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Equipment for Pharmaceutical, API and Fine Chemical Applications

Materials, Equipment, Design Features of Reactors, Heat Exchangers and Accessory Equipment For Batch Chemical Processes

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Introduction

The process of chemical synthesis for the manufacture for chemicals into API and fine chemicals is usually a complex multi-step process that can require reactors, receivers, crystallizers, heat exchangers, centrifuges, filter dryers and holding tanks made from corrosion resistant materials that will resist the ingredients and products being made during the manufacturing process. The material used is selected based on the potential products that will be made in the specific manufacturing suite upon preliminary conceptual design. Selecting the correct corrosion resistant materials for the process is a very important preliminary step in this process. Using a material that is not compatible with the process can cause premature equipment failure and process batches contaminated with service side fluids and metal residues a byproduct of excess corrosion.

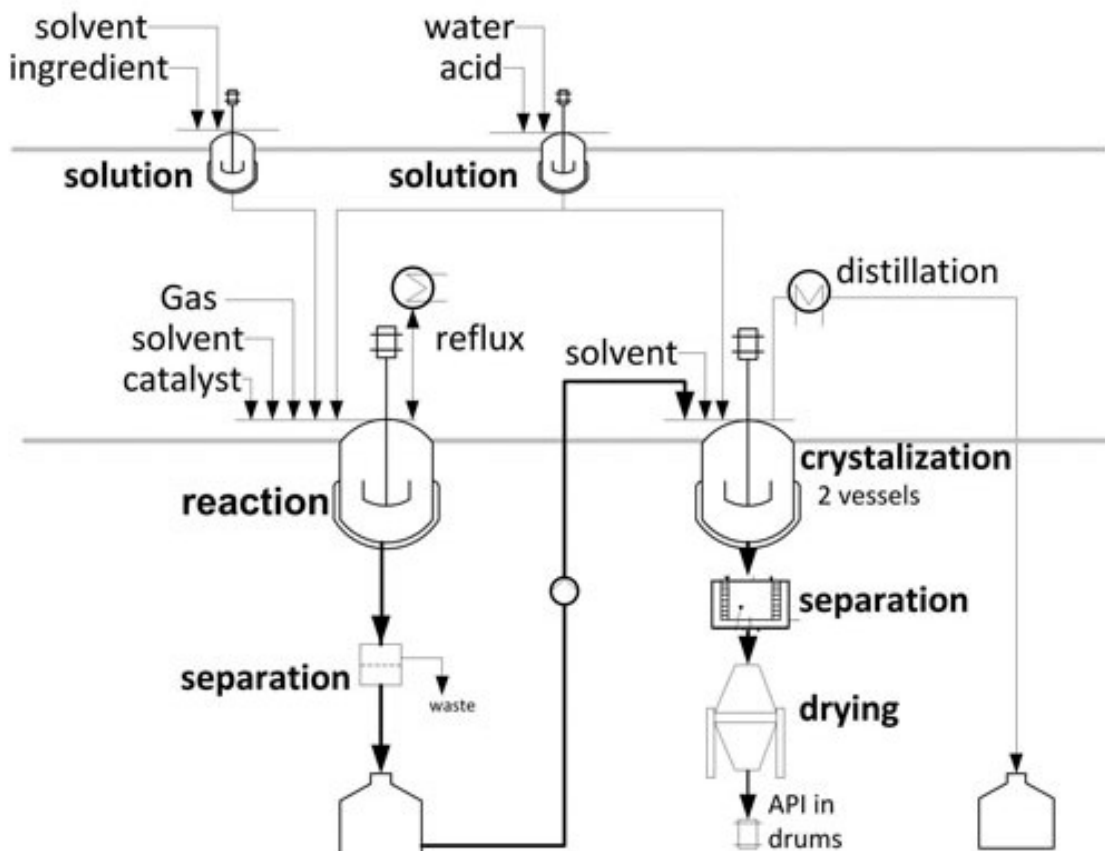


Figure 1 – Common Process Flow Diagram for API Application

Reference https://www.manufacturingchemist.com/news/article_page/The_modularisation_of_chemical_API_synthesis/150754

Materials

The three main metals used in multi purpose batch process facilities are tantalum, Hastelloy C and 316L Stainless Steel depending on the products that are going to be made in the process train.

Tantalum

Tantalum has been used for decades in the pharmaceutical industry because its versatility.

Tantalum can be used in applications where acids are used in the highest strengths, temperatures and makes a perfect complement to solid glass and glass lined carbon steel equipment because it has almost identical corrosion resistant properties as glass and also has excellent heat transfer properties as well as the durability of a metal.

The tantalum mill products used in the fabrication of condensers and other equipment meet the smooth surface finish requirements that are needed to accommodate fast and consistent cleaning between batches.

Equipment commonly manufactured using tantalum are heat exchangers, condensers, spray nozzles and dip pipe / spargers. Reactors are sometimes considered in tantalum however, the use of explosion cladding to accommodate the design conditions and heat transfer requirements of the application make the use of tantalum four or more times more expensive compared to glass lined carbon steel.

Alloy C-22

Alloy C-22 has found a place in applications where the corrosion resistance requirements are between that of tantalum and 316 stainless steel. Usually this is in applications where there is a wider variety of products being made using acids that will not exceed concentrations that would require glass or tantalum.

316L Stainless Steel

Of the three materials being considered in this paper 316L stainless steel is the least corrosion resistant however it's still very common in this application. The corrosion resistance of 316L stainless steel finds itself to be the workhorse in general in the pharmaceutical industry. It finds its place in applications where there are little to no chlorides.

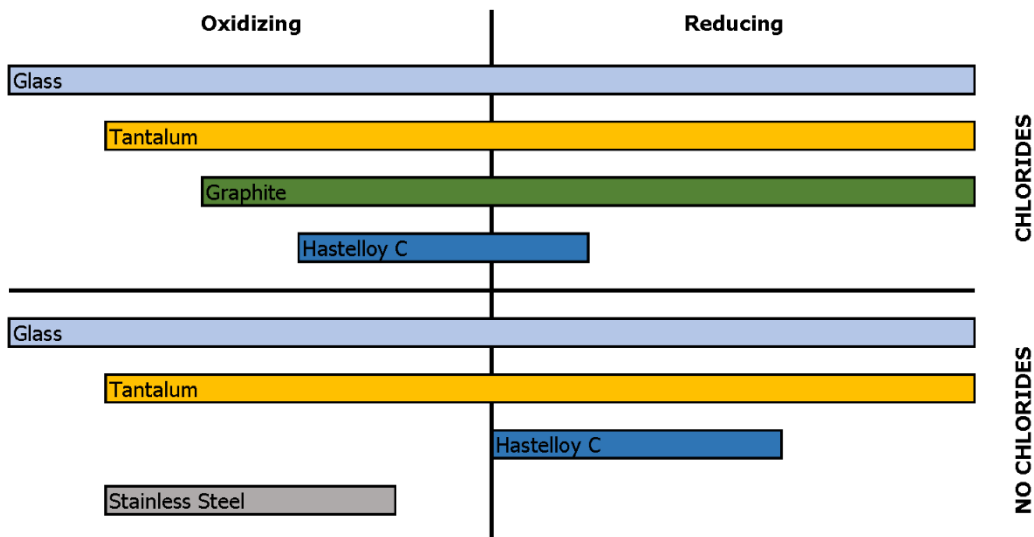


Figure 2 - General Corrosion Resistance Of Materials Used In API Applications

Reactors / Tanks / Receivers / Crystallizers

Reactors, crystallizers and receivers are the heart of multi-purpose batch pharmaceutical and fine chemical manufacturing processes. They can have all types of design attributes including, internal coils, external jackets, agitators, sight glasses and require polishing.



Figure 3 - Pressure Vessel with Internal Heating Coil



Figure 5 - Titanium Separator Vessel



Figure 6 - Jacketed Pressure Vessel With Jacketed Nozzles



Figure 4 - Half Pipe Jacket Reactor During Fabrication



Figure 7 - Half Pipe Jacket on Pressure Vessel Head During Fabrication

Heat Exchangers / Condensers

When considering heat exchangers for a batch process it is vital to consider the following heat exchanger design requirements:

- Equipment Reliability
- Product Purity
- Cleanability

Equipment Reliability

Metal shell and tube heat exchangers have been used for decades in the pharmaceutical industry. The fully welded metal design offers a ruggedness and reliability that can't be matched by graphite or silicon carbide.

Product Purity

The rigorous product purity standards mandated for the production of API / Fine Chemicals requires materials be corrosion resistant as well as not affect product purity.

Metal tube heat exchangers eliminate the possibility of contamination of graphite flakes or cross contamination of shell side heat transfer fluids when compared to graphite or silicon carbide heat exchangers.

Cleanability

Condensers / heat exchangers must be thoroughly cleaned in between batches to satisfy GMP standards. The cleaning time for metal tube heat exchangers is fast and very consistent when compared to other heat exchangers that require multiple gaskets or o-rings for sealing.

Tantalum, Alloy C-22 and stainless steel condensers all can be design to offer a fully drainable construction that ensures full drainability for fast and easy cleaning between batches. A 20 Ra surface finish can be met easily by all three materials.

The 3/4" diameter tubes allow for confirmation of the cleanliness of the inside of the tube after cleaning.

Sight glasses or solid glass end covers can be used to allow the use to view the condensation during operation. Spray Balls (CIP) can be applied to condensers to aid in the cleaning of the heat exchangers as well as the process piping. Riboflavin testing can be completed to confirm effectiveness of the spray balls being used.

There should be special considerations in the design of pharmaceutical condensers to the nozzle weld joint geometry and tube locations to promote full drainability in horizontal and sloped heat exchangers.

The fabrication of tantalum equipment often utilizes a weld joint that is flared away for the substrate material to eliminate the potential of contamination of carbon steel into the tantalum weld as well as to accommodate the argon purge necessary during welding. This joint can cause liquid hold up at the vapor inlet tubesheet and condensate outlet nozzles. When designing tantalum heat exchangers for batch applications it is mandatory to utilize a flush face fully drainable tubesheet design to meet the drainability standards required.

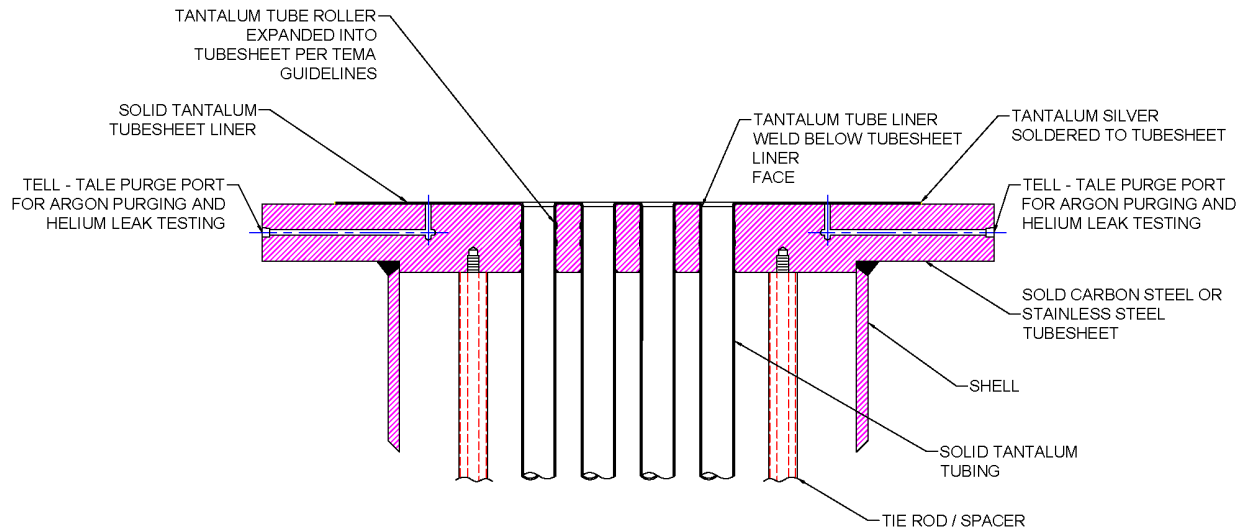


Figure 8 – Tantalum condenser with fully drainable tubesheet with 316L Stainless Steel Shell

Figure 9 shows the suggested configuration for a vertically mounted tantalum shell and tube condenser in a batch process to promote fast and effective cleaning.

Tricor Metals Fully Drainable Tantalum Pharmaceutical Tubesheet Design

INLET TUBESHEET DETAIL



OUTLET TUBESHEET DETAIL

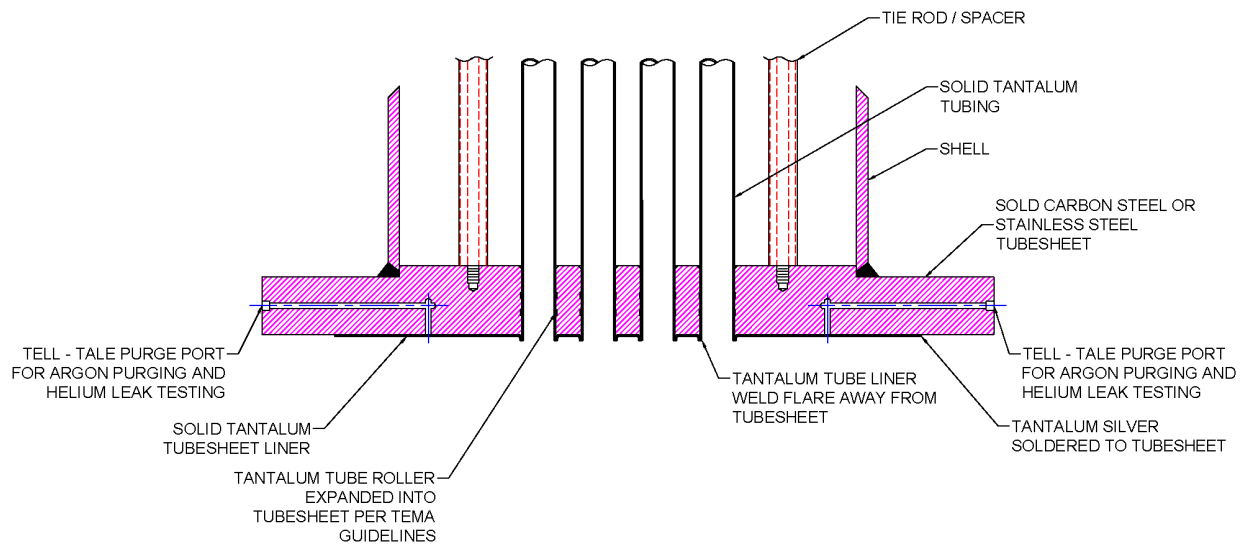


Figure 9 - Flush Face Fully Drainable Tantalum Condenser Configuration

Miscellaneous Reactor Accessories / Dip Pipes

Dip pipes, spargers and manway covers are common accessory items that can be supplied and tantalum, Alloy C and 316 stainless steel for Pharmaceutical, API and Fine Chemical applications.



Figure 10 – Mixing Dip Pipe



Figure 11 – Stainless Steel Dip Pipe



Figure 12 –316L Stainless Steel Manway Covers



Figure 13 – Polished Reducing Flanges

References:

1. Figure 1 - www.manufacturingchemist.com/news/article_page/The_modularisation_of_chemical_API_synthesis/150754

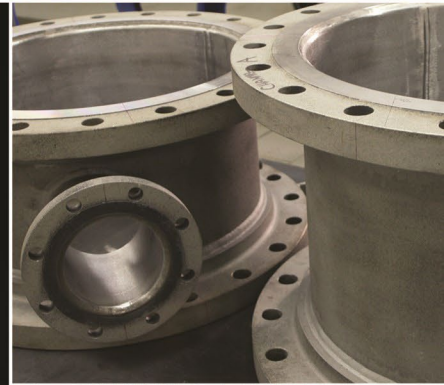
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