Demand, Design, Delivery: High Potent Packaging at PCI Pharma Services

In a fragmented marketplace, drug discovery organisations are increasingly looking to work with fewer outsourcing partners. As such, CDMOs that are able to provide true end-to-end services are becoming more in demand. By partnering with full-service CDMOs, drug discovery organisations simplify and de-risk their supply chain, saving both time and money by maintaining production under one roof, or within one organisation. Shaun Engelhardt, PCI Pharma Services' Director of Engineering and Innovation, discusses how recent investments in their UK-based high potent facility has created this ideal scenario for clients.

Demand-led Investments in PCI

Drug products containing highly potent APIs (HPAPIs) present unique challenges to CDMOs, and not all of them have the true capability to manufacture or package them from clinical to commercial scale. PCI has significant experience in this arena, with our first Contained Manufacturing Facility (CMF) launched in 2013. With industry-leading containment solutions capable of handling APIs down to an OEL of 0.01 µg/m^3, and geometrically scalable equipment trains able to manufacture lab- and commercial-scale batches, the CMF proved hugely successful.

However, PCI is always looking for ways to provide a greater level of services to our clients. As such, recent CAPEX investments have led to the construction of a brand-new potent packaging facility at the Tredegar site, alongside a second CMF that doubles our commercial-scale high potent manufacturing capacity. The result is a true end-to-end, integrated service solution for clients who need their highly potent solid oral products manufactured, packaged and distributed globally from a single site.

This investment is a significant milestone for PCI and particularly the Tredegar site, allowing an increased capacity to manufacture and package our clients' products from clinical supply to commercial launch. By investing in these new facilities now, we are confident that PCI can remain a major player in this arena for years to come.

Design Considerations

When designing such a facility, an important early step is for the team to consider what an ideal, best-in-class facility should include. Amongst these considerations were the needs and demands of the marketplace; any fundamental regulatory requirements; the industrial best practices, and whether any of these are likely to remain steady or change in the years to come. Once these aspects were determined, we can then identify a 'wish list' and an outline specification. For example, having an excellent flow of materials is vital, ensuring a seamless movement of the drug product from manufacture to primary and secondary packaging, and onto the final step of serialising the packaged product. Another important factor is ensuring a good flow of personnel in terms of how staff enter the facility, where they gown, and how they enter the production areas.

These expansions at the Tredegar facility are the largest in terms of footprint that the site has undertaken. As such, a great deal of consideration was required in terms of the aforementioned personnel and material flows, as well as the facility design, engineering requirements, environmental monitoring systems for the critical environments, and regulatory influences. The integration into the existing site was therefore vital, particularly in light of any potential future site expansions.

The growing emphasis on small-volume products, such as orphan drugs or highly targeted therapies for very small patient populations, means that as a service provider, we need to build flexibility into our equipment to ensure we can cope with these requests. The new blister line installed within our new packaging suite is a key example of how we achieve this goal. For example, the installation of our first HAPA digital printer means that with just one reel of lidding foil, we can print artwork for multiple different market requirements on a single line, whilst retaining a high standard of control over airborne particulates. The result is considerable flexibility when packaging commercial products and a reduction in the waste of pre-printed materials, the latter being a key initiative in PCI's Environmental, Social and Governance (ESG) commitments.

Due to PCI's extensive experience in contained manufacturing and packaging at both clinical and commercial scale, we had a deep understanding of the equipment needed to ensure a successful expansion of the Tredegar site. By selecting the industry's leading equipment for the new facility from our range of existing suppliers, this meant our staff were incorporating a known equipment train into the facility, with an established knowledge base from which to draw.

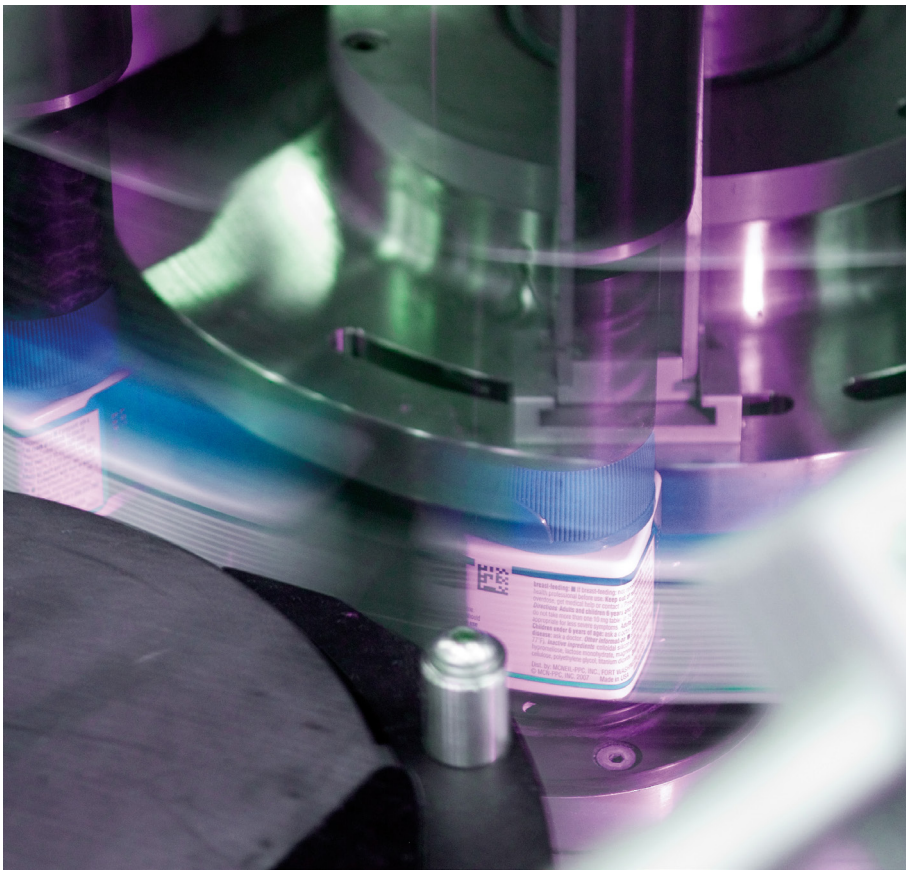
This experience also meant that we understood that containment of highly potent products, throughout the process, was vital, not just for product protection but also the safety of our operational staff. For example, we assessed processes and containment levels by conducting SMEPAC testing, which involves running a surrogate drug through the production lines to model the generation of airborne particulates. We then analyse how well we are able to contain those particles, for example by ensuring a robust system involving the segregation of rooms, conditioned environments for packaging activities, dust extraction units and dedicated HVAC systems.

PCI Tredegar utilizes HVAC throughout the facility. In high risk areas, we have isolated conditions with a minimum of 20 air changes per hour, meaning air is constantly being circulated through the facility. As such, any loss of highly potent material is captured in the HVAC and drawn through very high classification filters. The HVACs also help provide a pressure cascade in the area.

Delivery Challenges: Cleaning, Regulation and Product Integrity

PCI Tredegar is a multi-product facility. We therefore factored very robust cleaning procedures into the facility design. For example, the walls are made of an easily cleanable surface and the Ra (surface roughness) value of the equipment is 0.8 or less, which essentially provides a mirror finish to the equipment and prevents drug product from ingraining into the surface. This makes cleaning much more efficient and prevents the risk of contamination and carryover.

As automated cleaning methods are difficult to employ with packaging equipment, we rely on manual cleaning techniques. We perform risk assessments on the equipment, identify the hard-to-clean areas, and create an ever-growing knowledge base of how to clean the equipment. By performing regular cleaning checks, we ensure that standard procedures remain robust and there remains no risk of carryover. Additionally, purchasing dedicated tooling as part of client onboarding allows us to manufacture and package products with an even greater reduced risk of contamination.



As the pharmaceutical industry has a global supply chain, we at PCI have embedded Global regulations and industry best practice into our design, processes and procedures, ensuring the delivery of right first time quality products with increased customer satisfaction. Our team of dedicated experts on site are experienced in the preparation and hosting of Regulators from a range of Competent Authorities including MHRA, FDA, ANVISA, Turkish Ministry of health, Russian Trade and Industry ministry of health and PDMA.

In recent years, several audits have highlighted the use of cardboard within our facility, leading to the implementation of policies to reduce this as much as possible in the expansion. For example, we have introduced a de-boxing room as part of the new packaging facility, where raw materials and packaging materials are removed from the secondary packaging, cleaned within the de-boxing room, and then taken into the facility in polyethylene bags.

Additionally, the fundamental design of both sides of the production floor now separates the primary packaging from the subsequent secondary packaging using physical barriers, in line with regulatory requests.

To ensure a high degree of confidence that what is coming off the end of the line matches the client specification exactly, we installed specific systems on our automated production lines. For example, a sophisticated array of measures and checks on or bottling lines ensures the right label is applied to the right bottle, the desiccant is present, the bottle is sealed correctly, and the cap is tight enough. Our tablet-counting technology utilises EMF and infrared sensors play both sensors off against each other to ensure that both have seen the right count of product through the counting head. We also employ similarly smart technologies for capping, labelling and serialization in line with the EU Falsified Medicines Directive), and so on. Our serialisation line uses cameras that perform and enforce multiple checks and standards to reinforce finished product integrity.

Why PCI?

In spite of the global pandemic, PCI has

maintained focus on achieving continuous progress as a global organisation. By continuing to push forward in terms of building capability, capacity, adding new technologies and expertise, we feel confident that we are positioning ourselves as a major player in the CDMO arena.

PCI has been operating at the Tredegar site since 1985, providing a range of services to an international client base. In 2013, we reviewed our business model based on the demands of the marketplace and constructed our first, flagship Contained Manufacturing Facility (CMF), which was a significant investment in our site capabilities. This met the growing demand for highly potent solid oral dosage forms, and was instrumental in the site's success in the years that followed. This success led to PCI investing further, adding a second CMF which doubles our commercial manufacturing capacity, alongside the new high potent packaging facility. These new facilities will be operational in early 2023, with the increased capacity enabling PCI to become an even stronger CDMO partner. Our ability to supply highly targeted and lifesaving therapies to patients around the globe, from concept to commercialization, remains industry-leading, ensuring our clients products achieve speed to study, patient, approval and launch.

Shaun Engelhardt

Shaun has 17 years' experience in the pharmaceutical industry, working in a number of roles ranging from logistics to CAPEX programme management. In the latter role, Shaun oversaw the construction of Tredegar's new potent manufacturing and packaging facilities. He now serves as Director of Engineering and Innovation at PCI Tredegar.