Automated Testing: A Critical Component of High-Throughput Tablet Production

Automated tablet testing is a key factor in ensuring quality and achieving optimal productivity in tableting operations.

Automated pharmaceutical testing is a critical component of developing and deploying quality at its highest level, resulting in increased productivity, greater customer satisfaction and ease of regulatory compliance. Automation is having an ever-important effect on the economics of pharmaceutical operations worldwide. In the case of tablet production, fully automated presses are now common with productivity measured in millions of tablets per day per press outlet.

**CORRELATION BETWEEN TABLET PARAMETERS**

Measuring the compression force for each tablet punch has become a standard feature of modern tablet presses in order to be able to take immediate corrective action in the event of a fault. Although the compression force allows conclusions to be drawn about product specifications – such as the weight, thickness and hardness of tablets – additional testing of each parameter is required to ensure that the product characteristics are within the limits specified. It is important to understand that, even though all three parameters are directly related, only their combined test results will provide a basis for reliable quality control.

The basic correlation between weight, thickness and hardness is illustrated in Table 1. As the table shows, tablet hardness not only relates to the disintegration time of a tablet, it is also an indicator of whether the combination of weight and thickness is correct. In other words, if hardness is out of limits, then either weight or thickness (or both) will also not meet product specifications. It does not, however, tell the operator which parameter needs to be adjusted in the production process (for example, compression force or filling quantity). Only testing of all three parameters will give a complete picture – and allow for appropriate corrective measures to be taken.

**FULLY INTEGRATED IPC**

In order to take full advantage of modern high-capacity presses, in-process tablet testing also needs to be automated. Modern tablet testers automatically measure the weight, thickness, diameter and hardness of tablets, and can be operated on a standalone basis 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 pre-set intervals without any operator interaction required. When making a purchasing decision for an automatic tester with fully integrated in process control (IPC), the following key factors need to be considered:

**Can the Tablet Tester be Used In-line with Existing Presses?**

A high-quality popular tester would usually have in-line interface software written for it by a wide variety of leading international press manufacturers. Tests are started automatically during the production process, and production parameters are adjusted automatically based on measured test results.

**Can the Tablet Tester Handle a Wide Variety of Tablet Sizes and Shapes?**

It is important 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.

**How Reliable and Precise are the Test Results?**

Force measurement of hardness must be reliable and consistent, and posses unquestionable linear accuracy. The best precision is achieved by an S-Beam type load cell; this state-of-the-art transducer is internationally accepted for its accuracy and reliability. To provide

| Table 1: Basic correlation between weight, thickness and hardness of tablets |
|-----------------------------|-----------------------------|-----------------------------|
| Weight | Thickness | Hardness |
| ✓ (Out of limits) | ✓ (Correct) | ✗ (Out of limits) |
| ✓ (Correct) | ✗ (Out of limits) | ✗ (Out of limits) |
| ✓ (Correct) | ✓ (Correct) | ✓ (Correct) |
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 need to be able to absorb vibrations from the tablet press, as well as air draughts in the production environment.

MECHANICALLY INTEGRATED IPC

Even tableting operations that still employ traditional, lower-output presses can benefit immensely by converting their manually operated tablet testers to fully automated models. Besides the obvious significant labour-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 (for example, Microsoft Excel) or graphic format. Data required for client or regulatory audits is easily compiled and generated. Automatic tablet testers can be networked with multiple tablet presses, and operational control performed by one, centrally located, Windows-based PC.

PRODUCTIVITY CASE STUDY

The advantages of automation are shown by a case study comparing a fully automated tablet test system with a manual tablet testing protocol. Contract manufacturing is very competitive, and the ability to offer unsurpassed quality, reduce direct manufacturing costs and provide clients with concise, easy-to-understand test reports can be paramount in maintaining a competitive edge.

A contract manufacturer with 17 press bays outputting as many as 15 different products a day – ranging from dietary supplements to OTC products – used five 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 waste of labour. Plausibility and T limits were manually calculated in the quality control (QC) lab using production tester printouts. Batches were then authorised for release. The entire process was incredibly inefficient, laced with opportunities for error and very time-consuming.

After reviewing internal IPC and QC processes, the contract manufacturer decided to replace the manual testers with four 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’ (see Figure 1) to allow the set-up of as many as 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 minimise investment costs. The two remaining automated testers were installed directly in the compression room in combination with portable tablet diverters and an air transport system (see Figure 2).

One of the main advantages of realising the press integration with a standalone testing system was that no modification of the existing presses was required. Stack lights were programmed to signal whether a T limit had 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 authorisations 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 were direct labour costs.

WHAT’S NEXT?

Automating tablet testing is one of the key determinants of achieving reliable quality and productivity in tablet production – making it an important factor for optimised, cost-efficient operations. Given the ongoing market consolidation and increasing cost pressures within the industry, manufacturers are under pressure to look not only at automation but also at 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 taking production and quality control aspects into account. The use of alternative technologies such as automated near-infrared (NIR) spectroscopy is being actively pursued by almost all international pharmaceutical companies and will continue to change the way that the industry operates. The first successful process analytical technology (PAT) projects where a real-time release (RTR) using automated NIR technology has been realised open up new possibilities in automated tablet testing and show how significant cost-savings can be realised.

Holger Hermann is Vice President of Sales & Marketing at Dr. Schleuniger Pharmatron headquartered in Switzerland. With more than 15,000 testers in the market, the company offers solid dosage form test equipment and specialises in complete tablet testing solutions for research laboratories, IPC and QC departments and manufacturing plants of pharmaceutical companies all over the world. Holger is responsible for international sales, business development and key account management. Prior to his engagement at Dr. Schleuniger Pharmatron, he has been working for international engineering companies in the field of process automation and handling systems. Email: holger.herrmann@pharmatron.ch