

CUNO Application Brief

Metal Catalyst-Carbon Complex Removal with a Self-Contained, Reclaimable, Filter Pack

Introduction:

In the manufacture of small molecule pharmaceuticals, active pharmaceutical ingredients (APIs) and excipients, there are often intermediate steps involving the use of precious metal catalysts such as palladium, platinum, gold, silver, rhodium, and ruthenium.

As catalysts, these materials are highly active and are used for such applications as adding hydrogen molecules to various organic molecules such as the hydrogenation of unsaturated hydrocarbons. These particular reactions are performed at both major pharmaceutical manufacturing plants as well as at contract manufacturing facilities.

In many instances these catalysts are coupled with carbon particles to provide a very large active surface area and exposure to the target molecule. High shear (aggressive mixing) is sometimes used to quickly contact catalyst powder with liquid-phase reactants and used to quickly contact catalyst powder with liquid and gas phase reactants in the case of hydrogenations.

As a result, a constant problem of catalyst-based reactions is the creation of fines that entrain (contaminate) the downstream process. Catalyst residue limits in active ingredients, excipients, and other intermediates are set by various organizations such as the United States Pharmacopoeia (USP) and the European Pharmacopoeia (Ph. Eur.) and are typically in the 10 - 50 ppm range.

Use of these catalysts can raise some difficulties:

- They are extremely toxic and must be both removed from the product and handled with care
- Some are highly active and in a dry state can burst into flame
- They represent a serious environmental pollution problem
- They are expensive

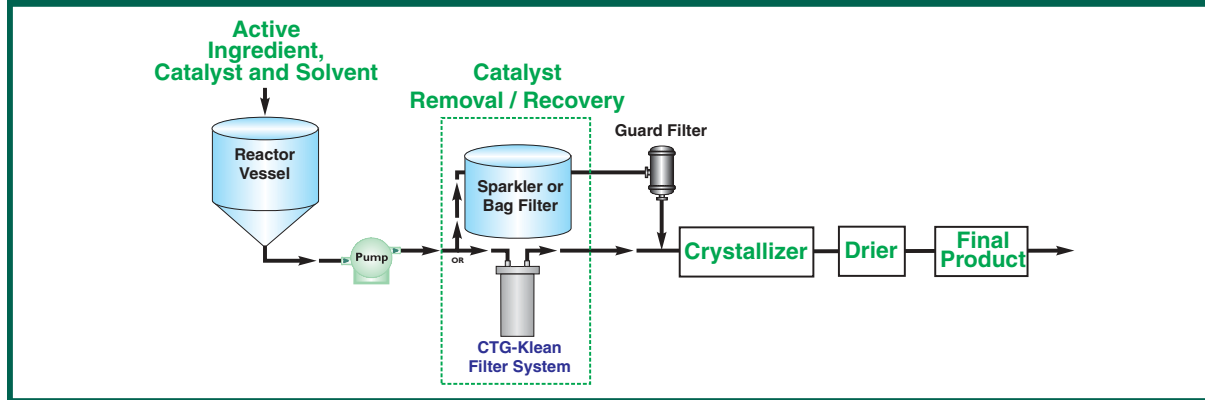
This CUNO Application Brief details how a self-contained filter pack, the CUNO CTG-Klean™ filter system, can safely and economically remove catalyst-carbon complexes, greatly easing cleaning validation and catalyst recovery.



The Process:

While many processes use metal catalyst in a variety of applications, the schematic in Figure 1 serves as a generic system by which to illustrate the use of the CTG-Klean filter system to remove and reclaim catalyst.

Figure 1. - Generic Metal Catalyst Removal/Recovery System



Problems Associated with Catalyst Removal and Recovery

Worker and Environmental Exposure

In many processes, catalyst-carbon complexes are removed downstream of the reaction vessel using one of three filtration methods: 1. Neutsche, Sparklers, or similar plate-style filters, 2. disposable filter cartridges, or 3. bag filters. Plate filters are typically composed of a pressure vessel containing a number of horizontal plates, each with an overlay of filter paper or fabric. In these filters, the catalyst is trapped on a filter paper held between filter plates. In cartridge filter and bag filter operations, the catalyst is trapped on the surface of the filter medium.

In all instances, workers are exposed to catalyst, solvents, and other potentially dangerous compounds when the filters are removed and cleaned. Plate filters are particularly problematic in that they require extensive effort to unpack, clean, and repack, often requiring two workers a total of 8 hours or more.

Limited Recovery Efficiency

Recovering expensive precious metal catalyst for reclamation and re-use is difficult using the conventional filter configurations described above. Plate filters often have recesses where catalyst accumulates and cannot be easily accessed in the recovery process. While less of a problem with disposable cartridge filters and bag filters, there is still an amount of catalyst that remains un-recoverable and is lost during clean-up, typically in the filter housing base or valving.

Extensive Cleaning Validation

The FDA has increased its emphasis in API manufacture on properly designed, documented, and executed cleaning validation protocols in recent years.

One point of particular concern is ensuring that all catalyst used in the process is accounted for at the end of the process. Using the conventional filtration operations described above, it can be difficult to account for all the catalyst used in the reactor. Often these systems allow for only a partial (90-98%) recovery of catalyst, begging the question: where is the remaining 2-10%? Assaying the final product usually documents the absence of catalyst; therefore, the missing amount is often lost in the process, often in the filter vessel, piping, and other equipment.

A second point of concern is ensuring that the equipment used in one process or batch is thoroughly cleaned before use in the next process or batch, to prohibit cross-contamination and carry-over. Fixed, difficult to clean equipment, particularly plate filters, are often cause for concern. Once the filter has been unpacked, it must be cleaned and flushed appropriately, with laboratory samples taken and analyzed to confirm cleanliness and the absence of catalyst fines, before it can be repacked for the next use. Typically cleaning, and especially validating the cleaning, requires greater time and effort than the original filtration itself.

The CUNO Solution:

The unique design of the CUNO CTG-Klean system has been found useful in dealing with catalyst removal insofar as it offers an easy and safe method of:

- Filtering the catalyst out of the product
- Providing complete capture of the catalyst
- Sequestering the catalyst in a safe container that can be filled with a quenching material if desired
- Providing a container that can be returned to the foundry for precious metal recovery and regeneration
- Easing cleaning validation concerns

The CTG-Klean system is a totally enclosed filtration device that uses a separate pressure vessel and disposable filter pack to isolate the product to be filtered from the housing. See figures 2 and 3.

CTG-Klean filter systems can accommodate a wide variety of CUNO filter elements, including all-polypropylene depth filters (PolyNet[®] filters), bi-component depth filters (Betapure[®] filters), pleated, all polypropylene surface filters (Betafine[®] XL and Polypro[®] XL filters), and sub-micronic membrane filters (LifeASSURE[®] and SterASSURE[™] filters). Filter systems provide retention ratings from 0.1 μm to 350 μm and standard models can accommodate flow rates from 1 - 130 gpm (4 - 500 lpm). Please refer to CUNO literature number LITCCK001 for further details regarding available configurations and supplemental equipment.

Figure 2. - CTG-Klean System



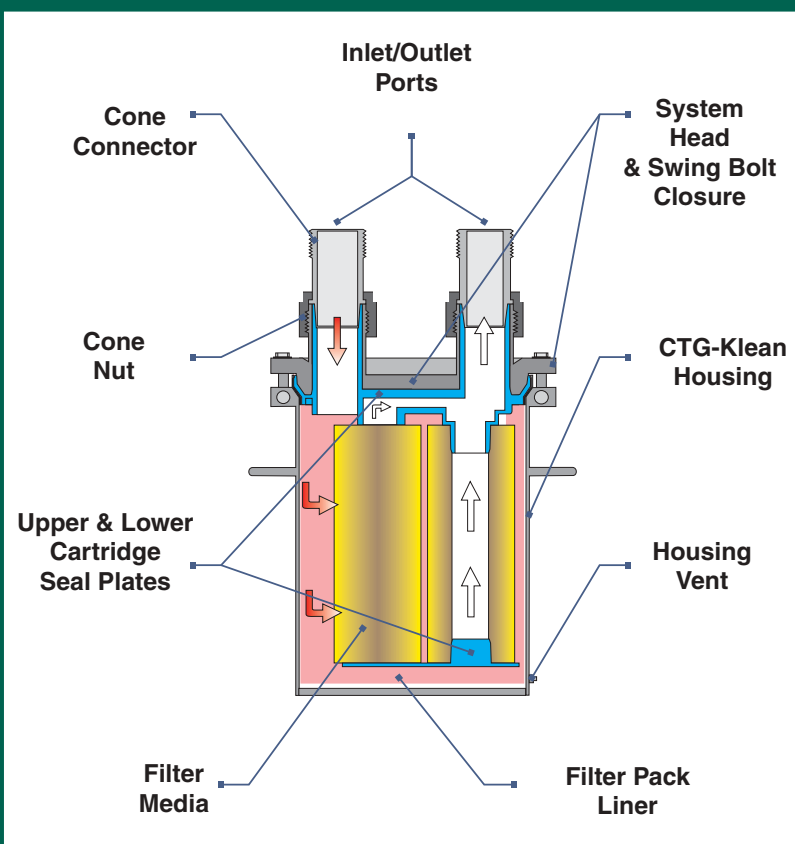
Significantly Limits Exposure

In the CTG-Klean system, the filter cartridges are enclosed in a self-contained pack, eliminating excessive worker exposure during filter change-out. Catalyst fines, solvents, and other hazardous compounds are contained within the pack and are not exposed to the filter housing shell. At the end of the filtration run, the operator simply disconnects the inlet and outlet lines, caps the filter pack inlet and outlet ports after removing the housing top plate, and removes the entire filter pack.

Allows for Complete Catalyst Recovery

Since 100% of the fluid flows through the CTG-Klean filter pack, all catalyst can be retained within the pack. There is no fluid/catalyst contact with the filter housing shell itself, as in conventional filters, so there is no potential for catalyst to

Figure 3. - CTG-Klean System Features



be caught in the recesses of the housing. With proper filter and retention rating selection, catalyst recovery is 100%. Furthermore, the unique design of the CTG-Klean pack allows for easy transport to a reclamation facility to recover expensive precious metal catalyst. In fact, revenues from reclaiming catalyst in this manner easily offset the cost of the CTG-Klean system itself.

Greatly Reduces Cleaning Validation

Since there is no exposure of product to the reusable CTG-Klean housing shell, cleaning validation is reduced considerably. All product contact is with the filter pack alone, which is disposed of at the end of each run. Therefore, filter housing flushing, sampling and laboratory analysis in regards to the filter housing are all obviated. This can drastically shorten the time needed to clean and prepare a system for the next processing run, increasing plant capacity and lowering processing costs.

Conclusion and Summary:

The use of precious metal catalyst coupled with carbon is common in processing small molecule pharmaceuticals, APIs, excipients, and other pharmaceutical intermediates. A constant problem of catalyst-based processes is the creation of fines that entrain (contaminate) the downstream process.

This CUNO Application Brief details how a self-contained filter pack, the CUNO CTG-Klean filter system, can safely and economically remove catalyst-carbon complexes, greatly easing cleaning validation and catalyst recovery.

The CTG-Klean system:

- Significantly limits worker and environmental exposure to catalyst, solvents, and other potentially harmful compounds.
- Allows for complete recovery of catalyst within the filter pack for easy disposal or reclamation.
- Greatly eases cleaning validation resulting in faster turn-around time, increasing plant capacity and lowering overall processing costs dramatically.



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