Particle size at Hovione: How small do you want it?

Pharmacists are looking for Active Pharmaceutical Ingredients (APIs) where the particle size is well controlled, batch after batch. Particle size is a major factor in the bioavailability of a drug product.
Initially, the only method available to obtain small particles was controlled crystallization but the final result was somewhat difficult to predict. Fortunately other technologies have appeared which give pharmacists what they want: a particle size with a narrow distribution – and reproducible.

Jet milling
Of all equipments used in the manufacture of APIs, the micronizing jet mill is one of the simplest machines. It has no moving parts and it does not wear out, reducing particle size by impact. From the pharmacist's perspective, the process is safe and it does not introduce contaminants or change crystal form.
Jet milling can achieve a *desired* particle size distribution with an average diameter down to 5 µm.
Hovione has a range of micronizers suitable for almost all products, ranging from grams to hundred kilos, operating in clean-room facilities.

Particles for inhalation
In order to understand the needs of the pharmacist in an area of enormous potential – inhalation APIs – Hovione has developed a battery of tests, which extend well beyond the determination of the size distribution by laser diffraction and now include inhalation development pharmaceutics.

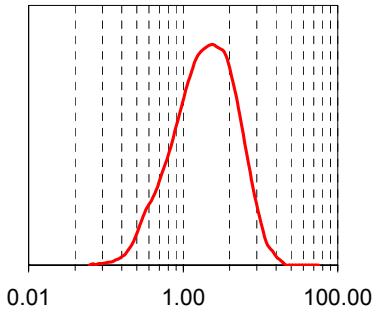

Fig.1.
Particle size distribution of a jet-milled corticosteroid by laser diffraction, d90 < 6 µm

In order to study how APIs perform in an inhaler, Hovione scientists formulate them as inhalation powders and test them using an impactor and determining the fine particle fraction.
This way, they can guarantee that the fine particle fraction, indicative of lung deposition, is always the same.

Spray Drying
In 2003, Hovione acquired an industrial spray drier from Niro A/S, capable of evaporating 35 to 90 kg of water per hour. It was an important step to design particles and control their size, mirrored at the lab scale by a Buchi unit, model B-290 with an inert loop B-295.
The advantages of spray drying are that one can go from solution to the desired particle size and the final particle can be either amorphous or crystalline, and discrete or agglomerated.

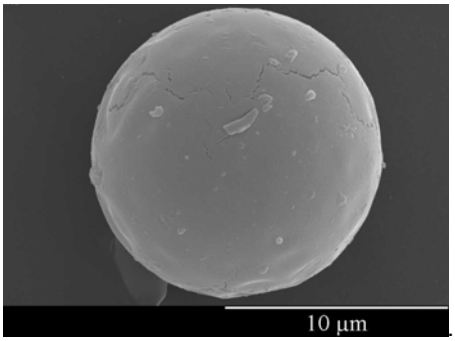

Figure 2. Spray-dried particle

By co-spray-drying different materials, it is possible to achieve micro-encapsulation, resulting in a particle which can be directly used in controlled release formulations.
Spray drying is possibly the one which shows the greatest potential now, largely due to its scaling-up capabilities, allowing the developed drug size to go from grams to tons and still obtain particles having the same size and morphology.

And in the future ?
Scalability is one of the differentiating factors between the various technologies that are presently available for reducing particle size.
Supercritical fluid crystallization is one technology where the final result is very attractive. Other processes are being investigated by Hovione. The challenges are simple: obtaining a material that has the desired particle size range and is physically and chemically stable.