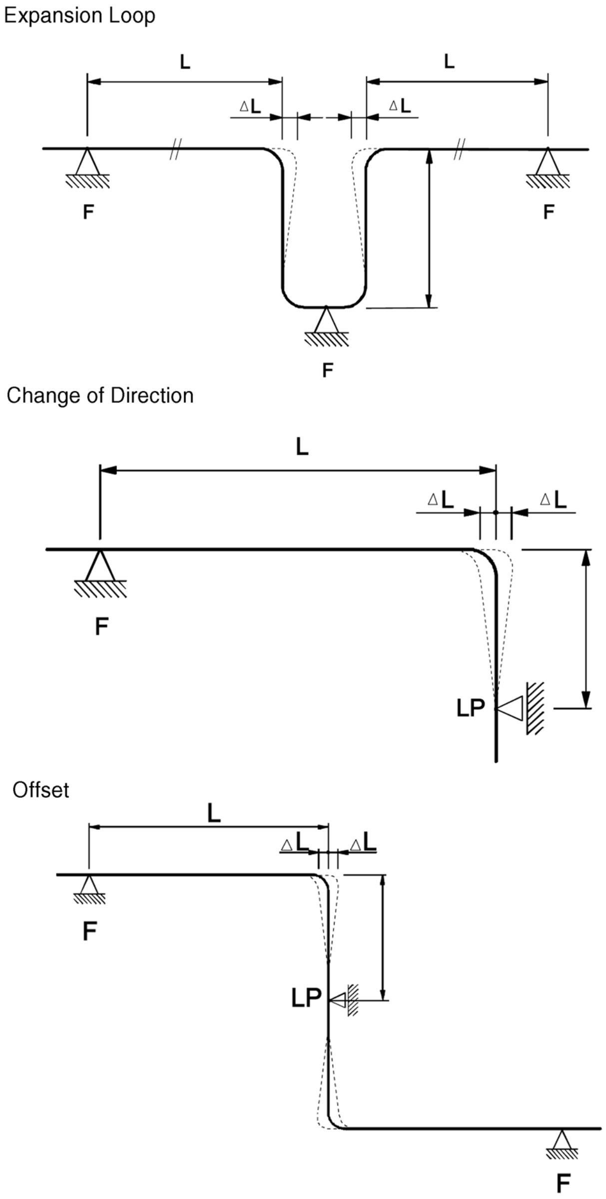


Figure 7: A special restraint fitting as provided from some manufacturers



Expansion Loop

Change of Direction

Offset

Figure 8: Expansion loop, change of direction, and offset loops used to help compensate fopr thermal expansion.

restraint fittings is always required to direct the growth. Qualified system suppliers are available to assist with expansion calculations and control means selection.

In conclusion, thermoplastic USP Water Systems are a viable and cost effective alternative to stainless steel. They provide clean operation with simplified maintenance. Reliable welding methods further ease the use of these systems in USP Purified Water or WFI applications. ISPE has acknowledged the expanding acceptance of plastics by noting their suitability in “Baseline, Volume IV”. It is helpful to understand the unique traits and characteristics of plastics when evaluating their merits for you next application. When properly designed and installed, thermoplastics systems provide years of trouble free service at less cost.

Acknowledgements

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Static Leach-Out Behaviour

Testing According to SEMASPEC

Description		Unit	Test Temperature 20°C (68°F)			
			PVDF	E-CTFE	PP-R	PP-H
Anions:						
	Fluoride	µg/m^2	1466	191	1.48*	13
	Chloride	µg/m^2	7.41	10.37	2.96	4.44
	Nitrite	µg/m^2	1.48*	1.48*	1.48*	1.48*
	Bromide	µg/m^2	1.48*	1.48*	1.48*	1.48*
	Nitrate	µg/m^2	1.48*	6.66	1.48*	1.48*
	Phosphate	µg/m^2	2.96*	2.96*	2.96*	2.96*
	Sulphate	µg/m^2	2.96	8.88	1.48*	1.48*
Cations:						
	Lithium	µg/m^2	1.48*	1.48*	1.48*	1.48*
	Sodium	µg/m^2	1.48	2.93	5.92	29.62
	Ammonium	µg/m^2	2.96	2.93	7.41	7.4
	Potassium	µg/m^2	1.48	1.48	1.48	22.22
	Magnesium	µg/m^2	1.48*	4.44	13.33	37.03
	Calcium	µg/m^2	3.7	4.44	13.33	32.59
Transition metals:						
	Fe 3+	µg/m^2	1.48*	1.48*	2.96	4.44
	Cu	µg/m^2	1.48*	1.48*	1.48*	1.48*
	Ni	µg/m^2	1.48*	1.48*	1.48*	1.48*
	Zn	µg/m^2	1.48*	1.48*	4.44	13.33
	Co	µg/m^2	1.48*	1.48*	1.48*	2.22
TOC:		µg/m^2	260	in preparation		

Table A: Static Leach-out Behavior at 20C * = Below Detection Level

Temp ºF	Temp ºC	PVDF Corr. Factor	PP Corr. Factor
68	20	1.00	1.00
80	27	0.95	
90	32	0.87	
100	38	0.80	0.64
120	49	0.68	
140	60	0.58	0.40
160	71	0.49	
180	82	0.42	0.28
200	93	0.36	0.10
240	115	0.25	
280	138	0.18	

Table B: Sample temperature correction factors for PVDF and PP