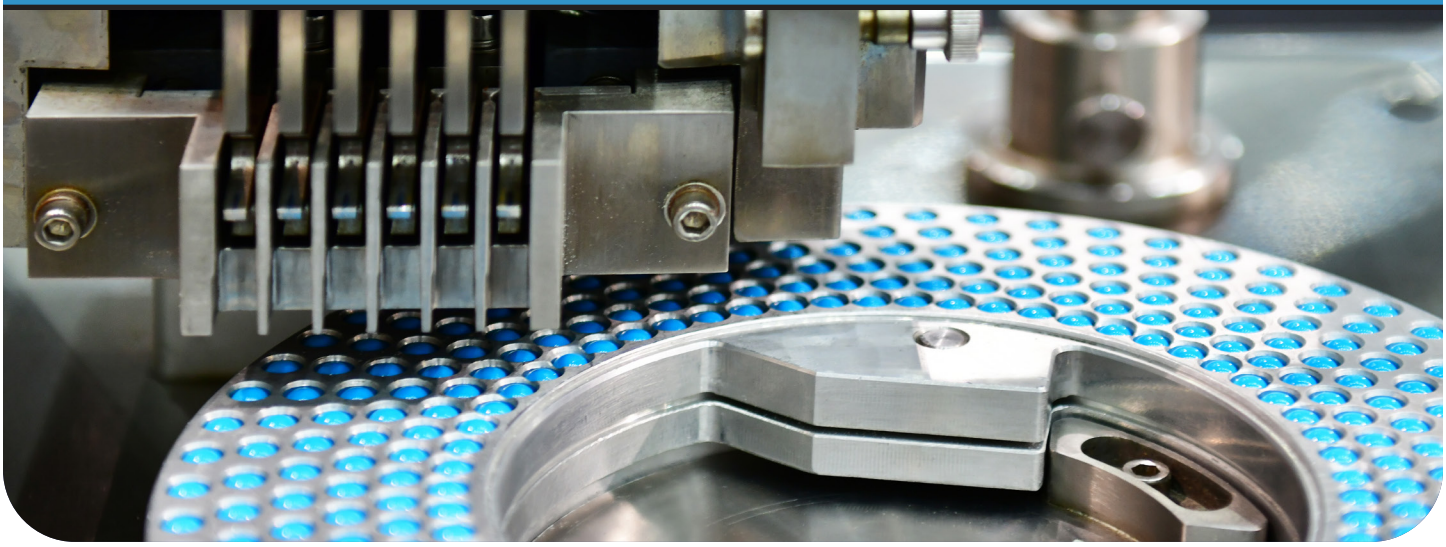
Clean Sweep: Increasing the Yield and Savings of Scrap Materials in the Pharmaceutical Industry



*Valued at **more than $1.49 trillion** and on track for ongoing investment over the next five years, the pharmaceutical industry shows no signs of slowing down. For first-party creators and contract development and manufacturing organizations (CDMOs) tasked with producing pharmaceutical products, however, generalized growth doesn't always translate to reliable revenue.*

In practice, issues related to full reagent use and cleaning validation are often linked to additional — and avoidable — costs. By implementing solution-specific spectrometry into existing processes, however, it's possible for companies to increase scrap material yields, reduce waste, and improve operational compliance.

The Challenges: Recovery, Waste, and Compliance

Different drug processes come with different challenges. For example, producing pharmaceuticals for rare diseases — also called orphaned drugs — and creating precision medicines require the use of highly specific and expensive components. If any of these components are wasted, the cost of loss could outweigh the benefit of production. When it comes to the large-scale production of more common products such as acetaminophen, meanwhile, extended cleaning validation processes can lead to wasted time and effort.

As a result, CDMOs typically face one (or more) common production challenges related to recovery, waste, and compliance.

Reagent Recovery

If chemical reactions are not entirely complete before the manufacturing processes end, reagents may be lost. For example, suppose a new drug requires the combination of three reagent types in specific quantities to produce the target result. In that case, companies must ensure that reactions are fully complete and all reagents have been fully combined and transformed.

While stopping the process early may still produce a portion of the intended results, the chemicals left behind are often wasted, in turn leading to a monetary loss. As a result, organizations need solutions that make it possible to continually monitor reaction performance and ensure reagents have been fully utilized.

As noted by a recent paper published in the **American Chemical Society's ACS Omega,** efforts aimed at unused tablets and capsules were able to recover 67.6 wt % of active pharmaceutical ingredients (APIs) from ibuprofen, and 73.1 wt % from tetracycline HCl. If

this process could be extended to the recovery of mid-production reagents, it could help organizations improve product output volumes.

Cleaning-Related Waste

While the Food and Drug Administration (FDA) requires pharmaceutical companies to follow current good manufacturing processes (CGMPs) when it comes to cleaning processes and validation, the specifics are often left up to individual organizations.

According to the FDA's Guide to Inspections Validation of Cleaning Processes, the agency expects companies to have documented general procedures for cleaning validation and expects firms to conduct and document their results. What the guide doesn't specify is exactly what this process looks like or how companies can ensure they get it right — failure to do so could result in a contaminated product batch that must be destroyed.

To help avoid this issue, many pharmaceutical organizations have opted to overextend cleaning times as a stopgap solution. For example, if a company has finished the production run of a product such as ibuprofen and plans to make acetaminophen next, it's critical to fully clean out all chemical vats before beginning the switchover.

Given the financial and reputational risk of creating contaminated products, many organizations opt for an over-cleaning method that sees them washing out vats with solvent for hours or days longer than necessary in an effort to ensure runoff doesn't contain unexpected reagents. While this accomplishes the goal of runoff regulation, it also comes with a substantial amount of wasted time, effort, and resources.

Chemical Disposal Compliance

Disposal is a key component of the pharmaceutical manufacturing process, both from a human safety and environmental stewardship standpoint. A **recent research article published in PNAS** details the results of a global study that measured API pollution in 258 rivers worldwide. More than half of the sites evaluated contained APIs including carbamazepine, metformin, and caffeine. In addition, 25.7% of sites contained at least one API in concentrations great enough that it posed a threat to aquatic life.

To help address this issue, new regulations such as the Environmental Protection Agency's (EPA) **Management Standards for Hazardous Waste Pharmaceuticals** codify the EPA policy on the handling and disposal of pharmaceuticals for manufacturers, healthcare agencies, and end users.

The result is an increasing need for CDMOs and other production enterprises to create and carry out compliant disposal processes. For these processes to be effective, however, organizations need to know precisely what chemicals — and in what concentrations — are found in their waste.

The Solution: Situation-Specific Spectronomy

Purpose-built spectrometers can help companies reduce reagent loss, minimize waste, and improve disposal compliance.

Consider production line reactions. By integrating spectrometers into production processes, companies can accurately determine remaining reagent amounts and ensure reactions proceed to completion, or choose to stop them at specific points for material recovery. In practice, this might take the form of a Raman spectrometer to measure the vibrational energy of molecules in both product and solution to determine if reactions are fully complete.

When it comes to cleaning validation, meanwhile, both absorption through flow cells and Raman spectrometers offer a way to ensure that chemical concentrations in vat runoff have decreased enough that new production runs can begin. Many vats are fully clean after 24 hours, but companies may run them for 72 hours or more as a way to ensure complete cleanliness. The use of targeted spectrometry can save both days' worth of time and hundreds of gallons' worth of cleaning solvent.

Ocean Optics also provides spectrometry solutions to meet specific pharmaceutical needs and ensure alignment with CGMPS. For example, many chemicals have a fluorescence band that reacts to specific wavelengths of light and renders observations useless. Custom-built devices can ensure that companies can always see what they need to see — when they need to see it.

Combined with Ocean Optics' repeatable production processes and global factory infrastructure, pharmaceutical companies can access the devices they need, when and where they need them.

The Benefits: Doing More With Less

As noted by the Congressional Budget Office (CBO) **April 2021 Research and Development in the Pharmaceutical Industry report,** the expected costs to develop and produce a new drug now average between $1 and $2 billion. This includes everything from research and development (R&D) to trials, manufacturing, and any resources committed to drugs that don't reach the market.

Given the significant time and investment required, it only makes sense for companies to prioritize both efficiency and oversight during the production process. By using precise and reliable spectrometry to ensure reactions are complete and cleaning validation is comprehensive without being wasteful, pharmaceutical producers are better prepared to deliver a sustainable return on investment (ROI).

But this is just the beginning. By implementing inline and at-line spectrometry, companies can do more with less to achieve benefits including:

Streamlined Processes

Inline and real-time analysis of chemical reagent reactions allows organizations to incorporate product evaluation as part of standard operating procedures (SOPs). In practice, this removes the need for product samples to be captured and sent to on-site or third-party labs for analysis, in turn streamlining the production process.

This also applies to cleaning processes. Rather than relying on staff to ensure that vats are cleaned for a pre-selected amount of time for validation, inline absorption or Raman spectrometers also allow companies to easily check current runoff levels.

Ongoing Oversight

Small changes in production line processes can result in wasted reagents or contaminated processes. Purpose-built spectrometers can detect even tiny fluctuations in chemical composition, making it possible for companies to pinpoint potential problem areas quickly. Not only can this help save money from unnecessary product waste if contamination occurs, but also help organizations find and address areas of common concern to help improve processes at scale.

Operational Innovation

There's also a case to be made for spectrometers as a source of operational innovation. Consider a pharmaceutical company running test batches of a new product. In-line spectrometry could help identify areas for process improvement based on how well reagents combine and how long the process takes.

When it comes to waste products, custom-built spectrometers can both ensure that waste product concentrations are aligned with regulatory expectations, and identify waste materials that may fall under the threshold for API-containing hazardous waste disposal, in turn saving organizations time and money.

The Results: Increased Yields, Better Savings, and Reduced Waste

By implementing inline or at-line spectrometry solutions from Ocean Optics, pharmaceutical firms and CDMOs are better equipped to monitor ongoing reactions and ensure completion, recover unused reagent portions, and streamline cleaning validation processes.

The result is an operational trifecta that allows organizations to improve product yields, increase scrap savings, and reduce total waste. This simultaneously provides more accurate insight into chemical disposal compositions and the actions required to ensure regulatory compliance.

Put simply? Advanced, accurate, and agile spectrometry is a clean sweep for pharmaceutical companies looking to maximize revenue and minimize waste in a rapidly expanding market.

If you're ready to see the difference, we're here to help. **Let's talk**.