SYMETIX®

Bulk Inspection of Tablets:

Assuring Product Quality at Manufacturing and Packaging

With the consolidation of tablet manufacturing plants, with the expansion of tablet packaging operations and with the increased separation of tablet manufacturing from packaging, come greater probabilities for mix-ups. The risk that foreign tablets and foreign matter could find their way into packaged product is rising. At the same time, product quality is being scrutinized by customers more closely than ever before and processes are increasingly coming under the review of regulatory agencies.

Now more than ever, manufacturers, packagers and brand owners of OTC and regulated pharmaceuticals need to take every precaution to deliver consistently high quality product. Inspecting the package is clearly not enough. The tablets need to be inspected too.

In the past, most manufacturers and packers of tablets have relied on labor-intensive manual inspection because automated systems were expensive and slow. But a new class of automated inspection systems – bulk vision inspection systems – have recently been developed specifically for tablets. The effectiveness of these new systems is prompting a new debate on what it means to be diligent in pharmaceutical manufacturing and packaging.

In this white paper, we will discuss the risks and consequences of relying on vulnerable verification processes. We also explore the various inspection practices available to tablet manufacturers and packagers, highlighting both the advantages and disadvantages of each. Lastly, we will suggest criteria to consider when selecting the ideal system for your application.

Risks and Consequences of Vulnerable Inspection

Of course, the ideal acceptable quality level (AQL) is zero defects, but in reality, technological limitations and business practices erode this ideal. The more production lines in the plant and the more "touch points" or distinct steps in the production process, the greater the risk of both cross contamination and the introduction of foreign matter – both critical problems.

If a foreign tablet or foreign matter is found in a packaged product, the consequences can be disastrous. At a minimum, such an incident will erode confidence in the company. More seriously, the event could trigger an expensive product recall call, or worse still, a consumer could ingest the foreign tablet and experience an adverse health reaction, which could result in litigation.

But even critical defects that were left in the product that left the manufacturing plant and are later found by a packager can have a devastating impact. Such an incident will cause the batch to be rejected or worse, product from that batch already packaged will have to be isolated and returned – both costly mistakes that affect a company's bottom line as well as reputation.

Reducing exposure to such risks is a high priority for quality-conscious tablet manufacturers, contract packers and brand owners. It's interesting to note that using effective inspection systems serves a dual purpose. Obviously, it reduces the risk that foreign tablets, foreign matter and defects reach customers. It also illustrates the company's due diligence, which reduces their financial exposure, should an incident occur.

To a lesser extent, even minor defects such as broken tablets, stained or off-color tablets and tablets with scratched or chipped coating can be a problem. Although these issues are not as devastating to a manufacturer, packager or

brand owner as the more critical defects (foreign tablets and foreign matter), they are common occurrences that have a negative impact on the perception of the company, which can affect customer loyalty and result in lost sales.

Types of Inspection Systems for Tablets
"Zero defects one hundred percent of the time will cost you an infinite amount of money," noted Lynn Torbeck, a consultant that specializes in cGMP statistics and their applications in the pharmaceutical industry.

Although no single inspection system is capable of achieving zero defects all of the time, some will get closer to that ideal than others. Furthermore, the commercial viability of various inspection systems differs dramatically, and these production and business considerations must also play a role in determining the ideal quality assurance program for any given situation.

It is important the every tablet manufacturer, packager and brand owner consider the benefits and limitations of each inspection practice and select the ideal program given their situation and objectives and implement the program to

RELATIVE CAPACITY

Manual Inspection

Mechanical Sorter

Bulk Optical System
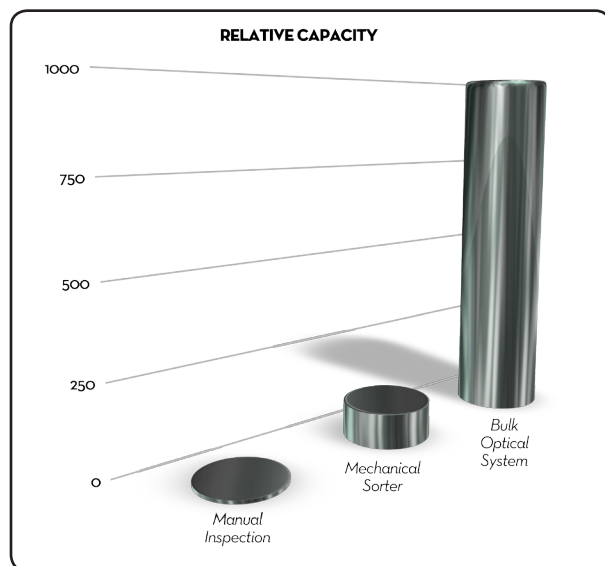
its fullest capability. Nothing less will serve to protect consumers and limit liability exposure.

No In-Line Inspection
Few tablet manufacturers and packers rely solely on sampling to assure final product quality because such a program puts the company at risk. Not only are they assuming the greatest risk that a critical defect such as a foreign tablet or foreign matter makes it way into packaged product, but they are fully exposed to a liability lawsuit and/or regulatory ramifications if such an incident occurs. Although this approach is cost effective in the short run, with no capital costs associated with automated processes or labor costs associated with 100 percent inspection, the long term costs can be significant. They are exposed to the most severe regulatory actions and the largest legal settlements should a problem arise.

Manual Inspection
Currently, the most common type of inspection in use on tablet manufacturing and packaging lines is manual inspection. The primary advantages of manual inspection are low capital costs and a strong basis for claiming diligence if the company is confronted with a liability situation. The disadvantages of manual inspection include high labor costs and most importantly, the fact that people are notoriously poor at inspection, especially over time as diligence decays. Furthermore, yield can suffer dramatically because manual inspectors often feel that their job is to pull product off the line and they won't succeed until their bucket is full. Lastly, adding people to the process can actually increase the incidence of foreign matter and the risk of contamination through both unintentional mistakes and malicious acts.

A variety of mechanical systems such as in-line conveyors and rotary tables are available to assist manual inspection. Although these systems are designed to facilitate the inspection process,

the benefits and drawbacks of manual inspection remain the same regardless of the technology that assists the operation.

Mechanical Sorting

Mechanically sorting tablets on manufacturing and packaging lines can be very effective in removing broken tablets as well as dust and coating flakes. But they cannot detect and remove foreign tablets that are the same size and shape as good product. They cannot detect and remove foreign tablets based on color differences and even their ability to remove product of a different size is limited to the minimum axis.

A common type of mechanical sorting system in use in the pharmaceutical industry today is the diverging roller sorter. In addition to its limitation in removing foreigners described above, its other disadvantage is its mechanical complexity. Such systems have many moving parts and wear parts, which require significant maintenance and operator intervention and reduces the repeatability of the systems' performance. Furthermore, these complex systems can be time consuming to sanitize during product changeover, typically resulting in the loss of two hours of production time.

A newer type of mechanical sorting system is the vibratory size grader. Although these systems are still limited to removing defects and foreign tablets based only on size, many of the drawbacks of diverging roller sorter have been resolved with this new technology. Vibratory size graders have few moving parts and no rotating parts. Mechanical simplicity reduces maintenance, which lowers the total cost of ownership. These vibratory size graders can be cleared and cleaned in only five minutes and, with fixed hole sizes in the removable decks, the process is fully repeatable and independent of the operator's skill. Lastly, a vibratory size grader can typically handle up to one million tablets per

hour – three times the throughput of a diverging roller sorter.

Single-File Optical Inspection Systems

Due to limited throughput and high capital costs, single-file optical inspection systems have not been widely adopted. Only when the need to assure the highest product quality outweighs other commercial considerations does this technology prevail.

These systems, first introduced 20 years ago, are spectacular at detecting and removing foreign tablets, foreign material and defects based on color, size and shape. However, low throughput (typically 50,000 tablets per hour), high capital costs and many expensive changeparts have made these systems unviable for most processors. Another drawback is that it often takes up to eight hours to change these systems over.

Blister Inspection

Many blister packing lines have integrated inspection systems that verify each of the blister pockets have a tablet. Because these systems do not typically verify the color, size or shape of the tablet in each pocket, they are not effective at detecting and removing blisters with foreign tablets or defects. To assure final product quality, additional inspection should be upstream of the blister packing equipment.

Bulk Optical Inspection Systems

Automated optical inspection systems, which have been widely adopted for decades in the food processing industry, have recently been developed for OTC and regulated tablets. Like single-file optical inspection systems, they use color cameras to inspect each object's color, size and shape. Unlike single-file optical systems, they need not single-file or orient products prior to inspection. The new bulk optical inspection systems are highly effective in detecting and

removing foreign tablets, foreign matter and defects. And, at roughly one third the cost of single-file systems based on equivalent capacity, bulk optical inspection systems are more affordable than single-file optical inspection systems. They can handle one million tablets an hour and can be cleared and cleaned in less than five minutes during product changeovers.

The Benefits of Bulk Optical Inspection Systems

The goal of a bulk optical inspection system is to assure high final product quality while maintaining high production throughput. This is achieved with high-resolution color cameras that are effective in inspecting shape, size and color. Some bulk optical inspection systems are so effective, they guarantee removal of 100 percent of foreign tablets, while also removing foreign matter, broken tablets, stained tablets and tablets with scratched coating if the coating is a different color than the underlying tablet.

But these systems provide additional benefits beyond superior product quality. Compared to manual inspection, bulk optical inspection systems reduce labor costs, often replacing 10 to 15 manual inspectors, and increase yield. Compared to diverging roller sorters and single-file optical systems, bulk optical inspection systems speed changeovers. And these bulk optical systems reduce capital costs and simply operation compared to single-file optical inspection systems.

However, there are less obvious benefits that can be achieved with bulk optical inspection systems – those associated with replacing batch processes with continuous, integrated automated processing and process control.

Currently, at every step between two batch processes, tablet manufacturers and packagers invest labor to move product and consume space to store work-in-progress inventory. But more importantly, at every step, the risk that a foreign tablet or foreign matter enters the product stream increases. Knowing all this, tablet manufacturers and packagers are racing to automate their production lines and continuous processes are replacing batch processes. Bulk optical inspection systems help facilitate this paradigm shift.

In addition to assuring product quality and reducing labor, bulk optical inspection systems can be used for process control. By capturing a continuous stream of data about products on the line in real-time, this technology enables manufacturers to improve upstream operations and streamline downstream processes immediately. And in the future, harnessing this data may be useful for integrating into Process Analytical Technology (PAT) initiatives.

Selecting an Optical Inspection System

Beyond looking for equipment that meets FDA requirements and complies with GAMP 5 guidelines, additional selection criteria must be carefully considered if all of the operational advantages outlined above are to be achieved.

The finest bulk optical inspection systems recognize subtle differences in color, size and shape to ensure every tablet conforms to product specifications. If the system offers ultra-high resolution (defined as 0.17 mm square pixels), then the system can detect and remove foreign tablets as well as the smallest foreign matter and the smallest color and shape defects. This is best achieved if the system uses four cameras that are located both above and below the product stream to view the product from all sides. Such systems are currently available to inspect up to 1,000,000 tablets per hour.

Of course, the effectiveness of the bulk optical inspection system relies not only

on the hardware but on the software – the algorithms – that manipulate raw data and categorize information based on the customer-defined accept/reject thresholds. The art and science of image processing lies in developing computerized routines that improve the effectiveness of the operation while presenting a simple user-interface to the operator. Thus, the equipment manufacturer's experience and success with optical inspections systems for the pharmaceutical industry and tablets in particular are key indicators of their ability to deliver systems that will achieve optimal performance.

The equipment manufacturer must be able to assist with the development and execution of the required qualification protocols, and produce systems that comply with GAMP 4 and 21 CFR 11 requirements. Furthermore, it is important to consider the level of service a supplier can provide in your region – from engineering to validation and after-sales support.

Conclusion

The arrival of modern bulk vision inspection systems designed specifically for tablets is likely to transform the industry. With their effectiveness in assuring final product quality and their commercial viability, both in terms of production throughput and capital costs, such systems appeal to product manufacturers, packagers and brand owners looking to deliver consistently high product quality and eliminate costs from the operation.