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Assessing Corrosion Risks For New Processes And Potential Impact on $$ and Safety

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MOC is Materials of Construction (not the other one) ☺

Agenda

Corrosion may be defined as the deterioration of a material (usually a metal) because of a reaction with the environment.

- Background and potential impact
- Corrosion basics for different materials
- Common materials of construction
- Testing strategy

The cost of corrosion

- "…Results of the study show that the total annual estimated direct cost of corrosion in the U.S. is a staggering $276 billion—approximately 3.1% of the nation's Gross Domestic Product (GDP). It reveals that, although corrosion management has improved over the past several decades, the U.S. must find more and better ways to encourage, support, and implement optimal corrosion control practices."
- *Corrosion Costs and Preventative Strategies in the United States – NACE, 2002*

NDK Crystal – 1 killed offsite

Silver Bridge – 46 dead

Impact of Corrosion -1

- **Batch contamination**

- Even a fairly low rate of corrosion (0.05 mm/yr.) can produce significant metal contamination
  - 0.2-0.3 mg/L of metals per hour of exposure for a typical 100 gal vessel.
  - Most metal corrosion products are strongly colored
  - Upon neutralization or transfer to organic solvents, can precipitate as gelatinous M(OH)x
- **Process Performance**
  - Metal contamination can interfere with catalytic routes, removing the chiral selectivity
  - Can alter reaction kinetics and overall selectivity
  - Iron and copper can enable redox schemes by serving as transfer agents M+2 <-> M+3

- **Vessel integrity**
  - Certain forms of corrosion can impair vessel integrity by reducing the stress the vessel can tolerate before failure
    - Environmental cracking, Intergranular corrosion, and Embrittlement are examples of this

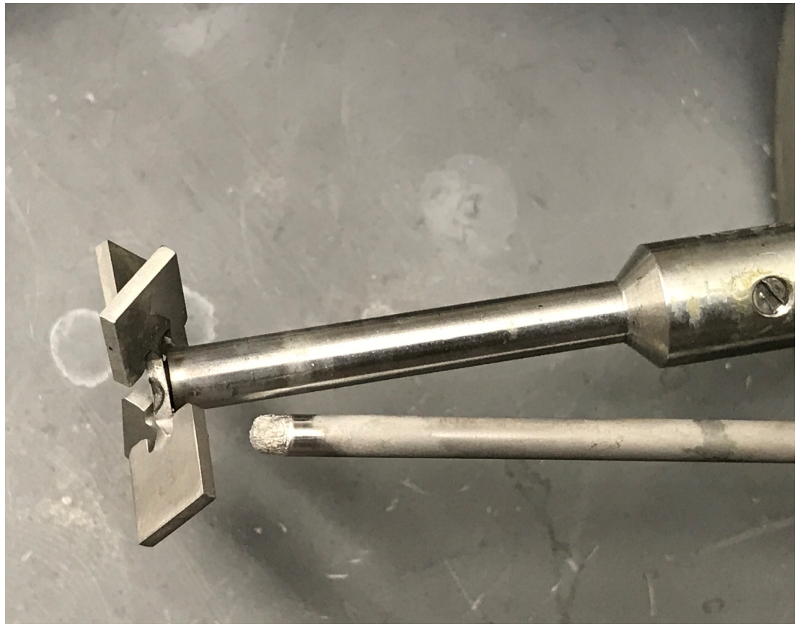
Impact of Corrosion - 2

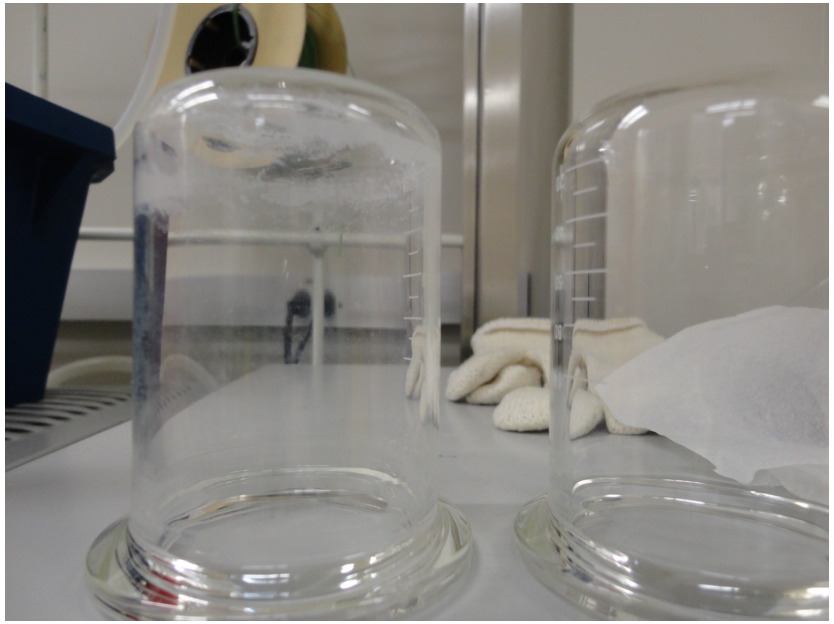
- **Vessel Damage**

- For metal vessels, general corrosion is usually fairly benign in terms of integrity – Thickness change is fairly uniform and can be measured via ultrasound.
- For glass-lined vessel general corrosion is a bigger issue as the glass lining is typically very thin (40-60 um) and is composed of multiple layers.
  - Reglassing a vessel can be $500K or more, and can take several months or longer.
- Crevice attack and pitting are more problematic:
  - Pitting can lead to vessel penetration in a small patch or area – and can be difficult to detect
  - Crevice attack by definition occurs in occluded or masked areas, and may not be seen until it causes leaks or other issues.
  - Can be difficult to repair, requiring electropolishing or grinding
- **GMP and cleaning issues**
  - For metal vessels general attack will dull the metal, but typically leaves a smooth surface
  - Pitting and crevice attack can lead local pockets that can trap product with poor access to bulk cleaning solvents
  - Glass and glassed steel will lose polish and become roughened as a result of general corrosion, making detection of soiling more difficult, and cause swabs and cloths used for cleaning to lose fibers (batch contamination risk)

Production Examples

- Corroded Hastelloy vent lines from HCl / SO2– Corrosion could be measured with a ruler.
- Severe discoloration after heat sterilization of NaCl solutions at 130°C –
  Testing showed that severe corrosion could be expected: vessel needed to be replaced.
- Badly corroded packing after distilling wet isopropyl chloride in a column with stainless steel packing –
  iPrCl + H_2O → iPrOH + HCl

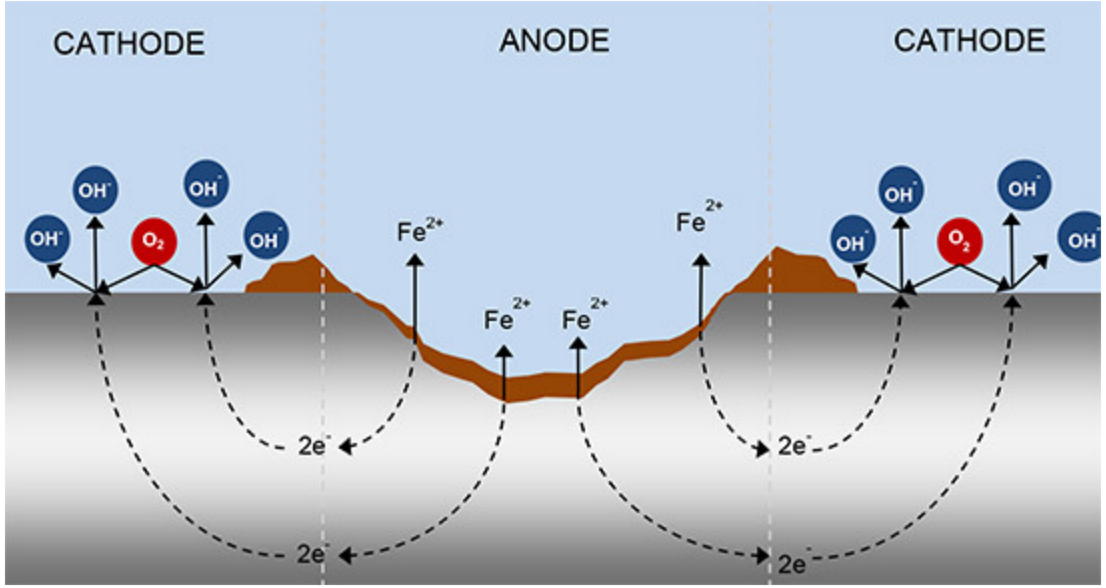




Metal Corrosion

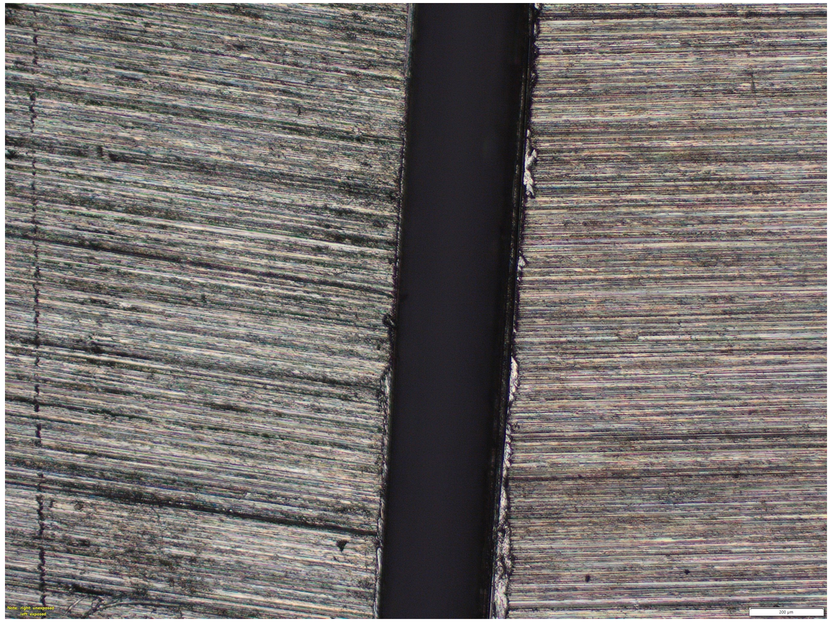
Fundamentals

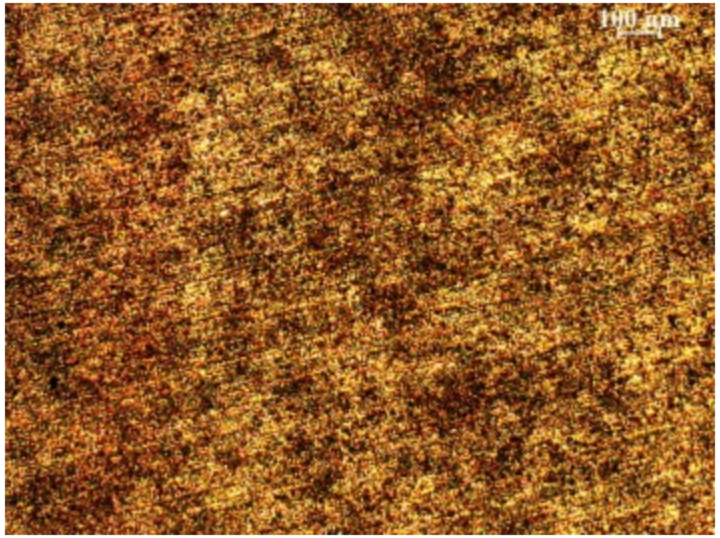
- Metal corrosion is a redox reaction
- Anode: $M^0 \rightarrow M^{+n} + n\ e^-$
- Cathode (most common):
- $H_2O + ½\ O_2 + 2\ e^- \rightarrow 2\ OH^-$
- $2H^+ + 2\ e^- \rightarrow H_2$
- $M^{+n} + e^- \rightarrow M^{+(n-1)}$



General corrosion (crystalline attack)

- Uniform corrosion across the surface. Most predictable form of corrosion.
- For passive metals (316L for example) this means the film has been reduced.
- The metal surface will appear dulled and possibly discolored.





Crevice Corrosion

- Typically associated with restricted access to an area of metal: Poorly sealing gaskets, poor welds, surface deposits and lap joints are common causes.
- Caused by local potential differences, either from oxygen depletion or corrosion product accumulation.
- Can be mitigated by proper design: eliminate stagnant areas, proper welding techniques, using sealants.

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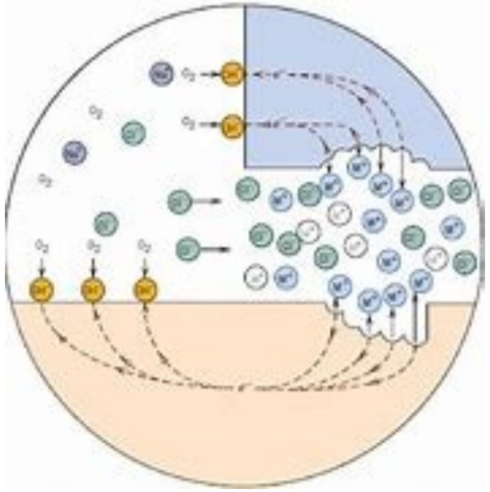
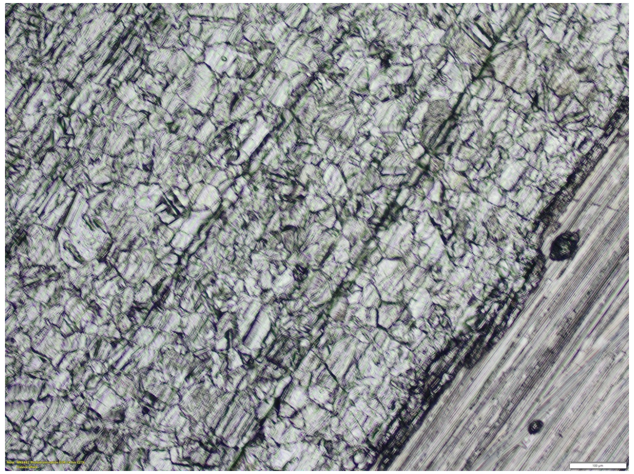
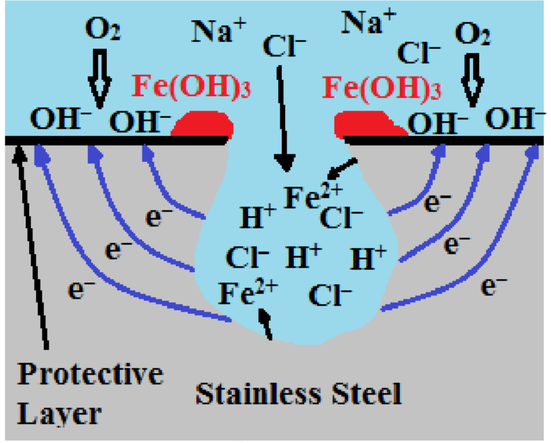
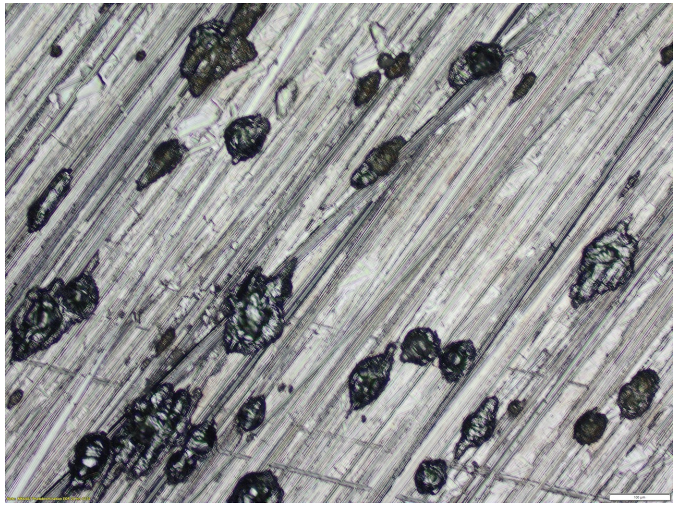




Pitting -

- Occurs in metals with a protective film
- Localized breakdown of the passive film allows corrosion in the defect
- Corrosion products accumulate and acidify the hole – increasing the local corrosivity.
- Pits can act as drills, rapidly penetrating the metal. This effect is amplified by the area effect (small anode, large cathode).
- Countermeasures include “passivation”, adding oxidizing inhibitors, deaerating the solution, increased flow





Galvanic corrosion

- Possible when dissimilar metals are connected, forming a circuit with an electrolyte solution.
- The more noble metal (copper, gold) serves as the cathode while the more reactive metal acts as the anode.
- Anode-cathode areas are critical: You want large anodes and small cathodes.
- Electrical isolation between different metals, or using easily polarizable metals. (such as Hastelloy or 316L)

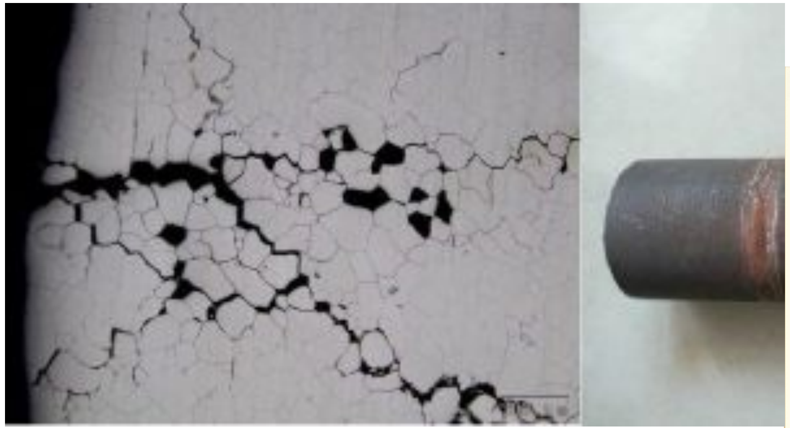
Proprietary

These forms of corrosion can cause catastrophic failure!

- Intergranular Corrosion
- Environmental Cracking
- Hydrogen Embrittlement

Intergranular Corrosion

- Selective corrosion of grain boundaries.
- Reason the “L” types of stainless were developed
- Issue with welding, heat-treatment



Environmental Cracking

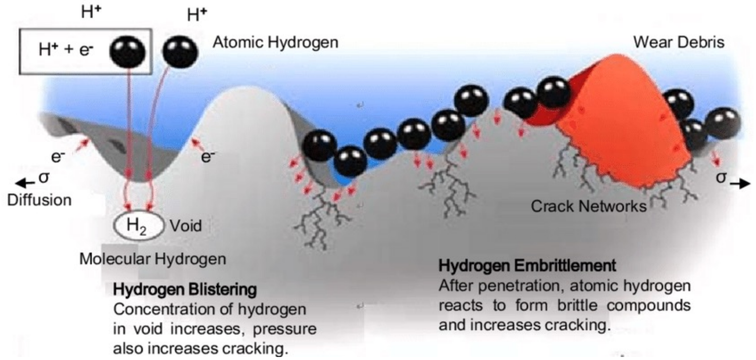
- A combination of tensile stress, with a locally corrosive environment. Cracking initiates at a local defect, and additional corrosion + the stress causes the cracks to propagate
- Environment specific:
- 316L + Cl-

Cu + NH3

Steel+ S-2

Hydrogen Embrittlement

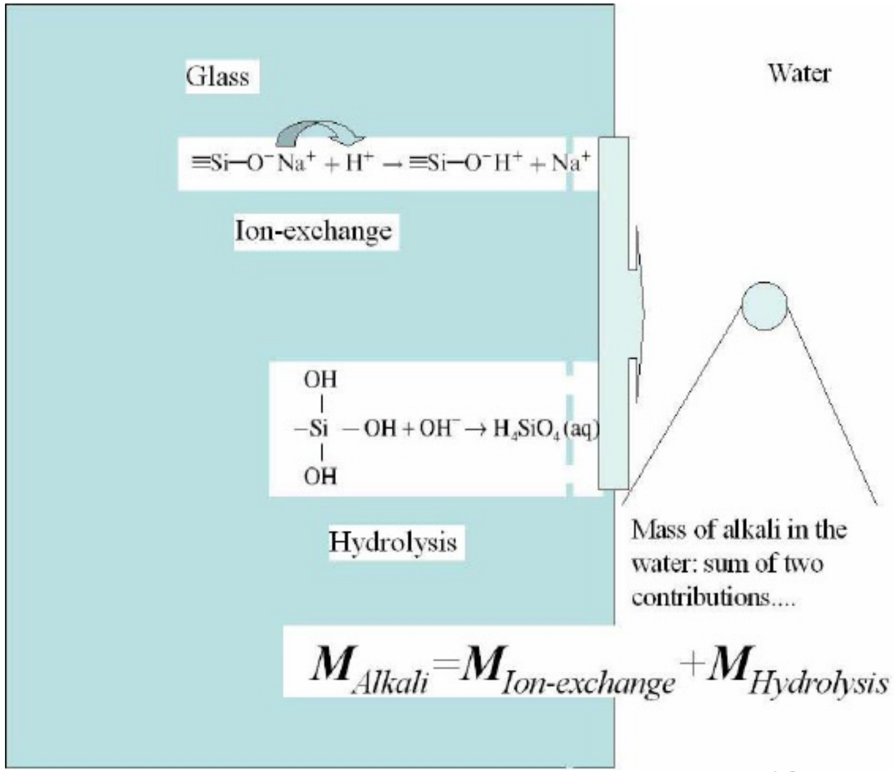
Diffusion of atomic hydrogen into the metal matrix, and formation of elemental hydrogen in the metal – causing high stress.
Titanium and Tantalum are very susceptible.



Other forms of material incompatibility

Overview

- Chemical reaction between the (O-Si-O) network and a corrosive species (OH- and F- are the most common, also hot phosphoric acid). Hot acids and superheated water can also attack
- Hot acids and water primarily use the ion exchange mechanism.
- Alkalis primarily use the hydrolysis mechanism
- Fluorides (HF) attack the silica directly
- (-O-Si-O-) + 4HF → SiF4 + 2H2O
- HBF4, HPF6 and KHF2 and other chemicals that can be written as HF.X can also be very aggressive towards glass.



Corrosion of Polymers

- Thermoplastic polymers: Formed of long-chain molecules held together by intermolecular forces
- *Can be heated, reshaped and cooled.*
- Polyethylene, polypropylene, Nylon, Teflon, PVC, Polystyrene, EPDM, Viton
- Thermosetting polymers: Crosslinked networks held together by covalent bonds
- *Decompose when heated: Once formed their shape is set*
- Epoxy resin, melamine, vulcanized rubber, Vinyl Esters, Polyurethane

Polymer attack

- Solvation: The general rule of thumb is that like attacks like.
- The solvent interpenetrates the polymer chains, typically causing softening and swelling
- Examples: Hexane and HDPE, DMF and Kynar
- Chemical Degradation: Attacks the linking bonds, cause permanent damage.
- Example: Acids and Bases with Nylon.

Common Materials of Construction in Pharmaceutical Labs Plants

And the associated warning flags

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C-276 and C-22

Grade	Ni	C	Mo	Cr	Fe	W	Co	Mn	V
C22	56	0.01	13	22	3	3	2.5	0.5	0.35
C276	57	0.01	16	16	5	4	2.5	1	0.35

Nickel-based alloys with excellent resistance to many acids, bases and salts.
Excellent resistance to wet chlorine gas, chlorides, hypochlorite.
Relies on a passive film for protection.
Workhorse for corrosion-resistant metal service at Merck.

Corroded by:
Warm HCl, warm H_2SO_4, bromine, chlorine water.

NOTE: Can catalyze the decomposition of hydrazine and peroxy-compounds (hydrogen peroxide, peracetic acid).

316L SS

Grade		C	Mn	Si	P	S	Cr	Mo	Ni	N
316L	Min	-	-	-	-	-	16.0	2.00	10.0	-
	Max	0.03	2.0	0.75	0.045	0.03	18.0	3.00	14.0	0.10

Austenitic stainless steel of the 18-8 family (18% Cr, 8%+ Ni).

Resists corrosion by most organic solvents, organic acids, neutral salt solutions

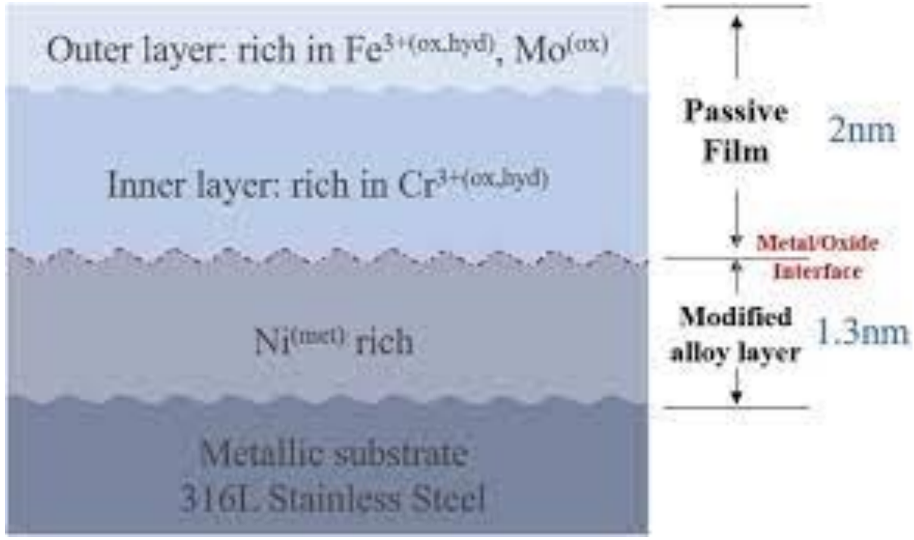
Relies on a passive film for corrosion resistance.

Remains ductile down to liquid N2 temperatures – used as backing for cryogenic glass lined vessels.

Vulnerable to:
Halogens, bleach, HCl, H2SO4 except very dilute and very concentrated, “acidic” cations (Fe, Cu for ex.), chlorides, bromides

Taking care of your passive films

- The corrosion resistance of austenitic stainless steel and Hastelloy depends on a thin passive film. This film forms spontaneously in air.
- To take proper care of this:
- Keep it CLEAN. Periodically expose to air.
- "Passivation" is a little of a misnomer. The main purpose to remove traces of grease, iron and rust from the surface and provide a uniform oxidizing environment for the passive film to grow.
- Be careful of scratching the metal under inert conditions, as the passive film may not reform.
- Try to avoid holding stagnant solutions, especially water, in stainless steel. Avoid allowing to dry out with salts, especially chlorides.
- If you have run strongly reducing chemistry in Stainless Steel, passivation may in order.



Other Metals

- Tantalum
  - Similar to glass in corrosion resistance.
  - Used for repairing glass linings
  - Vulnerable to HF, strong hot alkalis, oleum
- Copper and Brass
  - Ductile metals with poor chemical resistance, excellent heat transfer. Mainly used in gas and water services.
- Carbon Steel –
  - Strong material, no resistance to acid corrosion. In alkaline environments, the corrosion is controlled by access to air. Not commonly used for pharmaceutical processing – more likely in waste tanks.

Glass

- Soda-Lime glass – SiO_2 (69%) + Na_2CO_3 (plate glass)
  - Poor resistance to thermal shock, not very corrosion resistant
- Borosilicate “Chemical” Glass – SiO_2 (80%) + B_2O_3
  - Very low coefficient of thermal expansion allows to resist thermal shock
  - Somewhat more corrosion resistant than Glassed Steel
  - Glassed steel –
    - 20+ thin layers (2-3 mil each) sprayed on a metal substrate, and baked on in an oven:
    - Optimized for a combination of chemical resistance and mechanical properties.
    - Appearance / polish is the critical factor

Picture of good and bad dumbbells / micrographs

- Flags: Hot alkalis (Li →Na→K), fluorides
- NOTE: Even if a reaction is at a pH where attack by fluoride is not expected, if F is added to or removed from a molecule, it should be treated with suspicion.

Drums

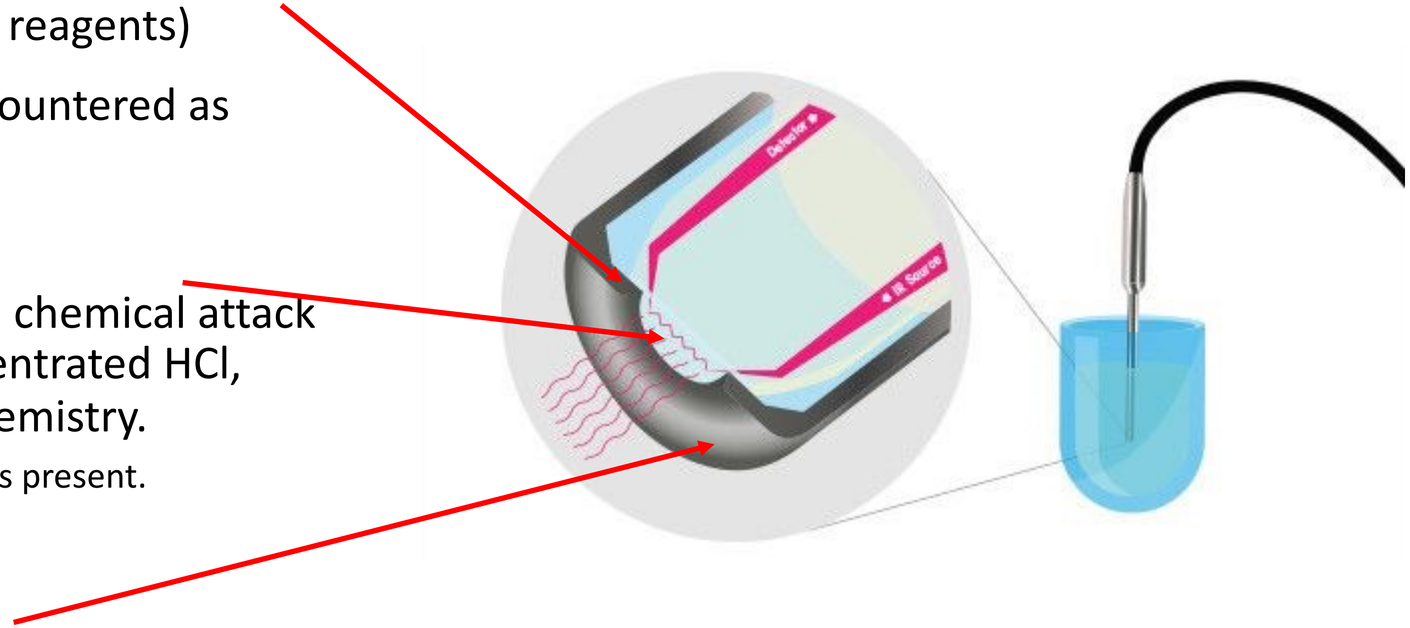
- HDPE
  - Compatible almost all aqueous solutions. Resistant to polar solvents. Does not typically contain additives.
  - Static may be an issue (drum is non-conductive)
- Polypropylene
  - Similar chemical resistance to HDPE. Typically contains plasticizers and coloring. May not be suitable for GMP batch handling.
- Carbon Steel.
  - Resists most “neutral” organic solvents. No real resistance to acidic conditions (pH <4). Under neutral and alkaline conditions the corrosion is controlled by dissolved oxygen.

Gaskets, seals, O-rings and tubing

- There is an excellent resource available online from DuPont to check compatibility of your elastomer / solvent pair
  - CRG: General Chemical Resistance Guide (force.com)
- Fluoroelastomers (Viton) – excellent resistance to aqueous solutions and **non-polar** solvents (hydrocarbons, long-chain alcohols). Polar solvents and methanol can cause severe swelling. Reasonable resistance to halocarbons.
- Ethylene Propylene Diene Monomers (EPDM) – excellent resistance to **polar** solvents, aqueous solutions. Poor resistance to hydrocarbons
- For challenging situations: Kalrez, Chemraz are perfluoro elastomers offer excellent resistance to most chemicals;
- Teflon: Highly chemical resistant and hydrophobic, the main concern is creep (the material can flow at elevated temperature) and permeability. Some chemicals can penetrate the lining and cause corrosion under the plastic coating, causing delamination

Unique to PAT Equipment

- Gold – warnings : Cyanides, Aqua Regia, Halogens and Halogen-like substances (DMDMH, Vilsmeier reagents)
- Platinum – Only aqua regia is likely to be encountered as attacking platinum
- Diamond and Sapphire–Effectively inert
- Silicon -Silicon is susceptible to abrasion and chemical attack by superacid (MSA, triflic acid) / bases, concentrated HCl, H_2SO_4 and HNO_3, as well as halogenated chemistry.
    - NOT attacked by HF or fluorides unless an oxidizer is present.
- Hastelloy C-22



Corrosion Testing

Addressing corrosion concerns early– a timeline

- Engage corrosion group early
- **Step Preview**
- Literature searches and consultation, lab observation
- **Before running in a kilo lab**
- Lab Screening (fluorides, hot caustic for the kilo lab, mineral acids for metal pressure reactors)
- Identify development targets that may present a risk
- **Before running in the pilot plant**
- The corrosion group reviews the process for corrosion risks and helps design appropriate experiments
- **Before running at a commercial site**
- The corrosion group and the plant evaluate the process for their equipment, including waste streams (stored in tanks). 316L SS should be reassessed. This may occur in conjunction with a PHA or HAZOP
- **Corrosion group additional expertise and equipment**
- Electrochemistry Metallographic microscopy (confocal) Hardness and swelling testing Specialized Corrosion Knowledge

Assessing corrosion risks – a tiered approach

- The first “concerns” typically will come from chemists' observations.
  - Etching, dulling or fogging of glass vials or reactors used to carry out experiments
  - The formation of color, typically yellow, green or blue, when the reaction is carried out with metal parts
  - Leaking or excessive swelling of rubber parts; swelling or cracking of plastic parts

- At this stage, a screening test at the 10-40 mL scale with weight measurements can help determine if the problem is corrosion or another issue.
  - For glass , a scintillation vial can be used as the test specimen
  - For metals, a coupon with a Teflon sling is submerged at an angle under 10-20 ml of liquid.

Stage 2

- **Carried out when the process is ready for scale-up** (either kilo lab or pilot plant).
- The reagents, products and chemistry is evaluated
- Outcomes are “No concern”, “Not recommended” and “Testing recommended”
- Process chemistry “paper” review
  - Historical experience
    - Species that generate HCl or equivalent, especially in polar solvents
    - Anything involving Br2 and most metals
  - Literature sources
  - <cite 3*metal, 1*glass, 2*polymers
- Be wary of general corrosion resistance tables – they may contain errors – always try to verify.

Stage 3

- Triggered by final commercial route
- Involves the most formal testing (150+ ml of solution, well-stirred)
  - For metals, will often use the 7 + 7 vs 14 technique
  - For glassed steel will use the actual glass
  - If a reaction is involved, will carry out in an appropriate reactor (EZ-Max for ex.)
  - Polymer tests are typically for 2 weeks, and may only focus on the solvent and any problematic reagents: The substrate typically has limited impact on corrosion behavior.

  - May involve evaluating or testing upset scenarios and waste storage tanks

Corrosion Testing Workflow

- The test is either initiated by the corrosion group reaching out with a potential corrosion concern, or the project team reaches out with a concern or observation
- The corrosion group and the project team discuss:
- Testing objectives
- Sample and coupon requirements
- Timing
- Who will carry out the testing
- The corrosion group is ultimately responsible for the materials of construction testing, but may need project team assistance, especially if the system has complex requirements that EPSE does not have the equipment for.
- NOTE: The impact of the metal surface and/or corrosion products on the process is more the responsibility of the project team. (Have some coupons)

Scales and types of test

- To screen glass (using borosilicate glass): 10+ mL, 20+ mL preferred per test.
- Confirms suitability for the prep lab, and can rule out possible use in the PP
- To screen metals : 20 mL / test.
- Confirms the suitability for wands and piping. Can rule out use in the PP.
- Formal corrosion studies: 150 mL / test.
- Suitability for Pilot Plant and Manufacturing use. For glass uses the actual glassed steel.
- Electrochemical Studies: 250 mL /test
- Identifies whether there is a long-term pitting risk, and can provide rapid turnaround on aqueous solutions




Thank You for your attention!

Any questions