Upgrading Your Containment Strategy for Potent API Processing

Thanks to an increase in potent active pharmaceutical ingredients, innovative filtration technologies have been developed to improve containment level without significant additional capital cost

‘Any technology option should be thoroughly risk-assessed by production personnel and industrial hygienists.’ By Gareth Leach, Ph.D.

The potency of pharmaceutical chemicals is characterized by occupational exposure values in g/m?; the lower the value, the more potent the chemical and the greater the level of containment required. Currently, there is a significant increase in the number of active pharmaceutical ingredients (APIs) coming through development and clinical trials into the production environment with potencies below 10 ?g/m, which is considered potent. This presents a major challenge for existing facilities familiar with handling non-potent APIs that need to upgrade their containment strategy for various unit operations. This article examines some recent developments in filtration containment technology that can provide improvement in containment level without significant additional capital cost and facility reconstruction. Particle filtration applications occur throughout the manufacturing processes that produce APIs. Application examples include: the clarification of incoming fluid streams such as reaction solvents, removal of heterogeneous catalysts, the recovery of crystallized actives or intermediates and the removal of insolubles from waste streams and venting lines. Filtration applications can be characterized in terms of the particle content in the feed stream. Applications for feeds with low particle concentrations are known as “polishing” and commonly employ cartridge filters to remove particles with high efficiency on solvent, gas and vent lines and also in-process lines after a bulk solids removal step. Cartridges typically consist of polymeric fibers, such as polypropylene, melt blown around a ridged polymer core or a thinner layer of porous polymer pleated to provide a higher surface area for filtration. Higher

particle concentrations generally require the formation of a filter cake of incompressible particles on a filter plate or on a thin layer of filter media to be cost-effective.

Cellulosic depth filters in lenticular format represent a convenient and cost-effective filtration technology for liquid applications with higher particulate concentrations and are widely used in API processing. These filters consist of lens-like cells or lenticles of cellulosic-based depth filter media stacked around a polymer core forming a module. Lenticular modules used for cake filtration have sufficient spacing to allow for the accumulation of filter cake between cells and between the media and the bowl of the housing. Unlike most filter presses, lenticular filters are fully enclosed while filtering; however, when filter change-out is necessary, the housing bowl is removed, exposing the cake, which might still be contaminated and could collapse. To reduce this exposure risk, a new generation of encapsulated lenticular modules has been developed. With such technology, the cake is retained within the capsule, which can easily be removed by the operator with no contact with either the cake or the wetted media. The inlet and outlet are capped off when the module is removed. Such technology is particularly suitable for the recovery of heterogeneous catalysts, which might not only be contaminated but also could present a pyrophoric risk should they dry out, an unlikely event with the catalyst trapped within the encapsulated and sealed module.

With processes incorporating filtration through pleated cartridges, another approach is to enclose the area around a pleated cartridge filter housing with a glove-box isolator and manipulate the filter change-out through glove sleeves. Such an approach is applicable to smaller cartridge applications and is generally more suitable for new facilities or parts of a facility that have been originally constructed with containment as a key design criterion. However, upgrading existing cartridge filter applications by enclosing the cartridge housings in glove-box isolators can involve significant capital expense and downtime. Flexible isolators or glove bags located around the housing or housing closure can provide a cost-effective solution. Glove bags are made of clear polymers, such as polyurethane or PVC, and can be tailored to suit a particular task. Glove bags are used in API facilities for applications such as sampling, dispensing, seeding process vessels and, of course, change-out. For filter change-out, glove-bag designs have glove sleeves and sleeves for feeding out waste material (spent cartridges) and feeding in new material (replacement cartridges). In many applications, glove bags are taped around the filter housing to seal them. Such an approach requires careful application of the tape and can introduce a procedural requirement for frequent inspection and replacement of the tape seal prior to each use to avoid the risk of failure during operation.

A significant recent improvement has been to design both housings and glove bags to seal together as a “containment system” that does not require adhesive tape. This entails modifying housings to incorporate a containment plate, which catches any spill and facilitates the secure sealing of glove bag and housing by means of a Vee-band clamp and O-ring. Safety evaluation studies have demonstrated that these

products can be used to provide containment to levels less than 1?g/m3, making them applicable to processes with otherwise high health risks. By modifying existing filtration formats through encapsulation or with flexible barrier approaches, the level of containment associated with filter change-out can be improved in a cost-effective manner. Any technology option should be thoroughly risk-assessed by production personnel and industrial hygienists in terms of its suitability to provide a required minimum level of containment. Considering the trend for more potent APIs, there is little doubt that the range of separation technologies providing enhanced containment during filter change-out will increase significantly during the next few years. *Gareth Leach, Ph.D., is the market manager of global API at Pall Life Sciences, 2200 Northern Blvd., East Hills, NY 11548, a leading global provider of filtration, purification and separation technologies. Additional information is available by visiting www.pall.com or calling 516-484-5400.*