When to use dimensional tablet sorters

Dimensional sorters are useful for removing off-weight tablets, but they should only be used as defined by an SOP, not as a means of quality assurance.

My first encounter with overweight (superpotent) tablets was in 1994, when a manufacturer sought my help after the FDA found some in a retained sample. Since that time, I've encountered over- and underweight (subpotent) tablets many times, none of which left the plant. But in early 2008, nearly 100 recalls stemming from off-weight tablets were reported in North America, and four companies reported “near misses” [1-5]. As a result, some manufacturers have opted to use dimensional sorters to identity off-weight tablets. Is that acceptable practice? It depends.

Weight matters

Weight defects originate on the tablet press. They do not indicate a formulation problem, since the same formulation usually results in on-spec tablets. Overweight tablets—far more common than underweight tablets—can pose a danger to patients because they contain too much active pharmaceutical ingredient (API). And most overweight tablets are between 130 percent and 210 percent of the target weight. Underweight tablets vary more narrowly, but regardless of whether the tablets have too much or too little API, the risk to patients can be serious, as noted in an FDA warning letter that also cited the company’s use of a dimensional sorter [6]:

Your Quality Assurance “Hold” documents for the lots noted that lots were sorted in a thickness sorter in an effort to eliminate aberrant tablets as a corrective action. However, your firm did not document the number of aberrant tablets that were rejected during sorting or any examination of other batches that may have been impacted. In addition, your firm did not evaluate the state of control of the process, including whether

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A gravimetric method (checkweighing) is the most accurate means of determining tablet weight, but many manufacturers opt for dimensional sorting, also called thickness sorting, because tablet checkweighers are slow and relatively expensive. Dimensional sorting—a technology used in many industries to separate parts by size difference—was first used in the pharmaceutical industry to eliminate foreign tablets (those with a different size or shape). Now the primary pharmaceutical application is separating underweight (thin) tablets and overweight (thick) tablets from those of the right size (on-spec), examples of which are shown above. The machines use either rollers that form channels (photo) or a rotating disc with machined slots.
Most tablet presses include systems that can control and/or monitor weight and thickness and can adjust the settings to ensure tablets meet their specifications. The systems can also identify, isolate, and reject off-spec tablets. But sometimes the system either misidentifies the tablet or isolates the wrong one. For this and other reasons, some manufacturers continue to rely on sorters to ensure they’ve made good tablets. They claim that dimensional sorting is equivalent to the automatic sorting method used with hard gelatin capsules, which removes empty and partially filled capsules based on weight. While I have no knowledge of the FDA ever objecting to the use of those systems to sort capsules, the differences between tablets and capsules raise some questions.

First, generally speaking, and assuming a nominal amount of API in the blend, there is much less risk of overfilled capsules than there is of overweight tablets. Second, there are fewer hard shell capsule products that contain APIs with a narrow therapeutic index [7]. Third, the FDA is likely to question manufacturers that rely on sorting to ensure quality, as the following excerpt from a 2010 warning letter indicates [8]:

> For example, it appears that as part of your batch release criteria you rely on a practice of sorting and rejecting tablets with quality defects as a quality control measure. It is our expectation that firms take a systematic approach to correcting and complying with CGMP to ensure the identity, strength, quality, and purity of their drug products.

In other words, sorting is seen as an attempt at “inspecting in” quality rather than adding a layer of protection.

**Roll sorter operation**

It’s important to recognize the limitations of dimensional sorters. No mechanical sorter can detect and remove foreign tablets based on color differences or foreign tablets that are the same size and shape as good product. Furthermore, in cases where a tablet’s thickness and its minor axis are the same or nearly so, some roll sorters will fail to distinguish between the two. Some machines are also mechanically complex and may require frequent maintenance and/or calibration. Critical operational features of roll sorters include:

- **Slide gate position.** The slide gate controls the flow of tablets from the feed hopper to the feeding track, and the tablets should reach the rollers in a controlled manner and without disruption.

- **Vibration amplitude.** Vibratory feeding provides more precise control than a slide gate. Excessive vibration, however, will cause the tablets to jump as they reach the rollers, possibly allowing unacceptable tablets to pass as acceptable.

- **Plastic tablet guide position.** Some machines use guides on the feeding track to divert tablets across the rollers (photo). Proper setup requires some trial and error.

- **Roller speed.** How fast the rollers turn determines how fast the tablets move over the rollers. Most machines allow you to adjust roller speed, but some don’t.

Whatever the setting, either a timing belt or a series of gears ensures that all rollers turn at the same speed.

**Roller gap.** The size of the gap between the rollers changes along their length: narrow at first, on-spec at the midpoint, and wide at the end (Figure 1).

![Roll sorter operation](https://via.placeholder.com/150)

**Figure 1**

Progressive gap between rollers for separating thin (underweight), standard (on-spec), and thick (overweight) tablets

![Progressive gap between rollers](https://via.placeholder.com/150)

**Standardizing the setup**

GMP requires that you calibrate and verify the accept/reject methods of your process [9]. Some dimensional sorters have a computer-assisted setup feature that
recalls and implements the thickness parameters for different tablet products. These parameters, however, are not independently verified, so be careful. In fact, the references may be dimensionless numbers that relate only to the machine, not to the tablet’s actual thickness specification. And the computer can’t detect or report part wear that can cause the settings to drift.

Another potential source of variation is using tablets taken from a good batch to establish the roller settings for another batch. That’s a bad idea because the tablets can wear and change thickness. They’re also likely to become lost in the batch, and you’ll spend all day trying to find them; when you can’t, regulators will presume they never existed.

Instead, use a caliper (photo) or standard tablets machined from brass or stainless steel. I prefer brass standards because they remain precise and don’t jump much on the rollers. Avoid using plastic or aluminum tablets, which tend to jump during sorting.

 sorting and GMP compliance

Sorting every batch of every product is not the solution, as the FDA made clear in the warning letter cited above. Thus, if you have a sorter and plan to use it, establish a standard operating procedure (SOP) that defines when to use it:

• As part of the operational qualification of a tablet press
• During initial product validation (three batches)
• When there is cause to suspect that the tablet press’ reject gate has failed
• As part of an investigation when absolute product quality is in doubt
• Occasionally to verify tablet press performance
• Every X number of months on a random batch of each size and shape of each product
• As a means to verify a process improvement to the tablet press [10].

Conclusion

Off-weight tablets are a genuine problem, and dimensional tablet sorters can help when used correctly. While the FDA has not addressed dimensional sorting recently, that could change if the practice becomes standard, as I’ve observed in India. To avoid problems with the FDA, establish an SOP for tablet press startup and the handling of rejected tablets. And train your staff to challenge the tablet compression process. If you’re sorting every tablet produced, inspectors can only conclude that your process is out of compliance with GMP.

References

1. Rowley, F.A. “Why overweight tablets are not going away.” Presentation at ISPE Facilities Conference: Learning from 483s, Tampa, FL. February 2012.
4. FDA Enforcement Reports. www.fda.gov/Safety/Recalls/EnforcementReports/

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