

**PHYSICAL FORM:****TECHNOLOGY TYPE:****1. What is Micronize?**

'Micronize' involves fracturing a coarse, poorly soluble drug using conventional milling techniques such as air-jet milling to produce fine crystalline particles. Micronized powders show a more uniform particle size distribution and, due to their smaller particle size, the dissolution rate is higher compared to unmilled drug. Typically, Micronize can reduce the mean particle size down to between 2µm and 5 µm.

**2. Which administration route is our Micronize technology suitable for?**

Micronized poorly soluble compounds can be used for oral, intramuscular, topical and pulmonary administration.

**3. Which types of compound are suited to Micronize?**

Poorly soluble drugs which are crystalline, fracture and do not change polymorphic form after micronization.

**4. How does Micronize increase bioavailability?**

If the drug is very permeable to intestinal membranes and the solubility is sufficient, dissolution rate determines the fraction of orally absorbed drug available at the absorption window at the particular time. Smaller particle size and increase in surface area encourage the drug to dissolve faster (enhance dissolution) compared to coarse and unmilled drug.

The poorly soluble drug slowly dissolves at the injection site. Therefore, the intramuscular route may result in slow release of the drug from the injected site.

**5. Which Phares services use the Micronize technology?**

If sufficient drug substance (gram quantities) is available, micronized powders can be fruitfully explored in Survey. However, this approach is not suitable for a very early stage compound if only 100 mgs are available. Micronized particles of poorly soluble drugs may be suitable for later stages of pre-clinical development if the bioavailability is found to be sufficient. If the oral bioavailability is sufficiently high, the powders can be used during Speed tox service. However, the particle size and crystal form of the insoluble drug must be characterized and amenable to control.

During Icebreaker formulation development, the technical development of aqueous suspensions of crystalline drugs with long term stability may be challenging because of crystal growth.

## **6. The advantages and disadvantages of Micronize**

### **Advantages**

- Standard technology to obtain fine powders with uniform particle size distribution
- The drug can be maintained in a physically stable crystalline form by using excipients
- Suppliers of micronising equipment and facilities for preparing micronised powders are available for highly potent and cytotoxic compounds

### **Disadvantages**

- The bioavailability improvement by increasing dissolution rate is often limited. It is generally more useful as a control rather than a bioavailability enhancing technique
- Producing sterile micronised suspensions can be particularly demanding. Sterile drug suspensions may require aseptic processing or separate end sterilization

## **7. Phares Micronize expertise**

Phares will assess the suitability of your poorly soluble drug by monitoring the micronised crystal form and its impact on dissolution. Because of somewhat less demanding processing requirements, Micronize is a useful first line approach for exploring bioavailability of a poorly soluble compound in man. Typically, the powders can be readily converted into a HGC or tablet formulation rapidly and more cost effectively.

## **8. Micronized product**

Two typical examples of micronized compounds are Progesterone 100 mg capsules (Prometrium®, Solvay) and Fenofibrate 160 mg and 54 mg tablets (Lofibra®, Teva).

**KEY SERVICES:**



**SPEED**  
*rapid solutions for tox testing*



**ICEBREAKER**  
*a clear path to the clinic*