



# PMPS

Pharmaceutical Manufacturing and Packing Sourcer

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## STOPPING THE TRANSMISSION

New measures are being implemented to stop the rise of counterfeit PPE during the pandemic

## PHARMA'S SILVER LINING

COVID-19 has brought together the pharmaceutical industry like never before in the fight against the virus

## LOSE THE LABEL?

As packaging gets more intricate, is it time to ditch the label and embrace packaging as a data space carrier?



### INSIDE THIS ISSUE

Parenteral Technology Supplement 2020





# Achieving Zero Defects in a Pandemic

**When lives and livelihoods depend on accelerating large molecule and drug production, pharmaceutical companies must ensure that they minimise potential defects and contamination**

Massimo Mainetti at 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 require manufacturers to address challenges with achieving zero defects and silicone contamination stemming from packaging and delivery.

Drug manufacturers have always aimed to minimise time to market while also protecting injectables against contamination. However, the challenges COVID-19 has posed to global supply chains have placed even greater emphasis on this goal. According to an FDA study, developing a new medicine takes on average 10 years and costs \$2.6 billion from discovery through approval. These are high stakes, so it is essential to utilise every available tool in creating an uninterrupted transition from the development stage to production.

As such, there is no time or resource to waste on the issues that stem from defective or problematic drug packaging. This is especially true considering that patients depend on drug manufacturers to supply them

with products that provide essential, life-saving treatments.

Though silicone contamination has been an issue for decades, it is still commonly used for plungers and stoppers in syringes, cartridges, and vials. Due to its ubiquity, the default tendency among pharmaceutical and biotechnology manufacturers is to 'work around' the possibility of silicone contamination in drug formulation rather than address this issue head-on. The thought of undertaking silicone contamination could seem daunting but contamination challenges like this one are not only surmountable, the solutions can save pharma companies time, money, and stress, while at the same time delivering a better product to the patients.

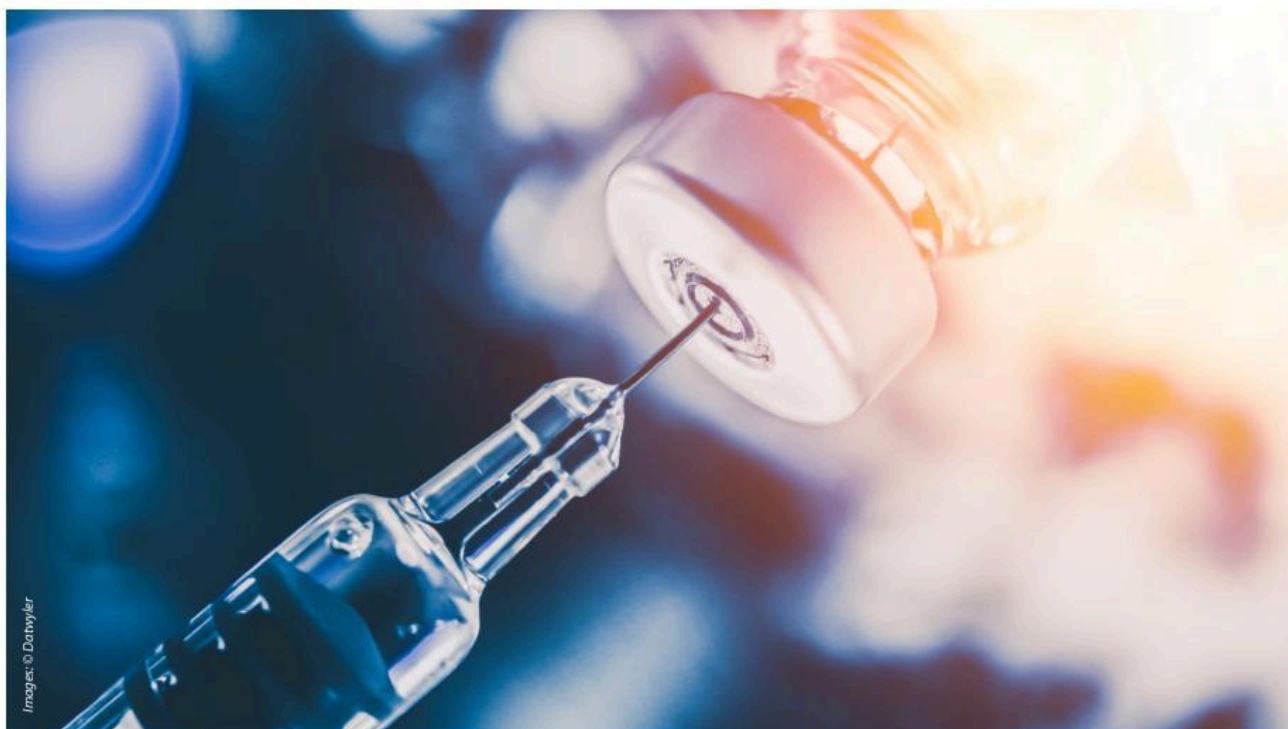
## Striving for Zero

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 pharma industry. In fact, injectable biologics therapies are rising in popularity partially due to the increased prevalence in chronic diseases, increasing occurrence of needlestick injuries and the benefits such as convenience, ease of use, and reduced pain associated with it. According to WHO, chronic diseases are the major cause of death and disability worldwide. In the UK alone, chronic diseases are projected to account for 85% of all deaths (1). It comes as no surprise that a new study from Market Industry Reports indicates the sterile injectable drugs market was estimated to be over \$500 billion in 2019, and is anticipated to grow at a double-digit compound annual growth rate from 2019 to 2030.

Though injectable biologics could change the way the pharma industry addresses patient needs, large molecule drugs are costly to manufacture and highly sensitive to extraneous contamination. Particles such as silicone, cellulose, or others could cause product adulteration and if the drug includes unsatisfactory levels of any of these contaminants, the whole batch must be disposed of, representing a significant monetary loss. Beyond potentially being a financial pitfall if improperly



managed, as we are reminded amid today's pandemic, disposing of an entire batch can result in precious time wasted in moments of potential crisis. Although there are industry-standard quality audits and third-party oversight, contamination of large molecule drugs still commonly occurs. This further emphasises the need for there to be strategic measures implemented throughout production that can help significantly minimise the risk associated with manufacturing biologics.

### Preventative Measures

Packaging materials have traditionally been viewed as secondary components to drug products and have not necessarily been manufactured in cleanroom environments. However, drug companies should not consider packaging an afterthought as it can significantly impact the viability of a treatment.

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 minimises the impact posed by extractables and leachables.

Additionally, drug and device manufacturers can seek ready-to-use components in rapid transfer port bags so that drug manufacturers do not also have to stretch themselves thin by sterilising components. Pushing the washing and sterilisation 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 minimise 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. As regulatory authorities' expectations rise, these key parties have the opportunity to enter a technical collaboration that could better achieve zero defects. For one, by using methods that scrutinise the complete packaged product, identifying

any opportunities of contamination and setting up the production line to defend against contaminants, manufacturers can ensure packaging is designed and produced with the same rigour of the drug itself.

Working closely enables specifiers to easily identify and troubleshoot any potential sources of contaminants and eliminate common defects throughout the supply chain. This is critical as visible particles accounted for 22% 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 manufacturing environment.

The most common contaminants in pharmaceuticals are cellulose (cotton and paper – more than 60% 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 (2).

Unwanted particles can serve as a major threat to drugs if found in the finished product. It is important to identify the source of any contaminants and establish measures that can eliminate them from the design of the packaging component and from the manufacturing floor.

However, 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 minimise human contamination of large molecule drug

packaging facilities, identify processes which 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. 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 pharma 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.

### References

1. Visit: [www.who.int/chp/chronic\\_disease\\_report/media/uk.pdf?ua=1](http://www.who.int/chp/chronic_disease_report/media/uk.pdf?ua=1)
2. Visit: [www.microscopedia.com/resource/microscopy/raman-microscope](http://www.microscopedia.com/resource/microscopy/raman-microscope)



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