White Paper-

# Market Insights and Solutions: Pharmaceutical Packaged Products


## Key Words

pharmaceutical packaged products, cGMPs, track and trace, safety, product inspection


## The Product Inspection Landscape

New approaches to selecting and using inspection and weighing equipment can help pharmaceutical processors better meet accuracy and safety objectives.

Metal detectors have long been a staple in pharmaceutical tablet press, capsule filling and deduster applications. This technology is also used in conjunction with packaging line operations. However, there can be challenges and limitations when metal-based packaging components, such as metalized film and foil seals, are part of the primary structure.

Implementing new technology—such as X-ray inspection—can help expand both inspection and detection capability.

Checkweighers and automated scales, also have been used in the pharmaceutical industry for decades to ensure packaged product weight accuracy. One of the biggest challenges for their use is lightweight products and variable weight packaging components that can pose challenges to weighing methodology. Incorporating two checkweighers—one prior to filling and one after—can help improve accuracy.

Pharmaceutical products come in various forms and package types. These include tablets, capsules, powders, liquids, creams, ointments and more. The most common package types are bottles, vials, blisters packs, jars, tubes and cartons.

Drug types include traditional over-the-counter, prescription, veterinary and extend into emerging nutraceutical, vitamin and other related categories. Selecting the right product inspection technology, such as metal detectors, X-ray inspection systems and checkweighers, will assist pharmaceutical processors to meet their product safety and brand integrity objectives.

## Physical Properties Challenges

The diversity of pharmaceutical product forms means that one solution doesn't fit all when it comes to ensuring packaged product safety and quality.

Obtaining the required weighing accuracy can be challenging when dealing with lightweight products. When you combine the variability in product weight with the acceptable tolerances in packaging component weight (bottles, closures, blister card material, etc.), the problem is compounded.

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Here's one example: a bottle is supposed to contain 30 tablets of a specific drug. But the variability in tablet weight could be such that 29 tablets manufactured at the upper acceptable weight limit could equal the weight of 30 tablets.

The bottle is checkweighed after filling and it meets the weight range previously determined as acceptable by the manufacturer. However, when the bottle is opened, only 29 tablets are inside, instead of the required 30.

This example illustrates how the combination of bottle and content weight can indicate false accuracy because each of the components has not been considered individually. When multiple components are weighed as one unit (bottle, label, closure, foil seal, patient insert, tablets, etc.), it becomes easy to see how a weight variation of one or more of these components can provide an end result that does not accurately reflect the requisite dose count.

This scenario also extends to powders, blister packs and other pharmaceutical product/packaging types where slight weight variations can negatively impact accuracy.

For this reason, pharmaceutical companies may want to consider the merit of installing two checkweighers on their manufacturing line: the first to weigh an empty container and the second to weigh the container after filling. Weighing empty and filled containers eliminates the potential for container weight variability adversely affecting pharmaceutical product weight accuracy.

Additionally, the lightweight nature of many pharmaceutical products is also pushing manufacturers to utilize checkweighing equipment with greater sensitivity so that measurement accuracy for these products can improve.

## Regulatory and Documentation Challenges

What differentiates pharma from other vertical markets is the level of regulation and documentation that must be adhered to in order to satisfy the requirements of the U.S. Food & Drug Administration's (FDA) current Good Manufacturing Practices (cGMPs). The cGMPs are minimum requirements needed to assure proper design, monitoring and control of manufacturing processes and facilities. They provide a formal system of controls to help prevent contamination, mix-ups, deviations, failures and errors so that drug products meet their quality standards.

Other markets (food, dietary supplements) regulated by the FDA must also comply with industry specific cGMPs. However, pharma market compliance requires more documentation, extensive equipment validation and qualification. In the not-too-distant future, the ability to track and trace drug products using electronic signatures will be added. Because of the need to comply with strict protocols when developing new

packaging lines, or adding a new machine to an existing line, pharma projects—from first discussion to equipment being put into operation—tend to take longer, on average, than in other markets.

## Clean Environment Challenges

Generally, pharmaceutical manufacturing and packaging is conducted in a clean environment, with equipment operating at speeds that typically do not push capability limits. Clean up usually requires machine wipe down, not full wash down, due to the antiseptic environment.  All of these have a positive impact on inspection equipment life expectancy.

## Inspection Needs from Sourcing to End User

There are several points in the pharmaceutical manufacturing process that benefit from inspection (metal detectors, X-ray equipment) and checkweighing technology. Here are some examples.

1. **Incoming ingredients.** Drop though and pipeline metal detectors can be used to locate contaminants.Depending on when the chemicals and other products were processed or mixed, potential contaminant types could include metal wire, a screen piece that the product may have been filtered through or a part (screw, nut or washer) that may have fallen off the mixer or other processing equipment itself. Additionally, the contaminant could have made its way into the product during transport from the ingredient supplier to the manufacturer.

2. **Tablet press or capsule filling.** After pressing or filling, excess powder must be removed. Typically, a vibratory device is used to separate the dust from the tablet or capsule, enabling it to be removed by vacuum. An ideal place to position a metal detector is after this process to make sure a small metal contaminant has not found its way into the medication.

3. **Packaging operation.** Checkweighers can be used in a number of different locations in the packaging line. As mentioned earlier, they can be used to weigh empty and filled bottles to assure the highest accuracy. Checkweighers also can be used to provide feedback to the filling machine to indicate when it is beginning to show a trend of under or over filling of product.

   Checkweighers also are frequently used after cartoners to assure that all required product and packaging components, by weight, have been inserted into the carton. Another typical location is after a blister form/fill/seal machine. Checkweighers also can be used to weigh a bundle or larger assembled group of products at the end of a packaging line.

When a foil component is part of the package, metal detector use is limited. That is why for most bottle applications, metal detectors are used after the filling machine, before the closure is applied. However, there is equipment that can be used to detect metal contaminants in containers after they have passed through an induction sealer.

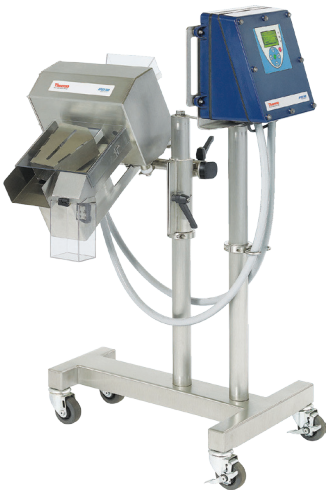
Converting to X-ray inspection will give pharmaceutical manufacturers additional inspection/detection capabilities. Metalized/foil components will no longer be an issue, inspection for broken/missing tablets is then possible and blister packs (with foil backing) can easily be inspected.

4. **Track and trace.** Checkweighers can play a significant role for manufacturers implementing track and trace, serialization or aggregation capabilities on their packaging lines.


Integrating code printing and verification equipment—the key elements of a track and trace/serialization/ePedigree solution—with a checkweigher, can save both cost and valuable floor space. Also, a checkweigher can automatically track products from the point of code verification to a reject mechanism. This means that reject verification and fail safe reject operation can be included in the system; both are of critical importance for most pharma applications.

A checkweigher designed specifically for pharmaceutical applications, and which complies with the industry's GMPs, has the ability to provide the highest level of weighing accuracy. This will serve as a good foundation for an integrated track and trace system. Another consideration is the system's operating speed. A system that will satisfy today's requirements, as well as having the capability to meet higher future speed requirements, is ideal.

## Meeting Applications Challenges



The **Thermo Scientific™ APEX 500 Rx Metal Detector** has been specifically engineered to meet the sensitivity, environmental and hygienic needs of pharmaceutical applications.

It features a patented multicoil design that consistently delivers industry-leading sensitivity and stability. Designed to detect even small slivers of metal, the APEX 500 Rx provides high sensitivity at high flow rates, while preventing product damage. Features and benefits include:

- Cost-effective solution for tablet presses, capsule filling and deduster applications
- High sensitivity—can detect metal pieces as small as 0.25mm
- Easy-to-use, password protected user interface
- Portable design for system mobility
- Quality assurance test and AuditCheck features to verify performance
- Complete IQ/OQ/PQ validation packaging available
- Integration with deduster system (optional)

**Thermo Scientific Versa Rx Checkweighing System**

The Thermo Scientific™ Versa Rx checkweighing system handles high-speed lines with ease and unparalleled accuracy. The system uses a single, brushless motor to power the infeed, weigh table and outfeed conveyors. It weighs products from 2 to 500 grams at speeds up to 600 parts per minute, depending on pack size.

Engineered for low maintenance, the Versa Rx has a unique closed cabinet design to reduce the impact of air drafts on weighing accuracy. Conveyors have a knife edge feature which help to ensure greater accuracy by minimizing product movement, such as bottle rocking or carton skewing. The system can be equipped with optional pharma-specific features and can be used for track and trace applications.

Its flexible design can handle a wide range of containers including plastic/glass bottles, blister packs, cartons, pouches, small aerosols and sachets. Features and benefits include:

- Easy-to-use, maintain
- Sanitary design
- High accuracy, speed
- 21 CRF Part 11 compliance option
- Marking and verification/data matrix optional
- Designed to GMP standards

Checkweighers, in addition to their primary function of confirming weight accuracy, can also be an integral component of track and trace methodologies.

## Protecting Brand Reputation

Reaching a high level of consumer satisfaction in the pharmaceutical segment has its own set of challenges. Oftentimes, the consumer doesn't have a purchasing choice; the specific medication has been prescribed by a healthcare professional. However, the consumer can and will react to problems with the medication and the packaging, among others.

What used to be a phone call or letter to the manufacturer complaining about a missing or broken tablet now results in a photograph and negative discussion on a social media site. Complaints are no longer a private matter between the consumer, the pharmacy and the manufacturer. Instead, they are voiced publicly and loudly, encouraging others to chime in with their negative experiences.

Consumers have learned that their concerns are more likely to be addressed quickly if they are made public. So now, pharmaceutical companies are having to employ costly human resources to monitor and address social media complaints. This is leading manufacturers to investigate all inspection options available, including X-ray, to prevent these issues from occurring in the first place.

## Key Takeaways

Pharmaceutical product safety and quality can benefit from the use of inspection/detection and checkweighing equipment. There are multiple places on the processing and packaging line where installing these systems can positively impact the quality, accuracy and safety of the pharmaceutical product being marketed.

Unlike many food processors and consumer packaged goods companies, pharmaceutical manufacturers have been slow to convert from metal detectors to X-ray inspection. This late adapter status has meant that these companies have not been able to take full advantage of the latest technology to keep products contaminant free and identify broken or missing components.

To review:

1. New approaches to selecting and using inspection and weighing equipment can help pharmaceutical processors better meet accuracy and safety objectives.
2. Implementing new technology—such as X-ray inspection—can help expand both inspection and detection capability.
3. The diversity of pharmaceutical product forms means that one solution doesn't fit all when it comes to ensuring packaged product safety and quality.
4. Obtaining the required weighing accuracy can be challenging when dealing with lightweight products combined with lightweight packaging components. For this reason, pharmaceutical companies may want to consider the merit of installing two checkweighers on their manufacturing line--the first to weigh an empty container and the second to weigh the container after filling.
5. What differentiates pharma from other vertical markets is the level of regulation and documentation that must be adhered to in order to satisfy the requirements of the U.S. Food & Drug Administration's (FDA) current Good Manufacturing Practices (cGMPs).
6. There are several points in the pharmaceutical manufacturing process that benefit from inspection (metal detectors, X-ray equipment) and checkweighing technology. Examples include: incoming ingredients, tablet press/capsule filling, packaging and track/trace.
7. Checkweighers, in addition to their primary function of confirming weight accuracy, can also be an integral component of track and trace methodologies.
8. It is critical that upfront efforts are made to minimize product complaints, otherwise posts on fast-paced social media sites may negatively impact your brand.

## Links and Resources

AuditCheck White Paper Thermoscientific.com/Auditcheck

Track and Trace White Paper Thermoscientific.com/trackandtrace

Thermo Scientific Checkweighing Solutions Thermoscientific.com/Checkweighingsolutions

Thermo Scientific Versa Rx Checkweigher in action Thermoscientific.com/Versainaction

Thermo Scientific Metal Detector Solutions for Pharma Thermoscientific.com/Metaldetector

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