

Ensuring Complete Product Packaging Quality

Liquid pharmaceutical manufacturers operate under great scrutiny and must set high standards of product quality. In three steps, Jürgen Kress, General Manager for Checkweighing and Vision Inspection, Mettler-Toledo Product Inspection, outlines how sophisticated weighing technology helps ensure that liquid pharma products are safe for consumers and compliant with regulations. He also examines the importance of serialisation and aggregation, and how product inspection helps drive transparency in the digital supply chain. Finally, he explains the importance of software connectivity as a critical part of making product packaging quality happen.

Step 1: Safety First – Getting Dosage Sizes and Pack Completeness Right

It's no exaggeration to say that quality assurance in liquid pharmaceuticals is a matter of life and death: give a patient too much or too little of a dosage, and the results might prove fatal.

Such potential consequences are bound to keep liquid pharmaceutical manufacturers on their toes. Their responsibility is to drive high standards in product quality, and to maintain these standards through the filling and packaging processes that ultimately deliver the finished product – be it a bottle, vial, ampule, or other vessel – to the patient or health sector organisation that will use it.

The Technology Solution

The solution for liquid pharma manufacturers lies in technical automation. Product inspection systems can perform the required technical tasks, in a fail-safe manner, and at the production speeds that manufacturers need to operate at to be profitable.

In this specific field, an advanced checkweigher is the best option to check that dosage sizes are correct within primary packaging. The system must be capable of extremely accurate weighing and of careful product handling. These products are very often small, light, fragile, and, in the case

of bottles, if not securely supported on the conveyor belt, are liable to tip over during processing. If a container breaks, there is spillage and possible glass fragments that can cause a line to shut down for clean-up, along with waste from the affected products on the line.

Getting the Sensitivity Correct

A checkweighing system based on high-performance Electro-Magnetic Force Restoration (EMFR) load cells has the required level of sensitivity to work with such lightweight products. It is not, however, just that the dosage amount might be under – or over – filled; there is also the issue of whether the bottles or vials themselves are of a uniform weight when empty. Even slight fluctuations in the tare weight of the vessel can have a profound impact on the gross weight of the product once filled. Therefore, each individual bottle's tare weight must be determined first, so that the correct dosage size leads to a predicted gross weight of product.

If fragile glass bottles and vials are not handled carefully during processing, they may break, leading to machine downtime while the problem is rectified. Therefore, checkweighers must have sophisticated product handling capabilities, including sorting and rejection mechanisms, to minimise this risk.

Optimising Productivity

This brings us to further benefits that fill level control of liquid pharma can deliver. Less downtime equals greater productivity and speed to market. Eliminating the risk of over-filling and product give-away ensures that the stock of medicine the manufacturer holds is optimised for the maximum number of bottled products, making the manufacturer more profitable. The avoidance of serious safety incidents preserves the brand's good name in the market. All of these dimensions are of an economic benefit to the manufacturer.

Alongside this control of fill level, another key part of quality assurance is the product completeness check. This can relate not just to the liquid itself, but to other things – typically a folded leaflet with medicine information and instructions for use – that must also be included within the product packaging to meet compliance requirements. Once again, these are very lightweight components of the package, but a sensitive checkweighing system can determine whether a pack has a leaflet inside or not by detecting subtle weight differences. An additional countercheck function in checkweighers can also help to ensure that rejected products are indeed off-weight and were correctly rejected. These processes can usually be carried out without disrupting production speeds.





In summary, the checkweigher can inspect the fill level, comparing tare weights with gross weights to make sure the right dosage size has been filled. It can also identify that a packaged product has been completed with all the components that need to be included. Aside from the safety of the patient or consumer, the benefit to the liquid pharma manufacturer of product inspection being able to detect these issues before a product is shipped to market is that they can avoid the significant financial and reputational costs that are the result of product recalls.



With fill level and completeness control, however, the case for the importance of high performance checkweighing becomes more apparent: patient safety is the main priority, but there are financial benefits for the manufacturer too.

Compliance

Then there is compliance. Product inspection systems such as checkweighers constantly gather and share production line data. This can be used to demonstrate that the manufacturer is operating in compliance with governmental regulations such as FDA 21 CFR Part 11 (which requires an audit trail of processing changes to be created and stored electronically), as well as those contractually set down by retailers.

Next Steps

As supply chains have become increasingly digitalised, the collection of data has been linked more and more to individual products, each with a unique serial code, enabling it to be instantly identified. This is critical in liquid pharmaceuticals and forms the basis of the second step: Serialisation and Aggregation.

Step 2: Serialisation is The Key to The Digital Supply Chain

The pharma supply chain is a digital one, driven by the electronic exchange of data. It cannot operate without serialisation – giving each product its own unique and verifiable code – and aggregation of batches

of products under a similarly verifiable code.

Context is especially important here. A worrying trend in the pharma market is that of counterfeit medicines, with unscrupulous suppliers seeking to make money from copycat medicines, where the standards of product quality and therefore safety are extremely dubious.

Serialisation

The digitalisation of the pharmaceutical supply chain has helped to tackle this problem, and serialisation of products is required in marking out the legitimate products from the fakes. Far more than this though, serialisation also paves the way for digital transparency and traceability throughout the supply chain of individual packs, and manufacturers can benefit from that in many different ways.

For example, it is a fact of life in the pharma business that occasionally there are problems with a product, e.g. a single vial, and it needs to be recalled. With serialisation in place, the manufacturer can utilise the serial code and access an audit trail of events and stages in an individual product's progression through manufacturing and packaging to distribution. If a recall must be made, the manufacturer can therefore be much more targeted in the scope of its recall, calling back just the specific products that it knows have been affected, rather

than entire batches, many of which might be perfectly good products.

Aggregation

Serialisation is followed by aggregation, where large batches are grouped together in a box, case or pallet for global or regional distribution of products. Aggregation can also serve as an anti-counterfeit measure offering additional assurance by checking these secondary boxes at key distribution points. Aggregation is becoming a mandatory requirement for compliance in many countries.

Whether we are talking about the unique serial code on an individual product or that on aggregated batch, the existence of a verifiable code immediately suggests quality and legitimacy. It reflects positively on the pharma manufacturer. However, an important word here is “verifiable”: the application of the code itself needs to be carried out with high quality, so that it is readable, with no smearing or skewing.

Partly, this is an issue of labelling and printing, in that printing onto labels or directly onto the side or top of a package, must be approached with a view to producing a code that is both clear and legible. That is only half of the story, though – inspection of the code is the second part.

Vision Inspection

Vision inspection systems are responsible for reading and quickly identifying packs with incorrect or poor-quality codes. This can save a great deal of time, money, and resources in allowing line stops so that any faults can be quickly rectified, and good quality coding can begin again.

In liquid pharma, the shapes, and sizes of the primary packaging – bottles, vials, ampules – present their own problems for serialisation and aggregation. For a start, since these kinds of vessels are typically round, they will rotate on the conveyer without a clear orientation of the package label visible at any time. Good product handling is going to be required in printing or applying serial codes directly onto pharmaceutical bottles, if that is the application. In vision inspection, it may be necessary to have technology that provides a full 360-degree view of the product surface, so that serialisation codes can be verified. Such a system would be able to view the product from all sides, regardless of the orientation and thus verify the serialised codes on the package.

A common practice with aggregated products is to use “helper codes”, printed on top of the products, so that the code can be read even when the product is packed into a container with other products. This still requires some forethought and co-ordination, since not every vision inspection system is able to read codes on the top of products.

It is important for liquid pharma manufacturers to make an analysis of their applications, bearing in mind the type of packaging they want to use at the final point of sale. Understanding this will aid in the setup of serialisation and aggregation processes so they can assess what their vision inspection requirements will be. For instance, in liquid pharma, equipment should be able to handle different types of round containers, can read top or helper codes, and can verify small detail data-matrix codes or codes of various sizes.

Sharing Data

The analysis must stretch beyond the factory walls too. Serial and aggregation data needs to be shared with the supply chain, so it is also critical that the technology deployed to read and verify codes can also communicate this information to the next links in the chain.

That communication comes about through digital connectivity, requiring software systems that can talk to each other, and that's what the third step will look at: the role of software connectivity in quality assurance for packaged liquid pharmaceutical products.

Step 3: Connectivity Gives Product Data its True Digital Meaning

In the previous two steps, we have looked

at ways in which product inspection equipment such as checkweighers and vision inspection systems can help liquid pharmaceutical manufacturers to manage the quality of their products.

In this third step, we move onto the importance of software connectivity to bring this all together. It is a technical challenge to integrate software, but one where pharma manufacturers and their technology suppliers must not cut corners, because the benefits of getting this right can reach into every aspect of a manufacturer's operation.

Connectivity

Equipping product inspection systems with the right software connectivity gives manufacturers a chance to gain a real-time picture of production, processing and packaging lines, allowing them to spot potential problems in advance. It might help them to avoid issues arising in the first place, but at the very least, they will be able to mitigate the damage and costs that they might incur. Being able to quickly pinpoint where something went wrong, and then quickly taking the action required to put it right, will also be appreciated by supply chain partners.

If we consider the word “connectivity” itself, we can gain a greater appreciation of why software connectivity is so important. We exist in a marketplace that is increasingly inter-connected; where the supply chain is transforming towards a fully digital utility that every partner both feeds into and taps into. To achieve true transparency, such a supply chain requires data to be automatically gathered and shared by each partner and passed on via an efficient digital





handshake from machine to machine, partner to partner.

Neither the handshake, nor the exchange of data can happen efficiently without software connectivity. In the areas of serialisation and aggregation, in particular, it is crucial. The point of these activities, after all, is to enable easy tracking of products, whether individually or as batches, through the supply chain. The data and the codes are pointless if they go nowhere. Building and sharing an audit trail of actions linked to serial codes serves multiple purposes.

Importance of Data

Firstly, it is a record of actions taken during manufacture and onward processing of a product – information that might need to be referred back to in the event of a problem with the product and as reference against attempts by counterfeit operations. Secondly, the data gained is useful for proving good manufacturing practices are being followed and meeting the compliance requirements of different levels of regulations. Thirdly, without this access to digital data, real-time process monitoring, and inventory management cannot meaningfully happen.

Role of Product Inspection

Pharma manufacturers will typically deploy checkweighing (for fill level and completeness checks) and vision inspection, to make additional quality checks as needed. Track and trace is a requirement for serialisation and may be optional for aggregation (depending upon the region). Utilising all three of these technologies will help in supporting top-quality production methods and compliance.

Modern checkweighers and vision inspection systems should have advanced software already integrated, with robust security levels and process monitoring capabilities built in. This should be aligned to global and local regulations that follow Good Automated Manufacturing Practice (GAMP 5) guidelines. For track and trace systems, integration into MES- or ERP-systems (Level 5 software) ensures connectivity across single or multiple production sites and provides transparency into the production line data. Exchange of data should be managed through industry standard protocols and software architecture such as OPC UA, PackML and Fieldbus, which supports developments around the Internet of Things and Industry 4.0 initiatives.

Compliance

For European manufacturers, compliance with the EU Falsified Medicines Directive (FMD) requires reporting of serialisation data to the European Medicines Verification Organisation (EMVO). Solutions for tracking and tracing the data must also include connectivity to Level 5 software, which in turn reports the data to the EMVO. Partner organisations must be technically certified to do the reporting as they have demonstrated that they meet the technical feasibility to do so.

Additionally, the need to comply with requirements such as those set out by the US FDA CFR 21 Part 11 regulations must also be supported. This FDA clause specifically calls for machinery to create a local electronic audit trail, recording activity such as user logins and machine set-up adjustments.

Compliance, digital supply chain transparency, managing production issues and operating more efficiently and cost effectively are benefits that liquid pharma manufacturers stand to gain by taking a proactive view of software connectivity.

All of these have a bearing on overall product quality – a multi-faceted aspiration for manufacturers in liquid pharma, incorporating the medication and the many processes by which that medication comes through the supply chain to market.

Conclusion

The key point to understand quality assurance for liquid pharma packs is that strong product inspection capabilities are at the centre of any effective quality assurance program. They help in making the production of liquid pharma products safe, complete, trackable, and compliant with all levels of regulations. They play a critical function in creating and maintaining a transparent and connected digital supply chain.

Crucially, product inspection systems do this while supporting manufacturers in meeting productivity and profitability objectives, by keeping production lines running at the speeds required with minimal downtime. Robust and thorough product inspection solutions are a requirement for liquid pharma manufacturers, helping them to overcome some of the many challenges they face today.

For more information: www.mt.com/pi-pharma-liquid-pr



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