Quality control in the laboratory and in production

The holy grail of automated tablet testing

It may seem surprising at first glance, but the proportion of manually performed physical tests in quality control is increasing in many places – despite high cost pressure. The increasing use of "complex" shapes for tablets, such as convex, oblong, and oval formats, or the lack of automation solutions for their testing, poses new challenges for solid oral dosage manufacturers. Reliable alignment of a complex variety is a basic requirement for precise, meaningful measurement results.

Positioning the dosage form with repeatable accuracy ensures that the measurement of weight, tablet dimensions (height / width / length) and breaking force ("tablet hardness") can be carried out in a reliable, unattended fashion. What is comparatively easy with round tablets, often leads to challenges with convex oblongs and "bulbous", oval-shaped tablets – both during manual testing by the operator and in automated operation. Put simply: what aids in swallowing an oblong tablet makes it more difficult to measure it physically. Aggressively curved, convex shapes are easier to take orally for the patient but become difficult while positioning in the testing device due to their small contact surface and the resulting limited stability. Even very slight deviations in the alignment between the fracture jaws cause the test specimen to rotate out of the longitudinal axis during the breaking force measurement. These differences can sometimes have considerable effects on the breaking process and thus on the measured breaking force ("tablet hardness" / "breaking strength"). Frequent incorrect measurements or less meaningful results are the outcome. Pharmaceutical manufacturers therefore often have no other option than to perform the required tests manually or, at best, partially automated. Possible increases in efficiency in quality control (QC) and in-process control (IPC) are reduced and the repeatability of tests can be highly operator-dependent. A fully automated on-line IPC, in which the tablet testing system carries out the required tests in the press room at regular intervals without operator intervention and transmits measurement results in real time to the tablet press for automatic readjustment, is not possible without reliable, repeated accuracy of the tablets automatic positioning.

Figure 1:
AT50 tablet testing system with integrated sample collector for automated on-line in-process control with tablet presses

Figure 2:
Compact and robust for use in the press room. Thanks to its low overall height and integrated wheels, the AT50 can be easily and space-savingly used in combination with a tablet press and upright deduster in the press room for automated on-line in-process control

With the new AT50, the Swiss manufacturer SOTAX is now for the first time offering a fully automatic tablet testing system that addresses precisely this problem: maximum flexibility via reliable positioning of convex tablet shapes of all kinds. The device combines two patented orientation systems, which can be used flexibly and fully automated without any mechanical changeover, depending on the tablet shape.

AutoAlign™
Two counter-rotating rollers reliably bring convex tablets into the required position for measurement. In addition to the breaking force ("hardness"), the width and length of oblongs and oval tablets can also be determined with high precision. Special formats such as diamond and almond-shaped are possible with AutoAlign™ without tablet-specific parts.

SmartAlign™
By means of a flat platform with a programmable angle of inclination, not only conventional flat tablets but also special shapes such as hexagonal tablets, cylinders or spherically shaped test specimens can be aligned automatically and with high repeat accuracy.

Figure 3:
AutoAlign™ – Alignment with counter-rotating rollers ("Roller")

Figure 4:
SmartAlign™ – Alignment with inclined plane and programmable angle of inclination ("flap")

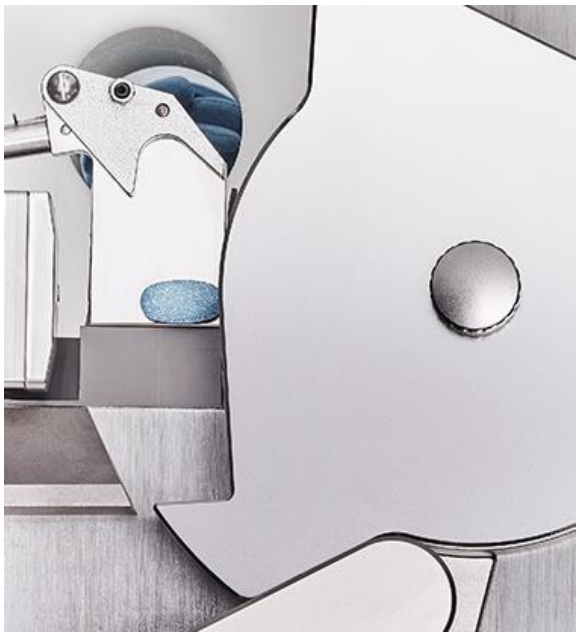

Figure 5:
Fast cycle times and short transport distances between the integrated measuring stations. Easy to clean with dust and water protected test area (IP52 or IP65).

A universal conveyor system ensures that convex test specimen shapes are always on their curved side even before positioning in the measuring station – and do not roll onto the tablet web as a result. The height measurement ("tablet thickness"), which is important for readjusting the tablet press, has also been optimised for maximum precision. A sensor integrated into the measuring foot prevents tablets from small plastic deformation during the test process or sticking to the foot of the thickness gauge caused by excessive contact pressure. Thanks to state-of-the-art measuring and sensor technology with polarised magnetic strips for linear dimensional measurement, vibration-resistant integrated precision weighing module and robust Dr. Schleuniger® breaking force technology, the AT50 sets new standards in measuring accuracy in the fully automatic quality control of five physical parameters.

An often-underestimated problem is the comparability of results, especially in the destructive breaking force measurement ("tablet hardness"). According to the Global Pharmacopeia (USP, Ph.Eur, as well as other harmonised pharmacopoeias) two different measuring principles (constant speed up to max. 3.5mm/s or linear force increase up to max. 20N/s) may be used to determine the tablet hardness. Comparability of the measurement results is only guaranteed if the test is performed under identical conditions – i.e. with the same measuring principle. This is complicated by the fact that for both measuring principles, only the maximum permissible speed is standardised. This implies that in the range below the maximum, any measuring speed is possible. In practice, this often leads to confusion when making hardness comparisons across departments and locations. Although results can be correlated product-specifically within the scope of complex studies, with any set-point violations, or out-of-spec (OOS) investigations, there is always an amount of uncertainty as to whether the product was produced incorrectly – or whether "only" the hardness testers used for quality control were operated with different measurement settings. Complicating the matter is the fact that the measuring principle is often not specified in test results, product specifications and work instructions.It may be surprising that different measuring principles and speeds can lead to significantly different breaking force results. Many of today's available hardness testers have an adjustable measuring principle – however, especially in older devices, the machines lack the corresponding documentation in the test results, the possibility to store the measuring principle for different products individually, or password protection to avoid an erroneous change of settings by the operator. In on-line in-process control, the problem regarding the measuring principle is different: until the introduction of the AT50, there was simply no automatic device on the market that would have made it possible to change the measuring principle. Comparability of the results from on-line in-process control with results in the quality control laboratory is therefore only possible if the corresponding laboratory instrument is operated with the settings of the on-line test system. However, as the product specifications are usually established using smaller laboratory equipment in Research & Development (R&D), this would require a change to the approved product specification and

Figure 6:
The universal circular conveyor of the AT50 separates everything – very small as well as large test specimen shapes. Fast and reliable. Tablet fragments or double tablets are automatically discharged from the further measuring cycle directly at the weighing station

Figure 7:
Oblong tablet positioned under the thickness gauge on the convex side

thus considerable administrative effort. Therefore, it generally remains the case that the data collected with in-process control are only partially comparable with the values obtained in quality control.

Conclusion

Increasingly complex tablet shapes and higher quality demands combined with steadily rising cost pressure require new automation solutions for quality control in laboratories and production. Increased efficiency can be achieved not only through short cycle times and low personnel costs. Reliably accurate test results, complete product specifications, and standardisation of the measuring principle for comparable measurements offer one thing above all: Reliability. In terms of measured results, but also in terms of the investment made.

Figure 8:
AT50 tablet testing system in the laboratory and during production

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