Optimizing Quality and Increasing Production Throughput with Automated Tablet Testing

Automated pharmaceutical testing is a critical component of developing and deploying quality at its highest standard. Resulting in increased productivity, greater customer satisfaction and ease of regulatory compliance. Automation is having an ever important affect on the economy of pharmaceutical operations world wide. Fully automated tablet presses are now common with productivity measured in the millions of tablets per day per press outlet.

Measured parameters & corrective actions
Measuring the compression force for each punch has become a standard feature of modern tablet presses to take immediate corrective actions. Although the compression force allows drawing conclusions about product specifications such as weight, thickness and hardness of tablets, additional testing of each parameter is required to ensure the product characteristics are within the specified limits. It is important to understand, that even though all three parameters are directly related, only their combined test results provide a basis for reliable quality control. The following table illustrates the basic correlation between weight, thickness and hardness.

Weight	Thickness	Hardness
× (out of limits)	✓ (correct)	× (out of limits)
✓ (correct)	× (out of limits)	× (out of limits)
✓ (correct)	✓ (correct)	✓ (correct)

As the table shows, tablet hardness not only relates to the disintegration time of a tablet, it is also an indicator whether the combination of weight and thickness is correct. In other words: if hardness is out of limits, either weight or thickness (or both) will also not meet product specifications. It doesn't, however, tell the operator which parameter needs to be adjusted in the production process (e.g. compression force or filling quantity). Only testing of all three parameters gives a complete picture – and allows for appropriate corrective measures.

Fully integrated IPC
To take full advantage of modern high-capacity presses requires in-process tablet testing also be compatibly automated. Modern tablet testers like the "AutoTest 4" from Dr. Schleuniger Pharmatron automatically measure weight, thickness, diameter, and hardness of tablets and can be operated stand-alone or fully integrated with a great variety of tablet presses from different manufacturers. Measured test results are transferred to the tablet press in real-time to automatically adjust production parameters or alert the operator. Often referred to as "lightly attended operation", the combined system of tablet press and tablet tester provides for maximum efficiency and reliability as tests are conducted automatically at preset intervals without any operator interaction required. When making a purchasing decision for an automatic tester in fully integrated IPC, the following key factors must be considered:

1. ***Can the tablet tester be used in-line with your (existing) presses?***
   A high-quality popular tester such as the "AutoTest 4" has in-line interface software written for it by a wide variety of internationally leading press manufacturers. Tests are started automatically during the production process and production parameters are adjusted automatically based on measured test results.
2. ***Can the tablet tester handle a wide variety of tablet sizes and shapes?***
   Be sure to select a tester that is capable of testing an assortment of tablet sizes and shapes. Oblong, hexagon diamond and custom designed shapes should be correctly oriented automatically and fed to sequential width, thickness, diameter, and hardness test positions.
3. ***How reliable and precise are the test results?***
   Force measurement of hardness must be reliable, consistent, and posses unquestionable linear accuracy. The best precision is achieved by a S-Beam type load cell, as this state-of-the-art transducer is internationally accepted for its accuracy and reliability. To provide for reliable weight measurement, there are two key factors: Precision of the integrated weighing system (balance) and vibration-resistant design of

the tester itself. As test equipment is located directly in the compression room, the tester needs to absorb vibrations from the tablet press and air draughts in the production environment.

Mechanically integrated IPC

Even tableting operations still employing traditional lower output presses can benefit immensely by converting their manually operated tablet testers to fully automated models. Besides the obvious significant labor saving advantages, automated weight, thickness, diameter and hardness testers provide real-time, accurate test data that can be identified and evaluated immediately. Resultant corrective action, if any, is therefore timely and prevents costly continued production of a substandard product. Productivity and quality are enhanced along with reduced waste and the need for costly remakes.

Additionally, test data generated by a quality automated tablet tester can be electronically captured, stored and secured on a PC with CFR 21 Part 11 compliant software. Data can be retrieved onsite or remotely at any time and displayed in either tabular – such as Microsoft Excel® – or graphic format. Data required for client or regulatory audits is easily compiled and generated. Automatic tablet testers like the "AutoTest 4" from Dr. Schleuniger Pharmatron can be networked with multiple tablet presses with operational control being done from one, centrally located, windows based PC.

Productivity maximized

A typical example comparing a fully automated tablet test system with a manual tablet testing protocol is very telling. Contract manufacturing is very competitive, being able to offer unsurpassed quality, reducing direct manufacturing costs and providing clients with concise, easy to understand test reports can be paramount to maintaining a competitive edge.

In one case study a contract manufacturer with 17 press bays outputting as many as 15 different products a day ranging from dietary supplements to OTCs, used 5 manual tablet testers shared by all the press operators. The quality control lab used the same model tester as production. Because of the extremely wide range of formulas in manufacture at any given time, plausibility and T limits were not programmed or recorded on the compression floor. To do so resulted in specification input errors, testing errors, confusion, avoidable production stoppages and unnecessary expenditures of labor. Plausibility and T limits were manually calculated in the QC lab using production tester printouts. Batches were then authorized for release. The entire process was immensely inefficient, laced with opportunities for errors and time consuming.

After reviewing internal IPC and QC processes, the contract manufacturer decided to replace the manual testers with 4 fully automated testers (in this case "AutoTest 4" tablet testing systems from Dr. Schleuniger Pharmatron): three in production and one in the QC lab. The automatic tester in the QC lab and one of the production units had a so-called "12-magazine feeder" to allow setup of up to 12 tests at the same time – making it possible to quickly and easily test multiple samples from a wide variety of products and batches. Whereas one tester could be shared among a group of press bays in production, it proved to be equally useful to use a 12-magazine feeder in QC to streamline processes and minimize investment costs. The two remaining "AutoTest 4" were installed directly in the compression room in combination with portable tablet diverters and an air transport system. One of the main advantages of realizing the press integration with a stand-alone testing system was that no modification of the existing presses was required. Stack lights were programmed to signal whether a T limit has been exceeded alerting the press operator. The benefits and increased efficiencies were immediately apparent. Test reports by batch including plausibility, T1 and T2 limits were generated with each tablet sampling in real time. Confusing data became a thing of the past and batch release authorizations took place in synergy with production schedules. Customers were pleased to receive test data by email within hours of their products being completed. Delivery times were reduced as was direct labor costs.

What's next?

Automating tablet testing is one of the key determinants to achieve reliable quality and productivity in tablet production – making it an important factor for optimized cost-efficient operations. With an ongoing market consolidation and increasing cost pressure, pharmaceutical manufacturing is forced to look into automation, but also into other possibilities along the value creation chain to increase production throughput without compromising quality. Holistic product development strives to design new products not only from a formulation and marketing point of view, but also takes production and quality control aspects into account. The use of alternative technologies such as automated NIR spectroscopy is actively pursued by almost all international pharmaceutical companies and will continue to change the way the industry is working today. First successful PAT projects where a Real Time Release (RTR) using automated NIR technology has been realized open up new possibilities in automated tablet testing and show how significant cost savings can be realized.

Stand-alone tablet testing:
Setup of multiple tests / samples
with 12-magazine feeder

Integrated tablet testing:
with portable diverter and air transport system