We are always ready to give you expert advise in issues concerning particle characterisation. It might be questions regarding particle behaviour in relation to manufacturing – or it might be advise on necessary experiments to clarify stability.
Do not hesitate to send us an email at info@particle.dk and we will get back to you shortly.

Particle Analytical ApS
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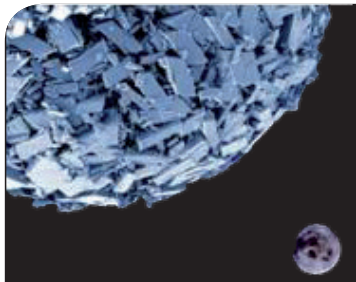
T: +45 4576 3060 - www.particle.dk



Particle Analytical ApS

Contract laboratory - GMP certified and FDA approved

Full solid state characterisation of particles
Method development and validation
Particle size and shape
Physical properties

About Particle Analytical ApS.

Particle Analytical is a contract laboratory performing full solid state analysis of particles. Our company values are based upon efficiency, quality and confidentiality, These are main reasons why leading API manufactures as well known international pharmaceutical companies choose us as their independent partner. Read much more at www.particle.dk

Particle Analytical support R&D, production and quality assurance. Our services can either be used in routine analysis, separately to solve specific problems, or in parallel to a larger drug development program. Furthermore we can take over the full responsibility of solid state characterization.

cGMP

We work according to cGMP within:

+ *Size*
+ *Morphology*
+ *Surface area*
+ *Crystallinity*
+ *Thermal analysis*
+ *Porosity*

We are certified by the Danish Medicine Agency as well as the FDA

Experts

We are experts in:

+ *Method development*
+ *Method validation*
+ *Routine analysis*
+ *Polymorph screening*
+ *Determination of crystallinity*

Time schedule

Routine analysis

+ *within 10 working days*
+ *3-5 working days*
+ *Next business day*

Inspection

You are welcome to do a free inspection when starting up a co-operation

Sample submission

When submitting samples, please provide:
Contact informations, type of analysis, deadline, storage conditions, MSDS, Invoicing details and VAT number

Access to result

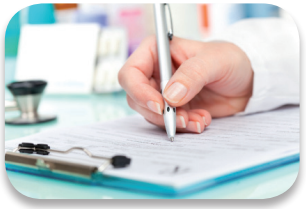
Regular mail, courier or email
Your own log-in to server for immediate access to results

What and why: Solid state characterisation

Particle Analytical ApS offers a full solid state characterisation of your compound

Solid state characterisation is an evaluation of a compound with regard to physical form, melting point, morphology etc. Solid state characterisation is indispensable in order to document that you have a comprehensive understanding of your API in regard to processing and bioavailability. Solid state characterisation is a requirement by authorities (ICH guidelines 6A, 8 & 9) as well as an important task in processing of the API.

At Particle Analytical we have all the needed equipment to characterise your compound. This includes a full package of instruments for particle characterisation with regard to size and shape, and instruments for determining the physical form with regard to relative stability. Particle Analytical ApS can support with routine analysis as well as more extensive development assignments.



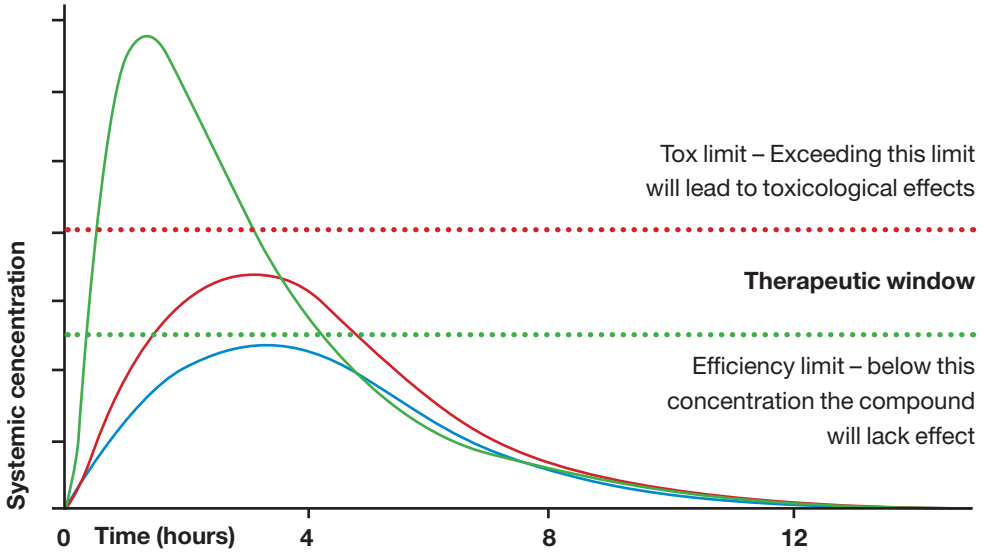


Figure 1: All compounds have a therapeutic window/concentration range that should be met in order to obtain effect. Decrease or increase in particle size might lead to either faster release (tox effects) or slower release (no effect). Also, change of physical form will change bioavailability towards either lower or higher exposure.

The primary risk

The primary risk of a patient in regard to a pharmaceutical compound is a change in release rate and/or composition of the product leading to a situation where the therapeutic level is either not reached - or exceeds far beyond the tox-limit. For all pharmaceutical compounds in development, authorities require a risk evaluation - a requirement based on a rational wish to improve patient safety. A **risk evaluation** demands measurement and specification of following parameters:

Particle size and/or shape: Changes in particle size is extremely important for poorly soluble compounds, as it has direct impact on the release rate.

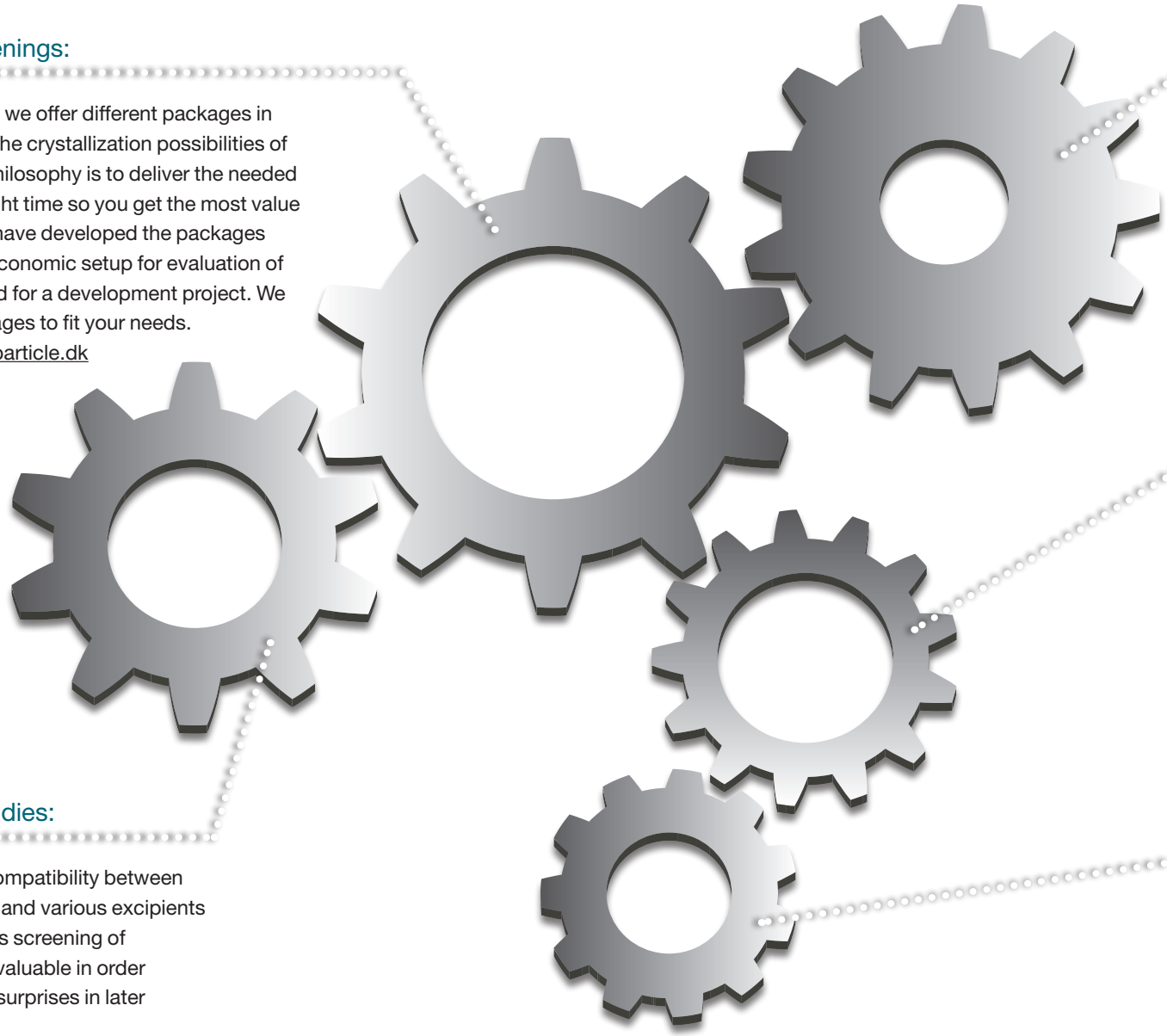
However, routine analysis of the compound is also essential to maintain stable processing, especially if a change in supplier or manufacturing equipment/ process occur.

Crystalline form: Almost all solid materials are capable of forming different crystalline structures, known as polymorphic forms. These polymorphic forms have different physicochemical properties that might have significant impact on the intended use, as for instance the release rate. Further, a sudden change of form would require a repetition of the full analysis program: Stability, dissolution, and compatibility as the new compound will have different properties.

Special services

Polymorph screenings:

At Particle Analytical we offer different packages in order to investigate the crystallization possibilities of your material. The philosophy is to deliver the needed information at the right time so you get the most value for your money. We have developed the packages to deliver the most economic setup for evaluation of polymorphs intended for a development project. We can adjust the packages to fit your needs.
Read more at www.particle.dk



Determination of % crystallinity:

The degree of crystallinity has high impact on the performance of the product.
At Particle Analytical we offer method development in order to quantify the crystallinity in various batches.

Method development:

A reliable method is needed in order to set specifications for particle sizes or to determine the content of, for instance, the degree of crystallinity of your product. At Particle Analytical we have extensive expertise in method development.

Compatibility studies:

Initial screening of compatibility between the active ingredient and various excipients in the solid state. This screening of excipients might be valuable in order to avoid unpleasant surprises in later development.

Determination of refractive index:

In order to make accurate particle size determination, especially of small particle sizes, it is necessary to know the refractive index of the compound. As one of the few companies in the world, Particle Analytical offers to determine the refractive index.

Fact Sheet: Following in-house equipment at your service

Particle size and shape

Instrument	Result	Use
Laser diffraction, Malvern wet and dry (Mastersizer 2000 and 3000)	Particle size distribution by volume e.g. $D_{10\%}D_{50\%}D_{90\%}$, in the range 0.02 to 3500 µm	Control of particles during manufacturing. Detection of batch to batch variations and agglomeration.
Optical Microscopy with digital image analysis	Morphology and particle size distribution	Insight into special characteristics of the particles (needles, plates etc.) Verification of laser diffraction results.
BET with N_2 including nanopores	Specific surface area m^2/g, volume and size distribution of nanopores	Especially relevant for high surface area items. Related to dissolution rate and thereby bioavailability.
Mercury porosimetry	Pore size distribution byvolume. Pore size in the range 3 nm to 360 µm	Useful in evaluation of product characteristics such as pores in tablet and granules. Moreover relevant for catalysts.
SEM (Scanning Electron Microscope)	Crystal shape, surface morphology and structure of particles. Size range is ~0,1 µm to a few mm	Insight into special characteristics of the particles (needles, plates etc.) Evaluation of product surface properties.
Particle Counting	Counting of particles by light obscuration. Particle size, number and size distribution in the range 2-125 µm.	For suspensions with a low content of particles - or if the total number of particles is of interest, e.g. injectables.
Photon Correlation Spectroscopy (PCS or DLS)	Particle sizes in the range 0.6 nm to 6 µm (nanoparticles)	Apparent sizes – including determination of agglomeration in solutions of proteins/ biomolecules.
Air permeability	Specific surface area on granules or micronised products	Evaluation of surface area accessible to water. Used in determination of coating surface. Related to dissolution rate and thereby bioavailability.
Helium pycnometry	Density, g/cm^3	Evaluation of behaviour during manufacturing
Bulk and tapped density	Ability to settle, Hausnerindex, cohesiveness	Evaluation of behaviour during manufacturing
Flowability with angle of repose	Ability to flow	Evaluation of behaviour during manufacturing

Fact Sheet: Following in-house equipment at your service

Physical properties

Instrument	Result	Use
X-ray Powder Diffraction (XRD)	X-ray diffraction pattern at angles between 3 and 40 ° 2Theta.	Crystal form and amorphous material. Determination of % crystallinity.
Thermogravimetric Analysis (TGA)	Weight loss upon heating. Measuring range RT to 1100 °C.	Identification of solvates and determination of solvent content.
Differential Scanning Calorimetry (DSC)	Detection of energetic changes during heating and cooling. Measuring range -65 to 700°C.	Determination of melting point, phase transitions, evaluation of relative stability etc.
Fourier Transform Infrared Spectroscopy (FTIR)	Infrared spectra at wavenumbers between 400 and 500 cm^{-1}	Identification of crystal forms. Detection of impurities. Quantification in mixtures.
Dynamic Vapor Sorption (DVS)	Sorption isotherm at relative humidities from 0 to 98%.Temperature range RT to 85°C.	Evaluation of hygroscopicity. Useful in setting specifications for storage conditions.
Hot Stage video	Microscope pictures upon heating. Temperature range RT-375°C.	Visual detection of thermal changes. Useful in polymorph screening.
Dissolution and IDR tester	Dissolution rates in aqueous solution. Temperatures 20-60 °C.	Evaluation of different crystal forms and particle characteristic with regard to dissolution behaviour. Useful in process control and in evaluation of bioavailability.
UV-VIS	UV spectrum of compound in solution. 200-800 nm.	Concentration measurements.
Karl Fischer	Water content determined from coulometric method.	Determination of water content in API or product.
pK_A titrator	pH measurement from titration of aqueous solution with acid/base.	Determination of pKA value. Useful in estimation of solubility at various pH values and for choosing relevant salts for salt formation.
Osmometry	Freezing point depression.	Determination of ”apparent concentration” and clustering in aqueous solution. For injectables and solutions with biological macromolecules.