Material Issues in the Pharmaceutical Industry

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THE OVERVIEW of materials of construction corrosion failure mechanisms in the article "Corrosion in the Pharmaceutical Industry" in this Volume continues to be a valuable resource for information on this topic. Some trends in the availability and application of materials in this industry, and current issues relative to pharmaceutical equipment construction, warrant closer examination.

Materials

In an industry conservative by nature, the change in material use is slow to occur and driven primarily by the failure of existing material systems to resist corrosion from new processes. Equipment involved in product contact has been constructed largely from austenitic stainless steel 304L (UNS S30403) and 316L (UNS S31603). The satisfactory performance of these materials in most applications, combined with good material availability at acceptable price levels, produces little incentive to change. Historically, in areas where 316L was not adequate, the high-Ni-Cr-Mo alloy C-276 (UNS N10276) was the alternate choice.

In the 1970s and 1980s, numerous alloys intermediate to 316L and C-276 were developed that offered the chemical and corrosion resistance necessary for the pharmaceutical industry. A few of these alloys are popular in the sense of market availability and use, and while alloy development continues, it is at a much slower pace. These alloys can generally be characterized into two families, identified as superaustenitic and duplex stainless steels.

Superaustenitic Stainless. Of the superaustenitic stainless alloys, the AL-6XN alloy (UNS N08367) has been the most widely used. This alloy is nominally 25Ni-20Cr-6Mo, with the balance essentially iron. See the article "Corrosion of Nickel and Nickel-Base Alloys" in *Corrosion: Materials,* Volume 13B of *ASM Handbook,* 2005, for information on other Ni-Cr-Mo alloys and aqueous and high-temperature corrosion. The high-chromium and molybdenum additions result in an alloy that is very resistant to

pitting attack, but more importantly, resistant to crevice corrosion. Laboratory tests for evaluating resistance to localized corrosion have been developed and are useful in determining the relative resistance of various materials to acid chloride environments. These tests should not be used to predict precise behavior in other environments, and comparison of one data set to another must be done with caution because there can be variability in results. However, materials showing resistance in these tests have demonstrated an ability to perform well under conditions where 316L has failed due to localized corrosion, such as crevice corrosion.

Crevice corrosion occurs in 304L and 316L stainless steels when the conditions in a tight crevice become more severe than the surrounding environment. Stainless steels gain their corrosion resistance by forming a protective oxide surface layer. This layer, composed primarily of chromium oxides, is readily formed in the presence of oxygen. This protective layer is susceptible to damage from halogens, but if oxygen is present in the environment, repair of the film is often rapid enough to prevent any significant damage. In the absence of a source to replenish oxygen, such as in a tight crevice, corrosion can accelerate as the available oxygen is consumed and the pH drops as a result of the corrosion process.

Another location where depleted oxygen can lead to corrosion of stainless steel is at low points of piping systems without adequate drains.

Duplex Stainless Steels. A number of duplex stainless steels exist. Alloy 2205 (UNS S32205) contains 22Cr-5Ni-3Mo and is widely used in industrial and chemical process applications. To date, duplex alloys have seen little application in pharmaceutical equipment, but their relative cost and properties make them suitable candidates to replace 304L and 316L. The chromium and molybdenum contents result in a material with pitting and crevice corrosion resistance superior to that of 316L stainless and that is also resistant to chloride-induced stress-corrosion cracking because of the austenite-ferrite (duplex) microstructure. In general, duplex alloys are magnetic, slightly less formable, and require more care in fabrication than the austenitic grades.

The correlation between resistance to chloride pitting and crevice corrosion and alloy content is shown in Table 1. Nitrogen has become an important alloy addition in these alloys as well. A pitting index, called the pitting resistance equivalent number (PREN), has been developed to predict resistance of an alloy based on its composition. The PREN is defined as $\%Cr + 3.3 \times \%Mo + 30 \times \%N$. Other PREN formulas use $\%Cr + 3.3 \times \%Mo + 16 \times \%N$, so it is important to know the basis of the value when making comparisons. There is a term for tungsten in other PREN formulas. The level of localized corrosion resistance offered by the duplex and superaustenitic stainless steel materials fills the large gap between 316L and C-276. The superaustenitic stainless grade should be seriously

Table 1   Typical corrosion characteristic values for materials of construction in the pharmaceutical industry

Alloy	UNS No.	Pitting resistance equivalent number (PREN)(a)	Critical pitting temperature(b), °C	Critical crevice temperature(c), °C	Stress-corrosion cracking, boiling 25% NaCl
304L	S30403	19.8	0(d)	<-3	Cracks in $<$72 h
316L	S31603	24.9	15	-3	Cracks in $<$72 h
2205	S32205	37.6	40	17	Resists
AL-6XN	N08367	47.2	80	43	Resists
C-276	N10276	65.0	$>$110	$>$75	Resists

(a) Using PREN = $\%Cr + 3.3 \times \%Mo + 30 \times \%N$. (b) ASTM standard G 48, method C, critical pitting temperature test. (c) ASTM standard G 48, method D, critical crevice temperature test. (d) Estimated

considered as a less expensive alternative to the higher-nickel alloy. Also see the articles "Corrosion Resistance of Stainless Steels and Nickel Alloys" and "Effects of Metallurgical Variables on the Corrosion of Stainless Steels" in *Corrosion: Fundamentals, Testing, and Protection,* Volume 13A of *ASM Handbook,* 2003.

Material Replacement. With advances in melting technology, primarily the argon-oxygen decarburization refining process that facilitated the development of these higher alloys, came the ability to control alloy content to more precise levels. One result of this advancement to the end user is that the alloy content of grades such as 316L is actually lower than it was 25 years ago. Given the ability to control molybdenum levels to tighter ranges, it is not surprising that the molybdenum content in 316L today (2006) is typically below 2.1%, while 25 years ago it probably averaged nearer 2.5%. This has resulted in a significant cost-savings to users of these alloys in most applications. In those areas where the alloy offered corrosion resistance that was barely adequate, the subtle change in chemistry may mean that replacement 316L component no longer performs well in areas where it was once satisfactory.

Passivation

Stainless steels offer useful corrosion resistance because they exhibit passive corrosion behavior as a result of the formation of protective oxide films on the exposed surfaces. Under normal circumstances, stainless steels will readily form this protective layer immediately on exposure to oxygen. This oxygen may be from any source, including air, dissolved oxygen in water, or other oxidizing media. When this protective film is violated or fails to form, active corrosion is likely to occur. Some fabrication processes can impede the reformation of the passive layer, and, to ensure that it is formed, stainless steels are subjected to passivation treatment. The common concern in this regard is contamination of the surface by carbon steel. This local contamination may result from a variety of causes, including handling equipment, forming tools, fixtures, and clamps.

Treatments. The production of stainless steels commonly involves the use of strong oxidizing acids such as nitric and nitric-hydrofluoric acid mixtures to remove the oxide scales formed during thermal treatment. This pickling process provides two benefits. First, it removes the oxide scale and passivates the underlying metal surface. Second, due to its aggressive nature, the process will remove any chromium-depleted layer that may have formed as a result of the scale formation.

For passivation treatments other than scale removal following thermal treatment, less aggressive acid solutions are usually employed. The primary purpose of these treatments is to remove contaminants that may be on the component surface and could prevent the formation

of the oxide layer locally. The most common contaminant is embedded or free iron particles from forming or machining tools. Mechanical polishing can be employed to provide a uniform surface finish and remove these contaminants. The polishing materials used should be devoted to stainless steel use only, because they can carry over small particles from one part to the next. In addition, these fine work-hardened particles, even from a stainless vessel, can have a lower threshold for corrosion and act as an initiation site if not removed. A dilute (10%) solution of nitric acid is effective at removing free iron or similar contaminants. For ferritic, martensitic, or precipitation-hardening grades, a nitric acid solution inhibited with sodium dichromate is used so as not to attack the stainless too aggressively. Phosphoric acid at 1% concentration and citric acid at up to 20% concentration are also effective for the more resistant stainless alloys. Other commercially available chelating agents can be employed. The use of these mild acids or chelating agents can also represent a significant advantage in terms of relief from environmental issues.

Welding. A passivation treatment is also advisable following welding. Welding processes, even with proper gas shielding, may result in some oxidation (heat tint) on or adjacent to the weld. Under severe corrosion conditions, these areas will be more likely to initiate corrosion. However, the magnitude of the increased tendency to corrode is difficult to quantify, and in many instances, this condition may have no impact on actual service performance. Only extensive corrosion testing or trial experience should be used to justify the serviceability of material exhibiting heat tint. Cleanup of localized areas is best addressed through conventional weld-cleaning methods, such as pickling pastes. Electrolytic pickling and descaling processes may also be effective. Stainless wire brushing is also an acceptable means of heat tint removal. The conventional postfabrication passivation techniques, such as dilute phosphoric, nitric, or citric acid, will not remove the heat tint from welding. However, such treatments will ensure that no free iron or active areas remain.

Further information on pickling, passivation, and cleaning treatments may be found in ASTM International standards A 380 (Ref 1) and A 967 (Ref 2).

Electropolishing

Electropolishing is a controlled corrosion process, resulting in the uniform removal of metal from the surface. See the article "Electropolishing" in *Corrosion: Fundamentals, Testing, and Protection,* Volume 13A of *ASM Handbook,* 2003. Electropolishing is not a passivation treatment, although the proper execution of the process will result in a passive surface. Proper electropolishing technique maintains the part in the electrochemically

passive range, while the passivated layer is only allowed to grow several atoms thick, at most. The electrolyte simultaneously promotes dissolution of this layer. The electropolishing process does remove surface impurities, as is accomplished with passivation. During the cleaning and rinsing process following electropolishing, the material does passivate naturally upon exposure to oxygen-containing rinse water or air. Ultimate passivation of the surface is assured, because any contaminants that may have been on the surface have also been removed by the polishing process. No additional passivation procedure is required. In fact, exposure to some passivation treatments, such as dilute nitric acid, may be detrimental to the intended result by dulling the luster of the polish.

Electrolytes used for electropolishing are usually proprietary mixtures with contents that are not quantitatively revealed. The electrolyte will typically have the ingredients to facilitate three different actions of the polishing process:

- An etchant that facilitates the breakdown of a passive film
- An oxidizer that helps form a passivating film
- A highly viscous constituent that promotes the formation of a diffusion layer

The oxidizer and the etchant assist in maintaining the part in a pseudopassive state, while the diffusion layer control is necessary to promote uniform metal loss. For electropolishing 316L stainless, the electrolyte will often contain perchloric acid, which can provide both oxidizing power and a halide etchant. Acetic anhydride may be used to control the diffusion layer. Stainless and higher-nickel alloys may also use nitric acid, sulfuric acid, phosphoric acid, hydrogen peroxide, and methyl alcohol. Determining the ideal electrolyte ingredients is an important part of the polishing process. Because electropolishing is an electrochemical process, other variables to be controlled include the voltage, current density, and solution temperature. Voltages that are too low can cause etching of the surface due to more rapid general corrosion. Voltages that are too high will result in pitting. Part geometry and cathode design are critical, because it is imperative that the current be distributed as uniformly as possible over the part surface. High current densities will also result in pitting.

The large majority of stainless steel production today (2006) is by the argon-oxygen decarburization (AOD) process, followed by continuous casting. The AOD process, along with other controls in the steel-making process, has resulted in a more consistent and uniform product. Continuous casting does create the opportunity for types of surface or near-surface imperfections that can have an impact on electropolishing behavior. Static casting of ingots can result in similar problems with cleanliness. Although electropolishing imperfections on AOD stainless products are rare, the use of a double-melted product will ensure an essentially imperfection-free electropolished

surface. The benefits of making this a requirement, however, must be weighed against increased cost and decreased availability.

Rouging

Rouging is a phenomenon of particular interest to the pharmaceutical industry. It is the presence of a surface layer of oxide on stainless equipment or piping typically handling high-purity water at temperatures above ambient. This includes stills, steam systems, purified water, and water for injection. The oxides can vary in composition, degree of oxidation, color, texture, and adherence. Although generally shown to be innocuous, the mere presence of these deposits can raise concern.

The rouge itself is typically composed primarily of iron oxides or iron hydroxides, but because these are developing on stainless surfaces, they may also contain oxides of chromium, nickel, and molybdenum. There is empirical data indicating that resistance to rouging increases with increasing chromium-iron ratios in the passive layer and/or the thickness of the passive layer itself. Because both electropolishing and passivation increase the chromium-iron ratio, application of these processes can increase resistance to rouging. Even with such treatments, the passive layer can break down due to the ionizing effect of high-purity water. The low oxygen content of these waters also slows the rate of repassivation and may cause the layer to linger in intermediate states of oxidation. Repeated cycles of this process result in the entrapment of various oxides in the passive layer, hence the wide range of colors.

Rouging has also been observed to result from deposits of corrosion products from upstream equipment. Such deposits can simply be wiped from the surface and reveal an unaffected electropolished surface underneath. Upstream equipment potentially identified as the source has included stills (often with carbon steel components), lower-alloy stainless steel piping (304L/316L) welds, and stainless pump components. Stainless pump housings are often produced from as-cast products. Foundry castings often contain higher ferrite contents than wrought stainless steels to facilitate castability. Ferrite contents in cast 304 or 316 products (CF-8, CF-8M) can exceed 20%, and these may be less corrosion resistant than their wrought counterparts that typically contain no more than 5% ferrite.

Removal of rouging can be accomplished mechanically but is usually addressed by chemical cleaning. Repassivation treatments with nitric, phosphoric, citric, or other oxidizing acid solutions have been effective in removing or fully reoxidizing this layer. As with any chemical reaction, the process is time-dependent and can be influenced by temperature. For more resistant rouge patterns, reducing acids such as hydrofluoric or hydrochloric may be used in combination with a passivation treatment. The use of these acids in strong concentrations, however, may etch the surface.

Potentiodynamic polarization studies have been conducted to measure the efficacy of passivation treatments. It has been shown that the breakdown (pitting) potential is raised by passivation or electropolishing techniques that result in higher chromium-iron ratios and increased thickness of the passive layer. These potentials can be increased by as much as 50 to 100 mV over mechanically polished or pickled surfaces and have been equated to increased resistance to rouging. Additionally, the breakdown potential of the molybdenum-bearing superaustenitic stainless alloy N08367 was shown to be in excess of 400 mV higher than 316L prior to enhancing passivation treatments, and another 50 mV higher following such treatments. Such studies would suggest that higher alloys, such as N08367 or the C-276-type alloy, are highly resistant to rouging.

Issues of rouging have recently attracted the attention of at least two organizations concerned with materials performance. ASTM International Committee G-1 on corrosion is considering the development of a test method that could be used to evaluate a material resistance to rouging. The existence of such a test method could help in understanding the conditions under which rouging will occur, as well as provide an indication of the materials that will resist its formation. The Materials Technology Institute of the Chemical Process Industries is developing a project designed to better define the sources and mechanism of the formation of rouge, and this program anticipates funding work to identify the mechanism and ways to prevent its formation. See the article "Rouging of Stainless Steels in High-Purity Waters" in this Volume for details on the water chemistry, materials of construction, and classification of rouge.

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