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"Aiming for Perfection in a Pandemic", an opinion by Datwyler

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"When Lives and Livelihoods Depend on Accelerating Large Molecule Drug Production, Biopharma Companies must Minimize Defects and Contamination" says Massimo Mainetti, Global Head of Marketing and Product Management, Datwyler

As the COVID-19 pandemic continues to unfold, the industry is working tirelessly to identify an effective treatment and vaccine. Amid the pressure to produce a vaccine in such a short time frame, there is also the pressure to ensure no valuable time and resources are wasted. Naturally, treatments that are being considered are large molecule drugs, which requires manufacturers to address challenges with achieving zero defects and silicone contamination stemming from packaging and delivery. Though this has been an issue for decades, silicone is still commonly used for plungers and stoppers in syringes, cartridges and vials. Because of its ubiquity, the default tendency among phealheharmaceutical and biotech manufacturers is to “work around” the possibility of silicone contamination in drug formulation rather than address this issue head-on. However, contamination challenges like this one are not only surmountable, the solutions can save pharmaceutical companies time, money and stress, while at the same time delivering a better product to the patients.

Striving for Zero

When producing parenteral packaging for vulnerable or sensitive products such as large molecule drugs, the goal should always be zero defects. This approach better preserves the drug, protects the patient and upholds the reputation of the drug manufacturer.

Aiming for zero defects becomes even more critical as highly sensitive drugs such as biologics and other large molecule compounds become increasingly common, with injectable biologics in particular emerging as chief drivers of sales growth in the pharmaceutical industry. According to a new study from Market Industry Reports, the sterile injectable drugs market was estimated to be over $500 billion USD in 2019 and is anticipated to grow at a double-digit CAGR from 2019 to 2030.

But large molecule drugs are costly to manufacture and highly sensitive to extraneous contamination such as silicone, cellulose or other particles. If the drug comes into contact with any of these contaminates, the whole batch must be disposed of, representing a significant monetary loss and, as we are reminded amid today’s pandemic, precious time wasted in

moments of potential crisis. Despite the quality audits and third-party oversight that are industry-standard, contamination of large molecule drugs still commonly occurs.

Preventative Measures

What best practices reduce incidence of drug contamination? In the case of silicone in parenteral drug packaging, it can start with complete coverage of any plunger or stopper with a no-silicone added fluoropolymer coating. Creating a robust barrier between the drug and rubber minimizes the impact posed by extractables and leachables.

Additionally, drug and device manufacturers can seek ready-to-use components in rapid transfer port (RTP) bags so that drug manufacturers do not also have to stretch themselves thin by also sterilizing components. Pushing the washing and sterilization of components further upstream to component manufacturers reduces the manufacturing footprint in a biologics facility, keeping the focus on the core competency of manufacturing and filling the drug product rather than on component processing—and the meticulous attention to detail required to minimize errors on that front.

Another best practice is to establish clear, transparent channels of communication between key parties: the drug company, the packaging manufacturer and other essential suppliers. By working closely, specifiers can easily identify and trouble-shoot potential sources of contaminants and eliminate common defects throughout the supply chain. This is critical; visible particles accounted for 22 percent of all injectable drug recalls between 2008 and 2012 and recall events due to visible particulate have been steadily increasing since 2009. For this reason, component manufacturers should consider redesigning production facilities for packaging and delivery systems used in large molecule drug applications to eliminate the presence of identified contaminants. Packaging production facilities should be designed to meet the highest manufacturing standards that serve as an extension of the active pharmaceutical ingredient (API) manufacturing environment.

The most common contaminants in pharmaceuticals are cellulose (cotton and paper - more than 60 percent of the time in the final product), fibers, synthetic fibers, silicone, plastics, rubber, metal particles and corrosion products, glass particles and vial delamination flakes, skin flakes and char particles.[1]

Eliminating cellulose from the vicinity of production is particularly difficult. Cellulose can be introduced via wood pallets, paper and bags present near-production environments. Eliminating paper from the production floor—and, if possible, in the surrounding offices and other areas—by transitioning a facility to all electronic records and communications, can go a long way to reducing cellulose particles that can circulate, potentially compromising a drug or drug packaging component. Substituting wood pallets with non-contaminating versions made of plastic substrate can also help reduce cellulose contamination.

Last but not least, to minimize human contamination of large molecule drug packaging facilities, identify processes that could become fully automated. A completely human-free environment isn't practical, so to further decrease risk of contamination, operators and repair staff need the right training and mindset, protective gearing and the right equipment.

Advancing Inspection

Finally, it's necessary to improve product inspection. Camera inspection adds a layer of security the naked eye cannot achieve alone. Cameras do not get tired and do not miss even the smallest anomaly. Among regulators, the trend is continuing toward more stringent standards, pushing drug manufacturers and the designers of packaging and secondary devices to higher levels of scrutiny in manufacturing and design. Lately, the FDA set the bar higher for injectable drug manufacturing, calling for implementation of improved specifications as mandated by regulatory bodies, increased inspection and improvement in analytical and inspection techniques.

This is fast becoming the new industry standard. And while large drug companies will move to anticipate these trends, smaller biotech firms and generic manufacturers are simply trying to meet the quality specifications already in place.

Contamination will always be an issue, and though zero defects is a lofty goal we may never achieve, we can come close. The creators and end-users of large molecule drugs are relying on parenteral drug packaging companies to get as close to zero defects as possible. Anytime there is a market recall—it is not just a financial liability, but a huge risk to the reputation of pharmaceutical company partners and to the health of waiting patients. Perhaps it's idealistic to work toward zero defects, but we in the industry need to meet this engineering challenge, continuously improving our processes toward reaching that goal for our partners and the patients whom we all serve.

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[1] http://www.microscopedia.com/Resource/Microscopy/raman-microscope