FITZPATRICK®

API Mills

INNOVATION IN PARTICLE PROCESSING TECHNOLOGY

The Fitzpatrick FitzMill™ and Its Role In Sizing Active Pharmaceutical Ingredients

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Pharmaceutical Formulators aim to match the particle size distribution of an API to that of the other ingredients in the OSD formulation. To address this need, bulk API manufacturers sometimes employ several styles of mills to achieve the desired range of particle size distribution. While this means the bulk API producer can add value and probably sell the API for more, in a lot of cases this extra processing costs time and investment as a result of all the different mills involved.

In some cases, the bulk API is only available "as is", as it comes from the last phase of manufacturing. In this instance, the particle size distribution (PSD) of the bulk commodity sold to the end user is not typically within the range needed to be blended or compounded into the final dose form. The final size reduction is performed by the OSD manufacturer to ensure a specific distribution profile is met that meets their individual processing program.

This White Paper identifies the reasons why the FitzMill Hammer Mill has become a popular choice within the industry for API milling.

HISTORICAL PERSPECTIVE

The original FitzMill was developed in the 1930's in response to the need for milling a variety of food substances ranging from dried potatoes and fruit, to herbs and spices. To accommodate early industry standards, a sanitary mill was developed to mill to a broad range of PSDs.

At the time, the cornerstone of the FitzMill technology was a pan-fed, multi-speed drive with a reversible bladed rotor assembly (Figure 1). The clever blade design remains as a cornerstone of the FitzMill's technology today, offering two distinct milling profiles (Figure 2) - one side is a knife edge while the other side has a blunt impact edge.

Figure 1: Traditional DASO6 FitzMill™ With Hand-Fed Pan

Knife/Knife Impact/Knife Impact/Impact

Figure 2: Typical FitzMill™ Rotor Blade Configurations

VERSATILITY

The pharmaceutical industry took note of the success of the FitzMill in food applications, and readily adapted the technology to address their own needs. As APIs became more complex and required improved PSDs, these pharmaceutical companies turned to the FitzMill as one of the most viable methods to not only mill APIs in a sanitary manner, but to be able to achieve a specific PSD target.

Over the decades, advances and refinements to the original FitzMill concept have primarily been driven by the adoption of the FitzMill as a size reduction mainstay of the pharmaceutical industry. Some of these technological breakthroughs include:

- Increase in the range of particle fineness through enhanced blade speed range and development of internal breaker plates.
- Development of application-specific tooling (i.e. blades and screens).
- The ability to delicately handle heat-sensitive materials using water jackets and/or throats that change the feed entry points.

Figure 4: PCS (Product Containment System)

Figure 3: Contained D6A FitzMill With Integrated Dosing Valves

- Automatic dosing systems in the form of integrated variable feed screw assemblies or contained valve-to-valve configurations (Figure 3).

API Mills

Today, FitzMills are readily employed within the pharmaceutical industry; in part due to Fitzpatrick's response to increased pharma industry regulations with enhanced designs and safety features including:

- Explosion protection and mitigation through nitrogen inerting and monitoring.
- Patented powder containment systems (PCS) for high efficacy/potency pharmaceutical materials (Figure 4).
- Electronic variable speed drive systems.
- Unique segmented milling chamber for 100% cleaning access.
- Complete validation documentation and validation assistance.
- One piece sanitary rotor designs (Figure 5).
- Advanced instrumentation, process controls, and data logging-archiving.

Figure 5: cGMP One-Piece Reversible Rotor. Knife or Blunt Rotor Configurations For Either "In Air" "Cutting" or "Impact" Milling.

FLEXIBILITY

With the introduction of the SLS-Scalable Lab System™ came the ability to alternate between multiple powder processing solutions in seconds within the R&D lab. The SLS utilizes *Smart-Detect™* technology, a unique feature that automatically ensures the appropriate scalable speed range is fixed by recognizing the head being installed. The PSD and capacity measures are completely scalable, and simple operating parameters are easily transferred from the small sample R&D tests to the full-scale production machines (figure 6).

Manufacturers will look for specific PSD values at D90, D50 and D10 percentiles. D90 is the relative indicator of "top size". D50 is the median particle size, whereas D10 is an indication of the amount of fines in the composite particle size distribution.

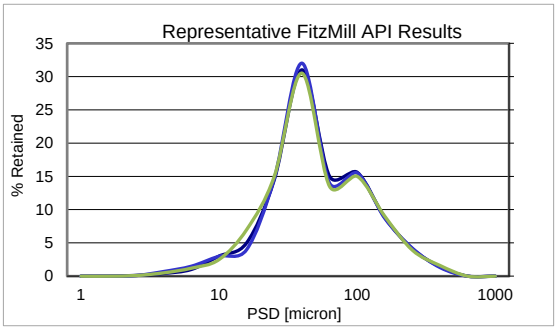

Figure 6: FitzMill™ PSDs Scalability From Lab To Production

To reduce capital investment, both bulk API and OSD manufacturers aim to limit the need for different milling systems. In response to this, the FitzMill was designed from the beginning to cover a broad range of fineness and PSD requirements. Dependent upon the mill set-up and the product's characteristics, it is possible to achieve typical API particle size targets between a D90 of 80 microns for friable/crystalline products, to a D90 of 300 microns for harder/pliable materials. The versatility is attributed to:

- *Rotor Speed*: Allows PSDs to shift from fine to coarse.
- *Knife Edge Blade Type*: Ideal for coarse grinds (typically with a D90 between 0.08 to 3mm) while precluding the generation of excessive fines.
- *Blunt Edge Blade Type*: Typical for finer grinds and to maximize the surface area of milled product.
- *"Free Air" Milling*: The relationship between the spinning blade tips and the distance to the mill's internal surfaces has a prominent effect on the amount of fines generated, thus impacting D10 results. However, if maximizing the D10 is desired, tolerances between the blades and surrounding surfaces can be adjusted by adding an additional plate or "boundary", thus increasing milling efficacy and consequentially creating more particle surface area.
- *Screen Aperture Size and Open Area (OA):* PSD top size D90 is primarily controlled with the mill's retaining screen. The aperture size and open area affects the residence time of the particles inside the milling chamber or so-called "action zone". Comparing two matched aperture screens with higher and lower open areas, shows the screen with the higher OA rating produces a higher capacity, lower milling temperature and fewer fines at D90. The lower OA screen produces a wider PSD curve (more fines) and increased powder surface area.

RELIABILITY

The versatility and flexibility of the Fitzpatrick FitzMill has made it the primary size reduction technology for APIs. Utilized universally throughout the pharmaceutical industry, it is used for milling a range of other "difficult –to-mill" pharmaceutical powders.

About the Author

With over 35 years' working with powder processing equipment and integrated processing systems, Jim Ruschmann has experience in size reduction, classification, roll compaction, mixing, blending and sifting. Jim's current tenure as a Field Application Engineer continues his commitment to end-to-end customer support. He is a graduate of The College of New Jersey and holds a BS degree in Industrial Engineering Technology.