

# **Spiral Jet Mill Systems Equipment Design and Applications**



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# FPS Food and Pharma Systems Organization

## Head Quarter (Como - Italy)

- Administration
- Marketing
- Sales



## Engineering Plant - Italy

- Activities:
  - Project and Design
  - Manufacturing and Assembly
  - R&D Centre and QA Dept.
- 5000m<sup>2</sup> surface
- 30 people



## Worldwide agent network

- In Korea: Sanitary Equipment Korea



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## **FPS Food and Pharma Systems Working “style”**

### **Each situation has its own solution**

We do not propose pre-defined solutions but solutions which correspond to end user needs

### **We always try to understand and know the needs, the history and the experience of our customers**

The starting point of a project is not our machine but our customer need around which we build our systems

### **We are open to new ideas and challenges**

We have a wide experience but we are learning something every day to improve our knowledge and face new challenges

## FPS Food and Pharma Systems Product Range

### Containment systems

- Isolators
  - Glove-boxes
  - Half-Suit isolators
- RABS
- LAF
- Down-Flow booths
- Pack-off systems
- Local Suction Arms



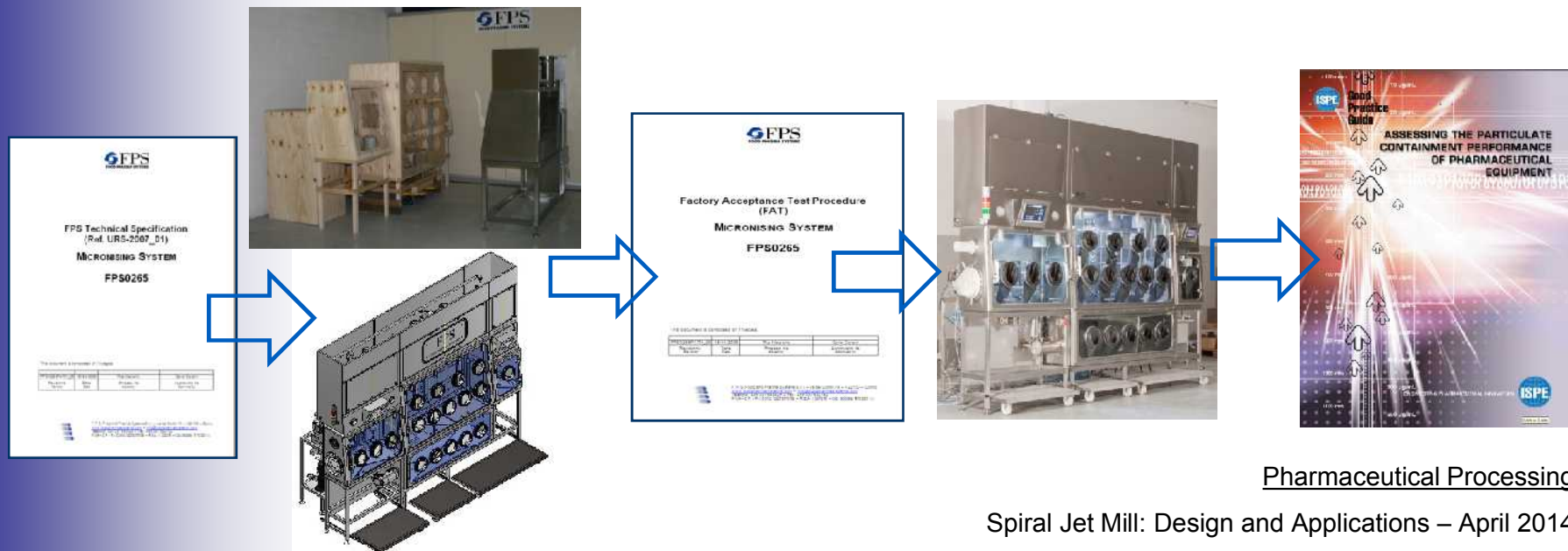
### Micronisation systems

- Jetmills
  - R&D units
  - Pilot units
  - Production units
- QMills
  - R&D QMill
  - Pilot QMill
  - Production Qmill
- PinMills



## FPS Food and Pharma Systems Project Activities

- On-site preliminary discussion
- Front-end design
- Detail engineering
- Manufacturing
- Document review
- FAT
- Transport & installation
- SAT
- Validation (IQ/OQ)
- Maintenance and operator training
- Lifetime assistance



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# **Spiral Jet Mill Systems Equipment Design and Applications**



## **Process Introduction**

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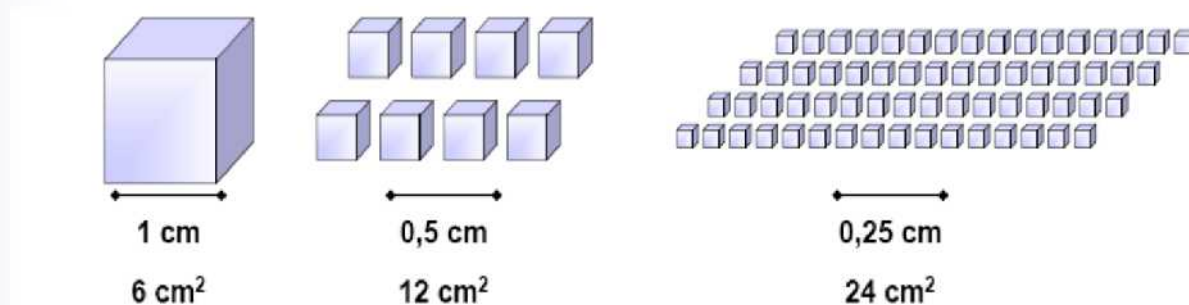
## Process Introduction

### Pharmaceutical need for size reduction

- ❑ Specific Surface increase
  - ✓ Pharmaceutical research is creating API with very limited solubility in water (<100µg/ml)
  
- ❑ Access to inhalation therapy
  - ✓ Reduced systemic toxicity
  - ✓ Quick availability of API
  - ✓ High concentration in lungs
  
- ❑ Acceleration of dissolution rate due to crystal structure change
  - ✓ Product amorphization
  
- ❑ Top-down particle size dimension control
  - ✓ Crystallization may be difficult for large/complex molecules

## Process Introduction Basic Notes

- ❑ Micronization is a high energy milling process
- ❑ Particle size reduction occurs without mechanical components intervention, but using a pressurized gas to impart high velocity to particles and determining high energy impact between particles.
- ❑ The micronization process allows to reduce the particle size of a substance in powder form down to micro-meter size ( $10^{-6}\text{m}$ ), highly increasing the exposed product surface.



## Process Introduction Pro/Cons Vs. Mechanical milling

With reference to spiral jet milling:

### Advantages

- No mechanical moving parts
  - no lubrication required
  - reduced metal contamination
- Easy components cleaning
  - reduction of X-contamination
- Temperature approx. constant
  - product characteristics preserv.
  - mill heat sensitive products
- Very fine particle dimensions obtained
  - D90 down to 3 $\mu$ m are possible

### Dis-Advantages

- Low productivity
  - e.g 20kg/h with large units
- Large equipment size
  - large foot print
  - large installation rooms
- High process gas flow
  - safety when using nitrogen
  - expensive
- PSD shape
  - no sharp cut above a given size

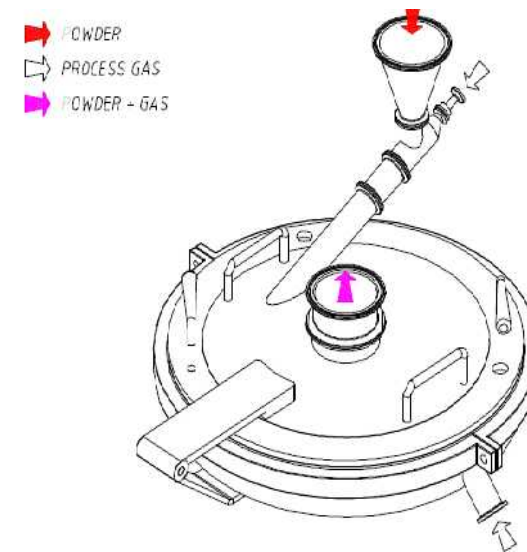
## Process Introduction Still poorly known...

Micronization process is often still considered as a **black box**:

- coarse particles enter the system
- fine powder exit the system

By adjusting the grinding pressure and the product feed rate into the system it is possible to get desired result, without much knowledge of the process.

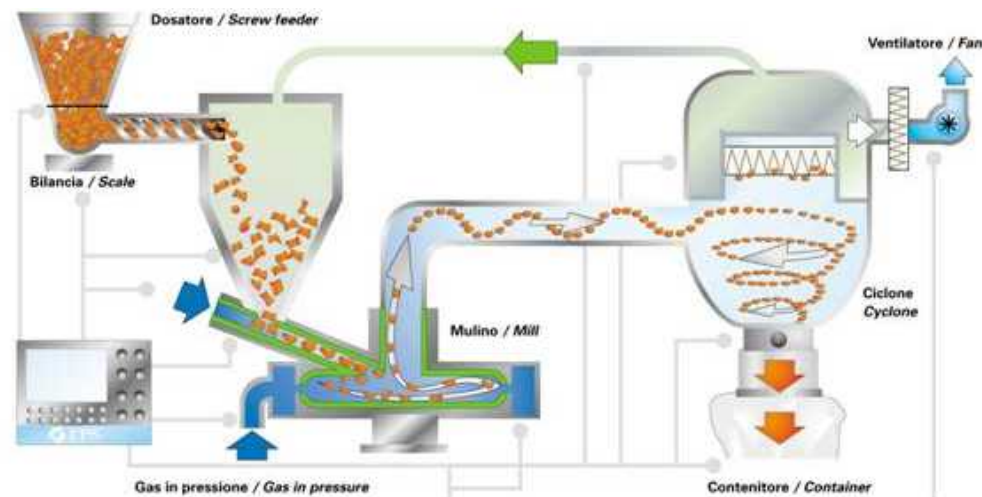
New molecules development, a better process control (PSD, amorphous content, specific surface value) and the requests from pharmaceutical authorities ask for a different process approach.



## Process Introduction FPS approach

The spiral jet milling process is not governed only by the jet mill itself. It is a process involving different machines and components which need to be properly integrated and controlled.

A strong empirical base is still used in jet milling operations.

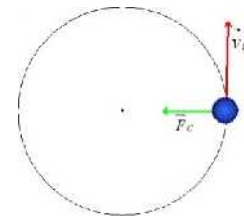


## Process Introduction Scientific bases

A particle inside the jet mill chamber is subject to two opposite forces:

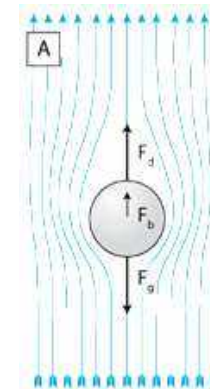
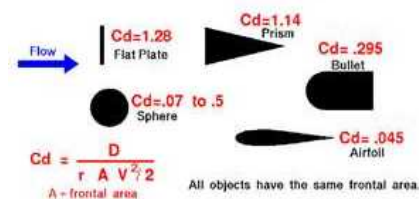
□ the centrifugal force, which depends on:

- ✓ the density of the particle
- ✓ the size of the particle
- ✓ the distance from the jet mill centre
- ✓ the tangential speed of the particle



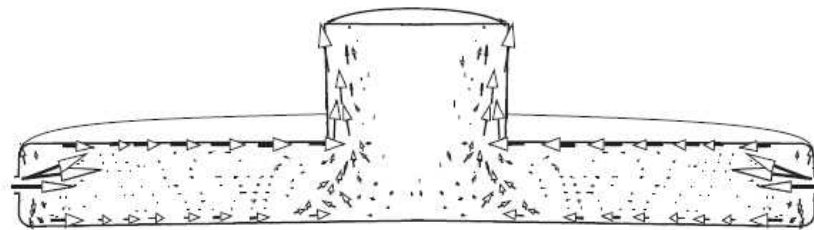
□ the drag force, due to the process gas flowing in the jet mill chamber, which (in a very simplified way) depends on:

- ✓ the size of the particle
- ✓ the radial speed of the flowing gas
- ✓ the aerodynamic coefficient
  - ✓  $C_D$  as per Stoke's law is  $8/Re$
- ✓ The density of the gas

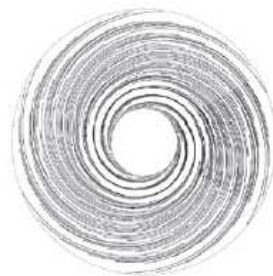


## Process Introduction Scientific bases

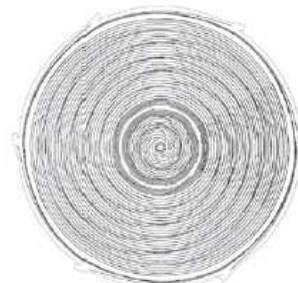
□ formula  $d_{cut} = 12 \sqrt{\frac{\mu r}{n_r \rho_p} \frac{v_r^2}{v_t^2} \left[ \frac{1}{\sqrt{\phi_p}} + 2/\sqrt{\phi} \right]}$



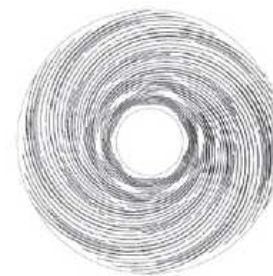
(a) Radial components of air flow in jet mill



(b) Streamline near upper wall



(c) Streamline at center of height



(d) Streamline near bottom wall



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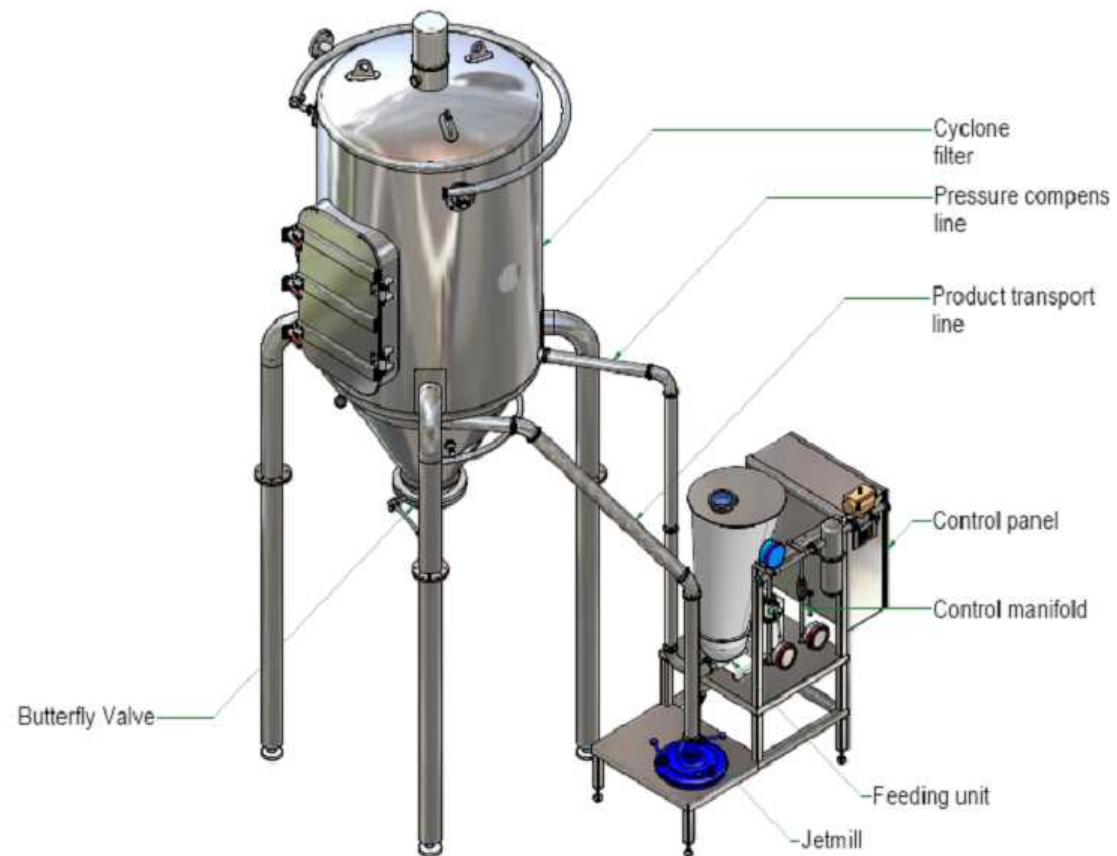


## **Key Components**

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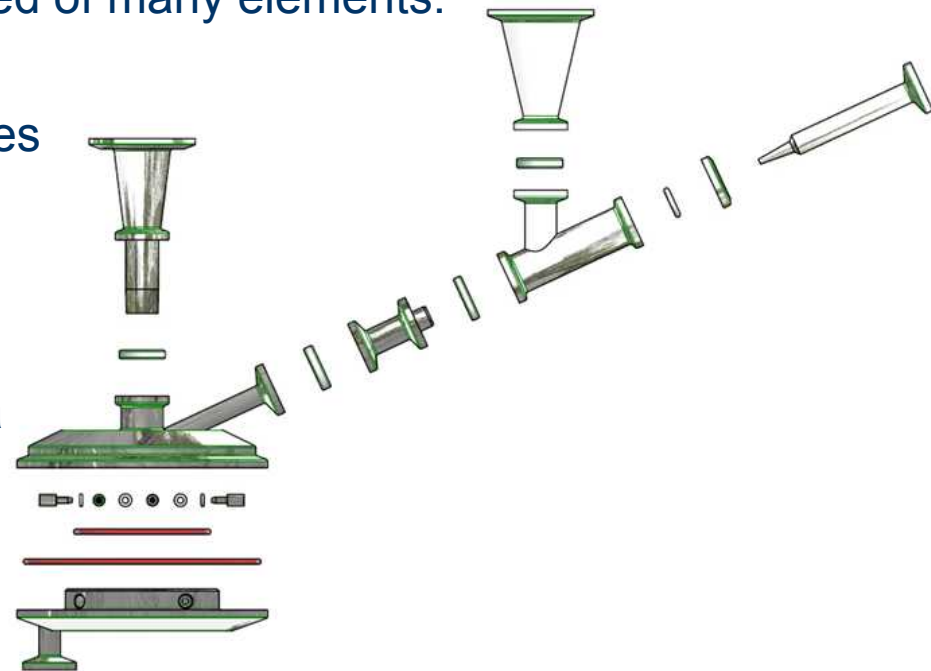
## Spiral Jet Mill System Key Components



## Key components The Jet Mill

The jet mill is composed of many elements:

- the expansion nozzles
- the classifier
- the top plate
- the bottom plate
- the pressurized area
- the injection line
- the Venturi nozzles



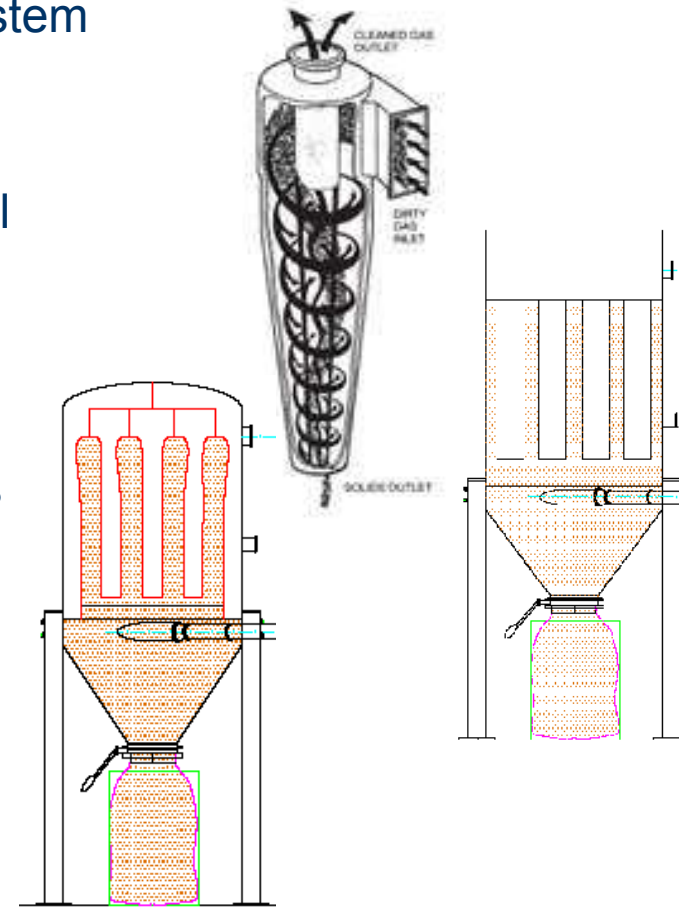
Exploded view of Pilot-size jet mill ¶



## Key components The separation cyclone

Different gas-solid separation system may be considered:

- Bottom discharge for the jet mill
- Separation cyclone
- Cyclone with filtering cartridges
- Cyclone with filter sleeve





# Spiral Jet Mill Systems Equipment Design and Applications



## Process Parameters

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## Process Parameters

### Chemical-physical characteristics of product

The powder to process is an important parameter. In many cases, two batches of the same product (same chemistry) obtained in different ways (different synthesis steps, different drying, mechanical milling, ...) have different behaviour during the micronization.

The typical product characteristics which may affect the process are:

- ✓ Humidity
- ✓ PSD
- ✓ Density
- ✓ Impurities

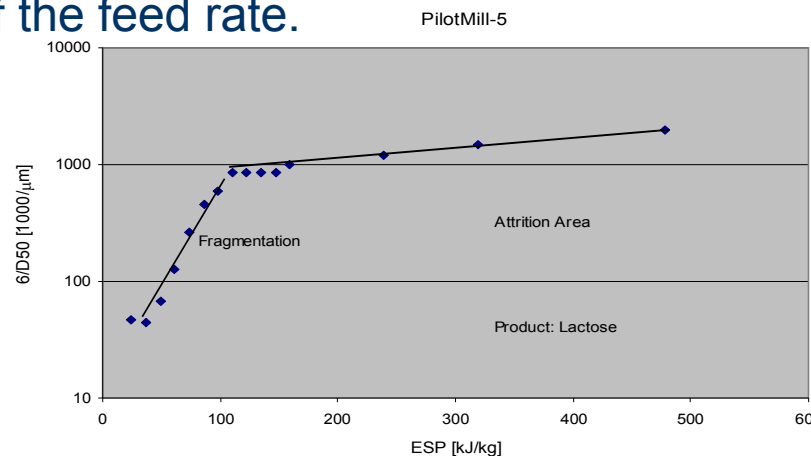
We can not change this situation. It is a process constraint and we have to keep it as it is. Anyway it is important to consider that the chemical history of the product may have an impact in the micronization result.



## Process Parameters Specific Energy

The energy given to the particles is one of the main parameter of this process.

The specific energy is proportional to the grinding pressure and to the ratio of the feed rate.



Their effect on the micronisation process is:

- At a fixed feed rate, the higher the pressure at the expansion nozzles is, the finer will be the product after the micronisation process
- At a given pressure, the higher the solid feed rate is, the coarser will be the product after the micronisation process

## Process Parameters Temperature

Micronization process is considered at constant temperature; in fact:

- + heat generation, due to particle-to-particle collisions
- heat absorption, due to gas expansion

The portions of the particles which are involved in each collision experience a temperature increase.

Temperature control allows to:

- make the material more brittle, allowing easier breaking and slimmer PSD
- process plastic type products
- reduction of amorphous content -> increased stability



## Geometrical Parameters Expansion Nozzles Geometry

The expansion nozzles are the elements bringing energy to the system. Throat section and geometry define the energy input. Can be:

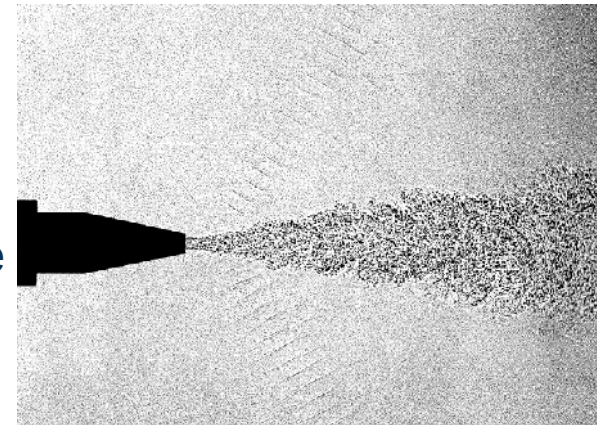
- straight
- convergent
- convergent-divergent

Also important is the way the nozzles are manufactured:

- Drilled directly in the nozzles ring.
- Separate nozzles, without O-ring.
- Separate nozzles, with O-ring.

Nozzles angle is also important:

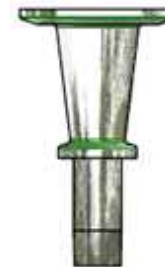
- too large: collisions against the jet mill walls
- too small: small grinding spiral with shortcuts



## Geometrical Parameters Classifier

The position and geometry of the classifier are important parameters directly affecting the PSD:

- Diameter
- Penetration of the classifier





# Spiral Jet Mill Systems Equipment Design and Applications



## FPS Innovations

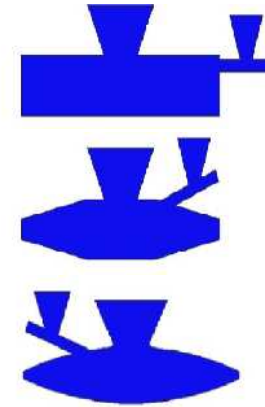
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## Innovations in API micronization Jet mills chamber shape

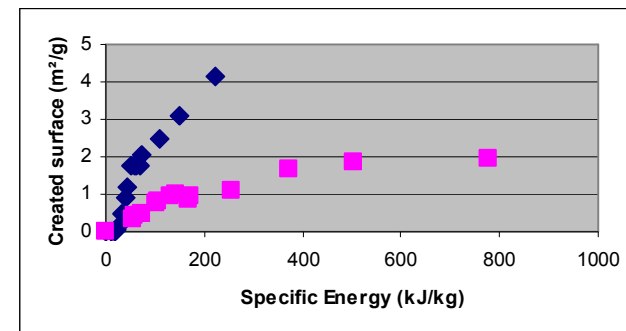
Historical development of jet mill chamber shape:

- Rectangular section
- Octagonal section ('70s)
- Elliptical section (FPS - 2003)



The final advantages obtained for an elliptical shape are:

- reduced process gas consumption
- higher productivity
- less product caking



## Innovations in API micronization “Fail-safe” pressurized chamber

A widely recognized problem on production jet mill is the tightness of O-rings in the pressurized chamber.

FPS new design for production units considers:

- easier access to milling chamber
- tightness of pressurized chamber independent of upper plate
- connections with quick release clamps for easy cleaning



## Innovations in API micronization Temperature control

The temperature control during the micronization allows to process plastic type products.

Temperature control is obtained by:

- cooling of process gas:
  - By liquid N<sub>2</sub> injection
  - Via cryogenic exchanger
- cooling of products before entering the system

Temperatures as low as  $-130^{\circ}\text{C}$  can be obtained in continuous mode.

Safety aspect have to be properly assessed.



## Innovations in API micronization R&D jet mills

### PilotMill-Zero

Worldwide smallest jet mill for early R&D

- Verification of possibility to micronize the molecule at an early stage
- Batch size: 10mg-200mg
- Tested product recovery higher than 75%



### LaboMill

Adopted for development phases

- Batch size: 200mg-100g
- Tested product recovery >85%
- Configuration with liners (AISI316L/Ceramic/PTFE)
- Feeding possibility
- Bottom or top discharge



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## Innovations in API micronization High potent drugs processing

Dust exposure is always a risk when operating a jet mill.

Exposure control is obtained by:

- Isolating the process
  - pressure compensation line
    - ✓ Reduced noise
    - ✓ Separated from installation room
  - protecting charge point
    - ✓ Feeder hopper lid
    - ✓ Pneumatic transfer system
    - ✓ Split valve
  - protecting discharge point
    - ✓ Pack-off booth
    - ✓ Continuous liner



## Innovations in API micronization High potent drugs processing

Dust exposure is always a risk when operating a jet mill.

Exposure control is obtained by:

- Enclosing inside a barrier isolator
  - Gloves or half suits
  - Containment level to  $<0.1\mu\text{g}/\text{m}^3$
  - Best integration
  - Sterile processing



## Innovations in API micronization Sterile processing

Sterile micronization is desired to avoid terminal sterilization

Sterile systems have different configurations:

- installation in sterile areas:
  - SIP with steam for production equipment
  - Sterilization in autoclave, for pilot/lab units
- enclosing inside an isolator
  - VHP sterilization for isolator
  - Steam sterilization for jet mill or autoclave and sterile transfer



## Innovations in API micronization R&D test centre

FPS company has its own test laboratory where it is possible to execute technical tests for micronization optimization according specific needs.

The lab is complete with:

- jet mills, spiral and QMill:
  - R&D
  - Pilot
  - Production
- Nitrogen as process gas
- Many geometrical configurations for jet mills
- Temp. control down to  $-100^{\circ}\text{C}$
- PSD instruments:
  - Microscope
  - Laser analyzer





## Final Notes and References

FPS has set up a small library collecting articles and documents specific on micronization.

In the preceding pages we made reference to:

- Images obtained from FPS archives or internet
- Van Dyke – An album of fluid motion
- Development of a spiral flow jet mill with improved classification performance – Kosumi Kozawa et al. – Advanced Powder Technology 23 (2012) 601-606
- Aerodynamic classification in a spiral jet mill – Viktor Rodnianski – Powder Technology 243 (2103)

If you are interested, we can share our bibliography as regards specific subjects: let's stay in contact.

## Thank you for your attention!



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