# Malvern Spraytec

Laser diffraction

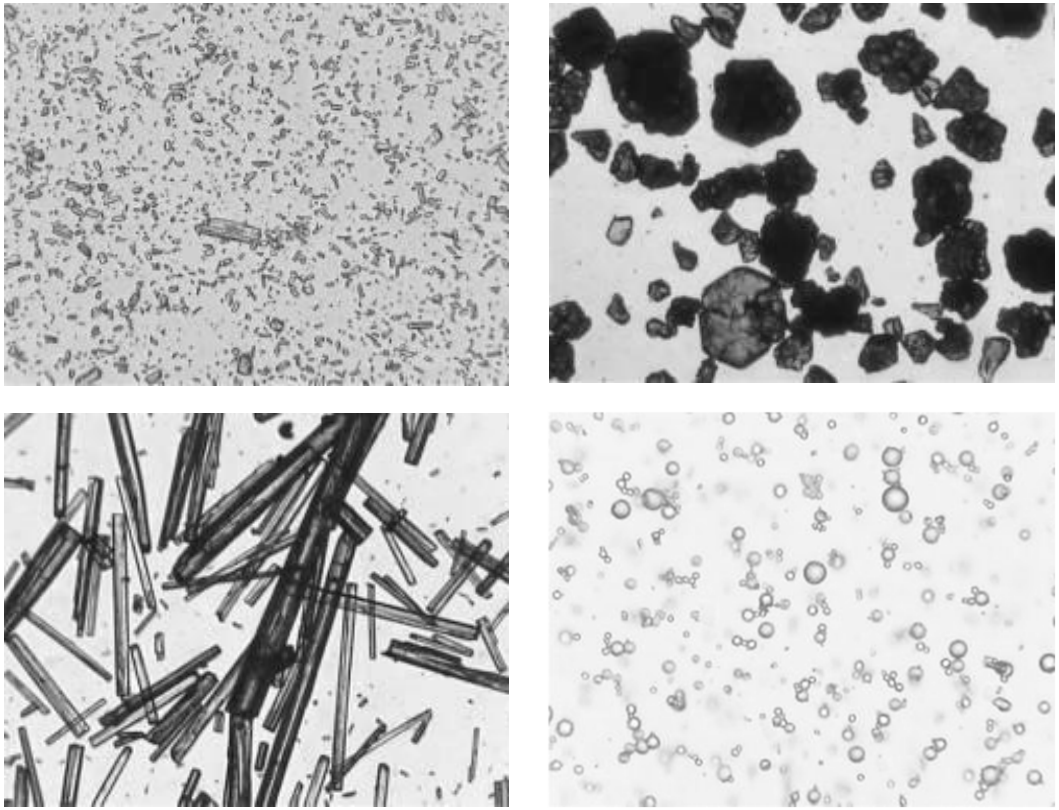
# Spraytec training overview

- Introduction to particle sizing
- Introduction to laser diffraction
  - The diffraction pattern
  - The Spraytec
  - Optical models
- Measuring sprays
  - Multiple scattering
  - Vignetting
  - Beam steering
  - Low signal
- Spraytec measurement process – at the instrument
  - SOP wizard

# Introduction to particle sizing

# Particles come in many different shapes

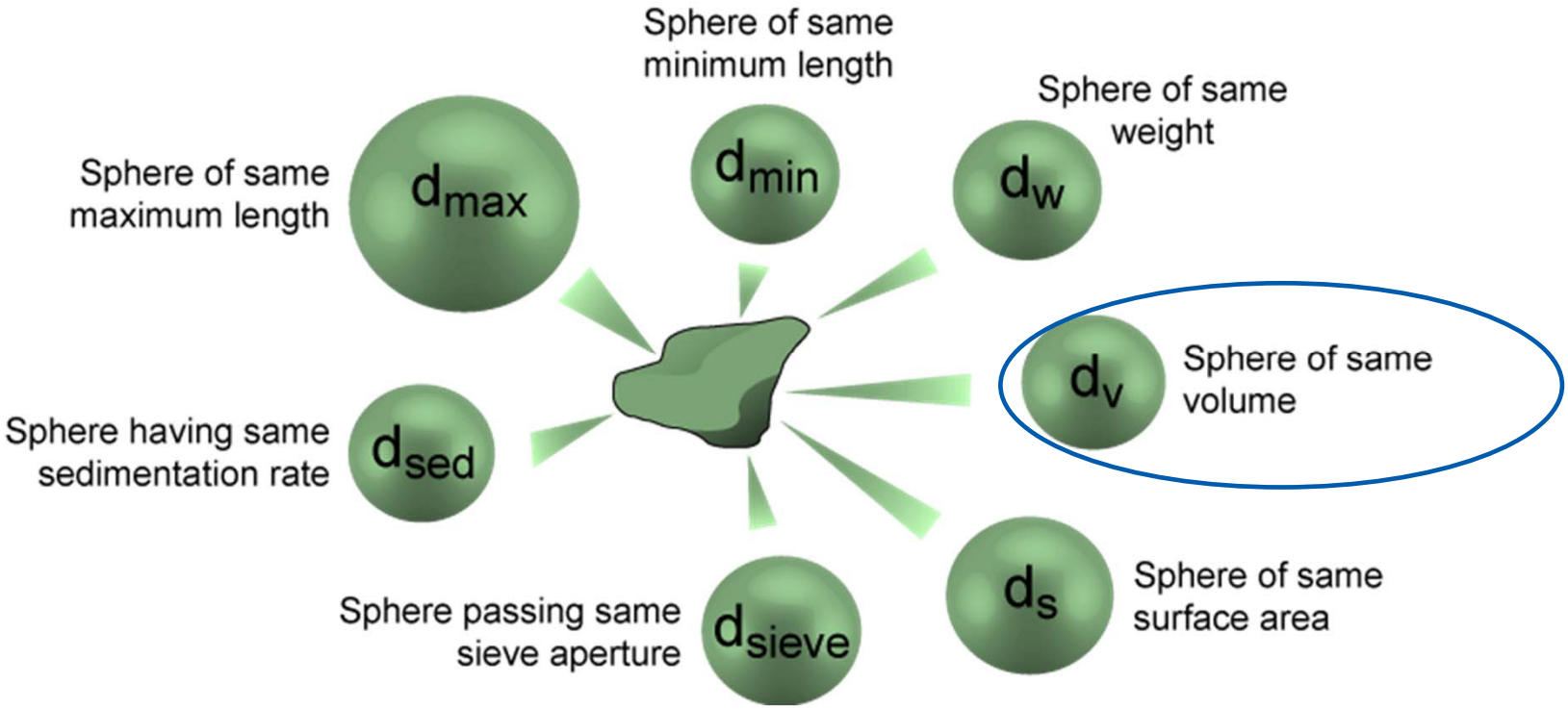
**(as well as sizes)**



- How do we describe the size of these particles?

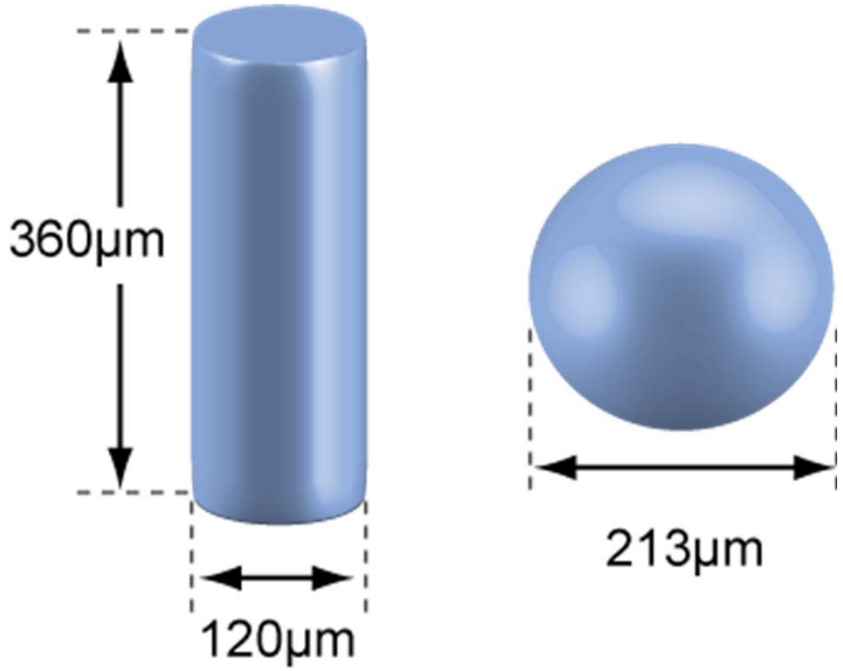
# Concept of equivalent spherical diameters

- Different particle sizing techniques report different equivalent spherical diameters
  - » Dependent on the physical property that is measured

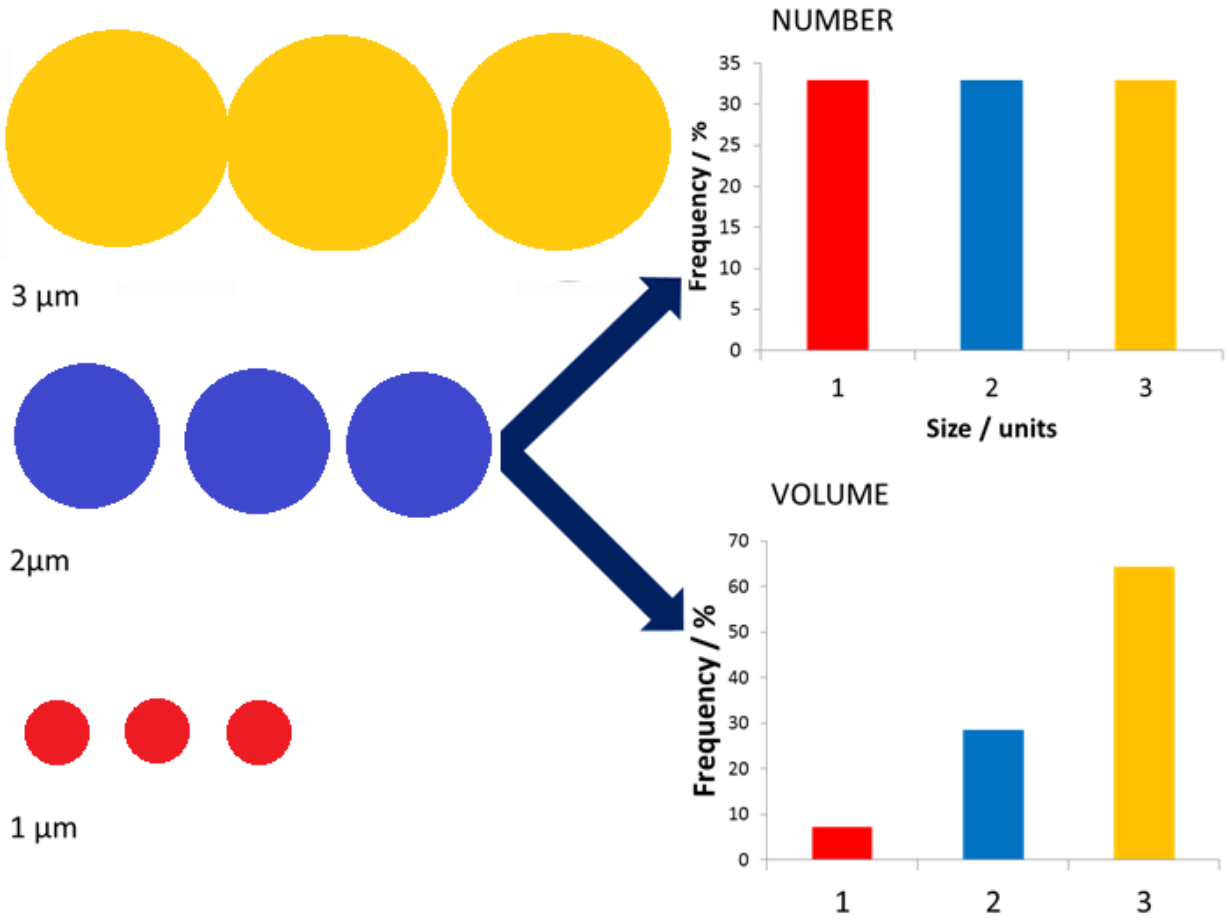


# Equivalent sphere theory

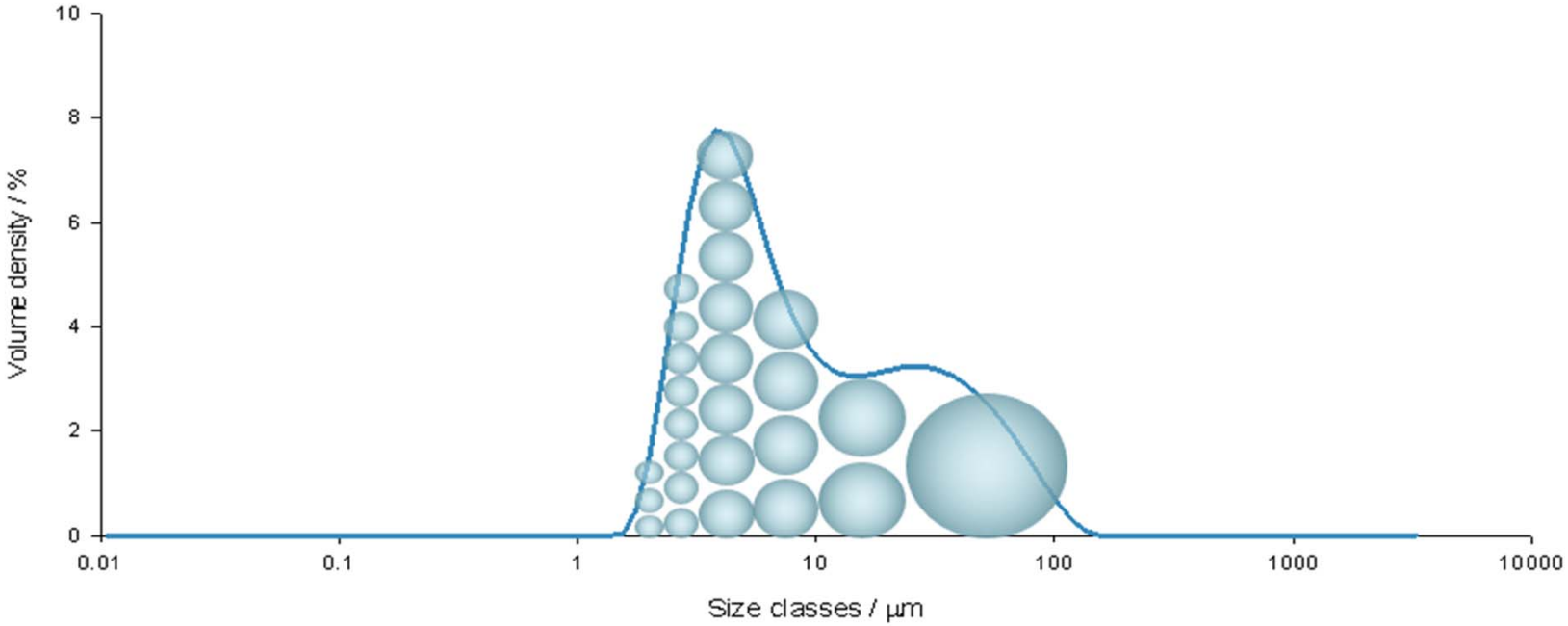
- Laser diffraction describes a 3D shape as the diameter of a sphere that would exhibit the measured effect



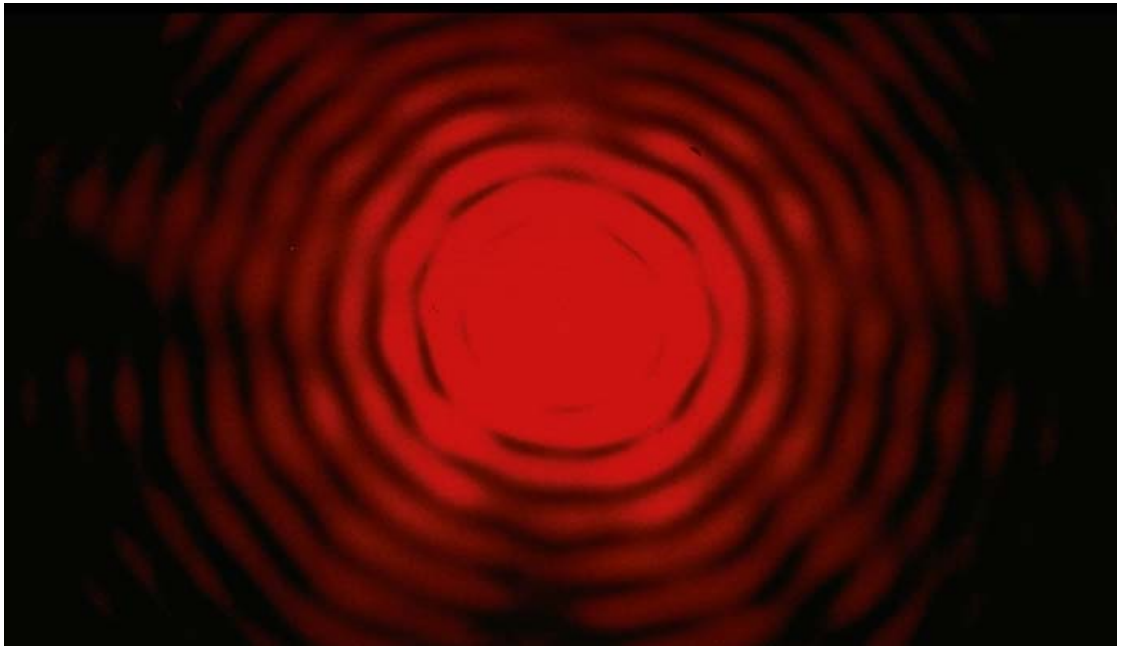
# Number versus Volume



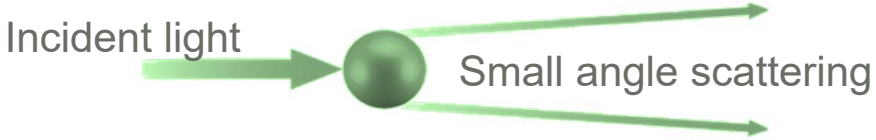
# Result = Volume weighted

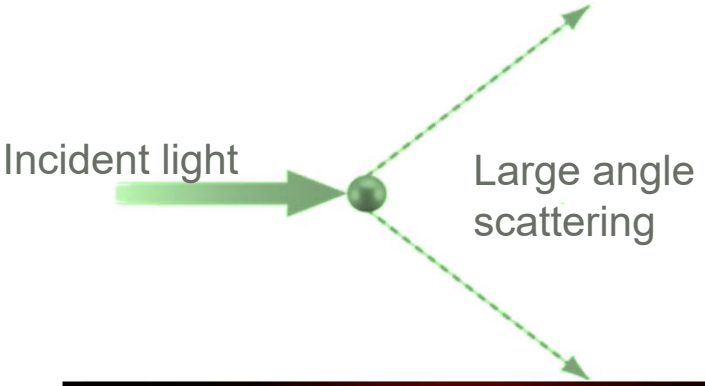


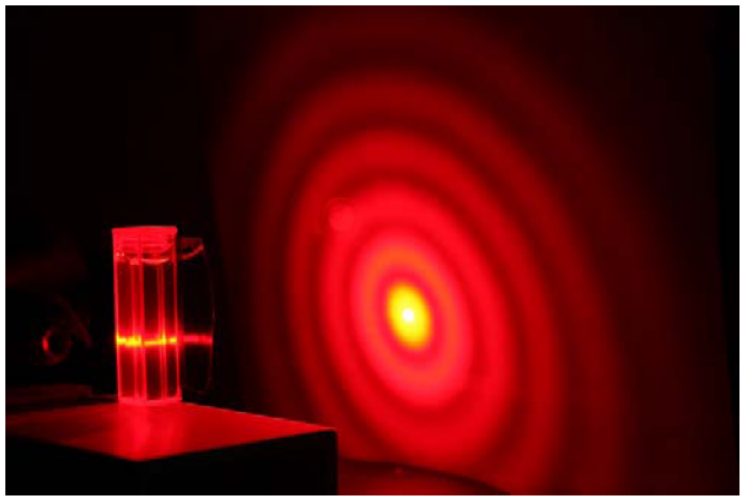
# Introduction to laser diffraction



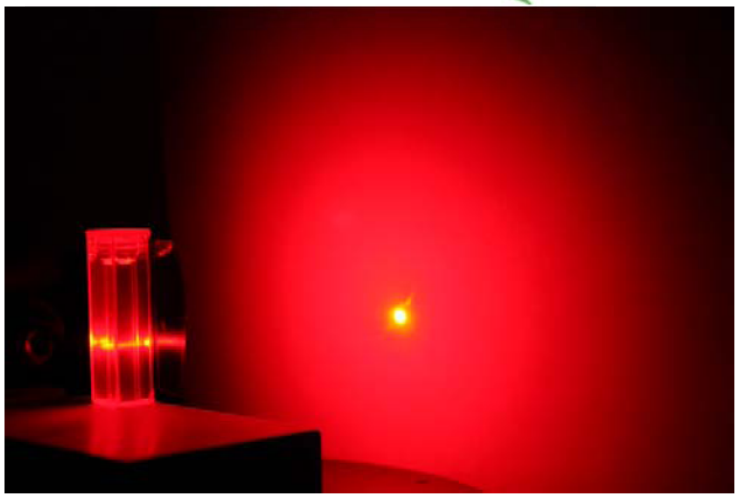
# Dependence of diffraction pattern on particle size



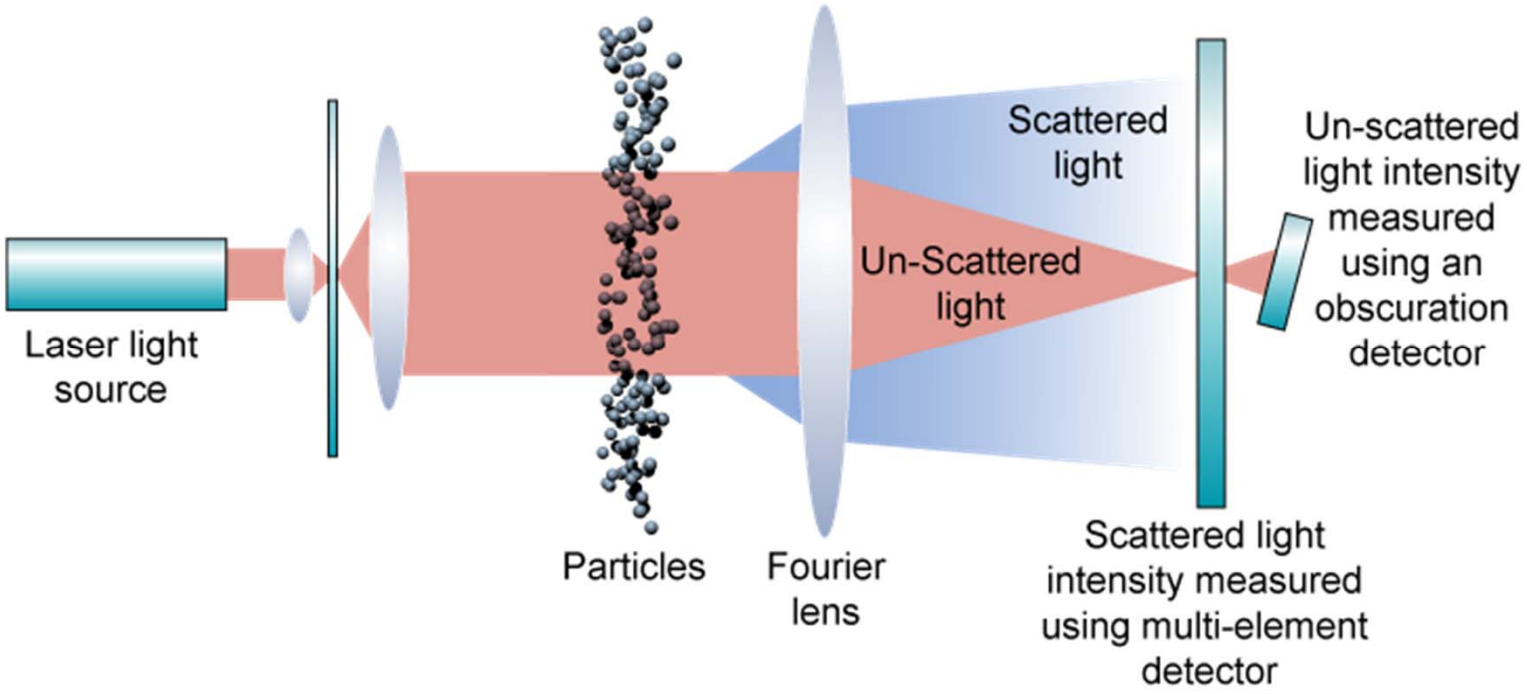



**Large particle**



**Small particles**

# A basic laser diffraction system…



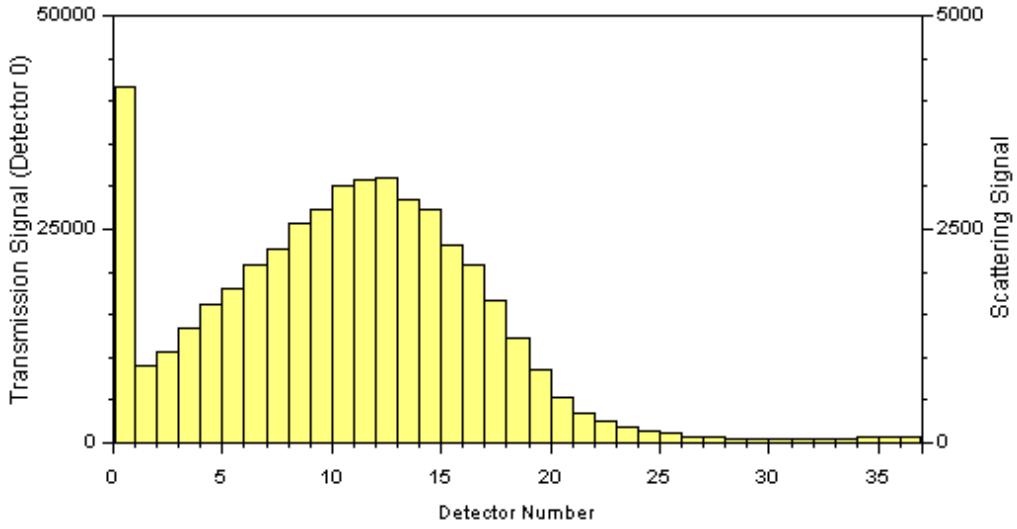
# Spraytec system detail

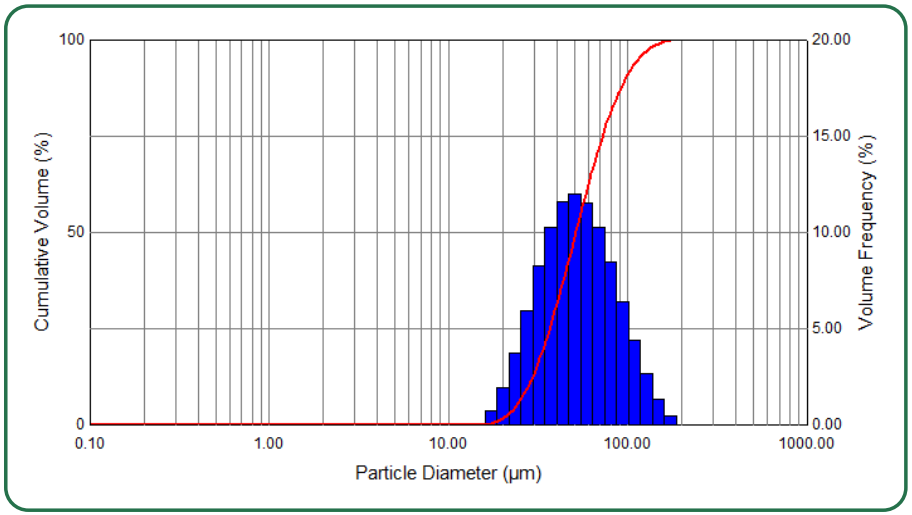
# Spraytec Lens Ranges

- Wide Dynamic Range
  - 300mm lens: 0.1 – 900 microns
  - 750mm lens: 2-2000 microns (5 – 1600 microns for Dv50)
- Large working distance
  - 150mm at 0.5 microns
  - Over 1000mm at 5 microns
- Small Surface Area
  - Minimises exposure
- Purge system available for large volume sprays

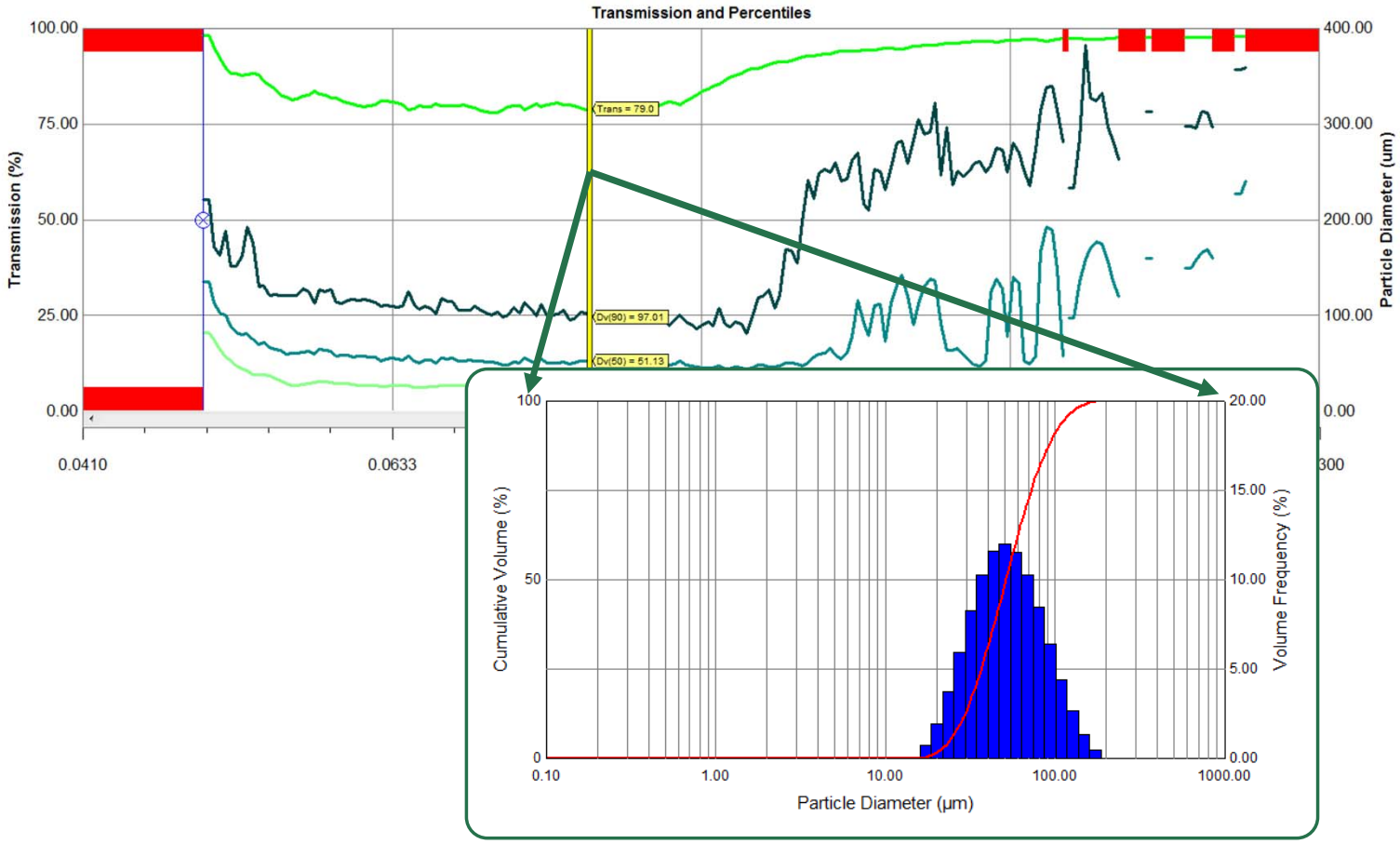
# Spraytec Data Capture

- The collected diffraction pattern is converted to a Volume Particle Size Distribution (equivalent sphere) following the Mie theory (or Fraunhofer)

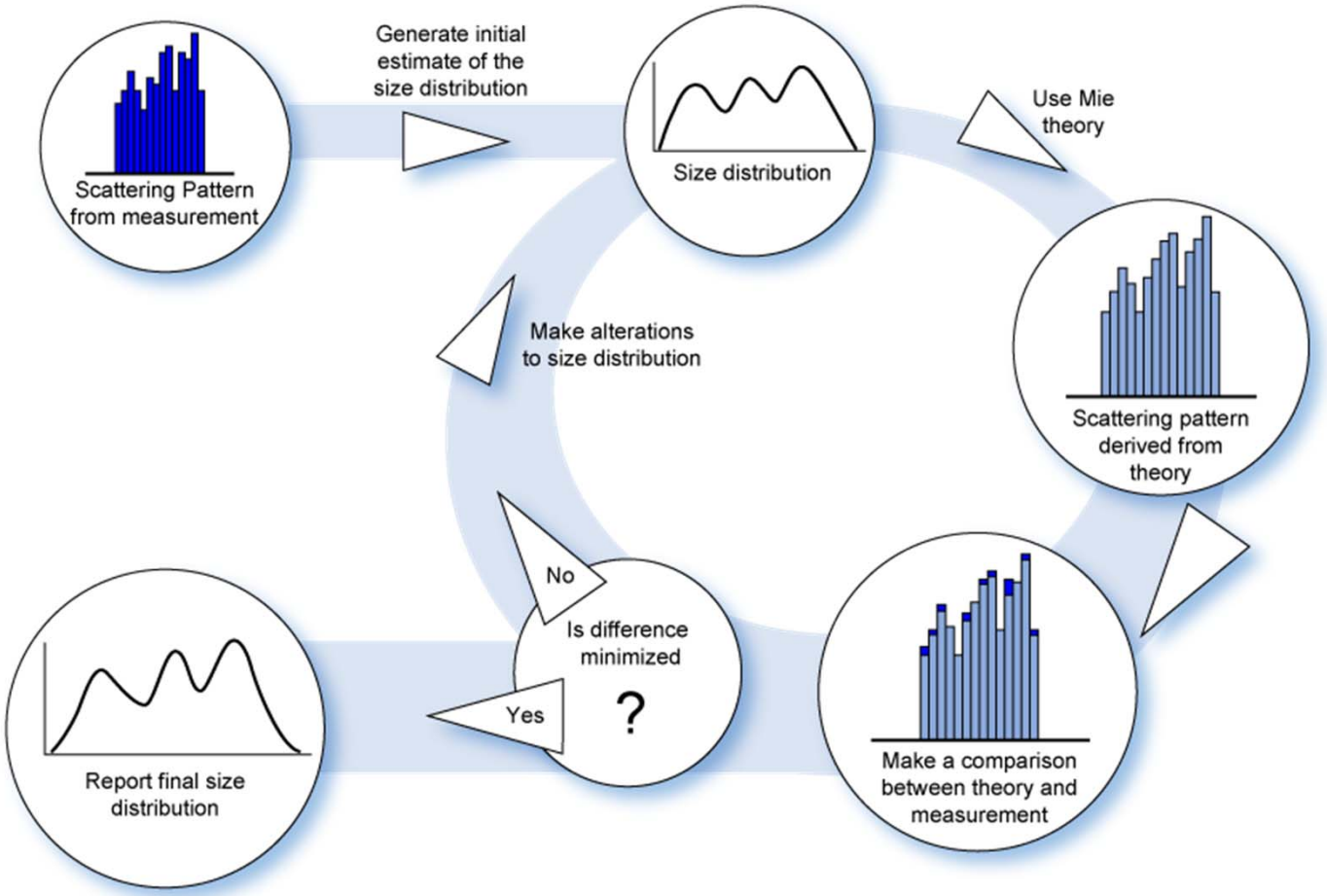


# Spraytec dynamic particle size analysis

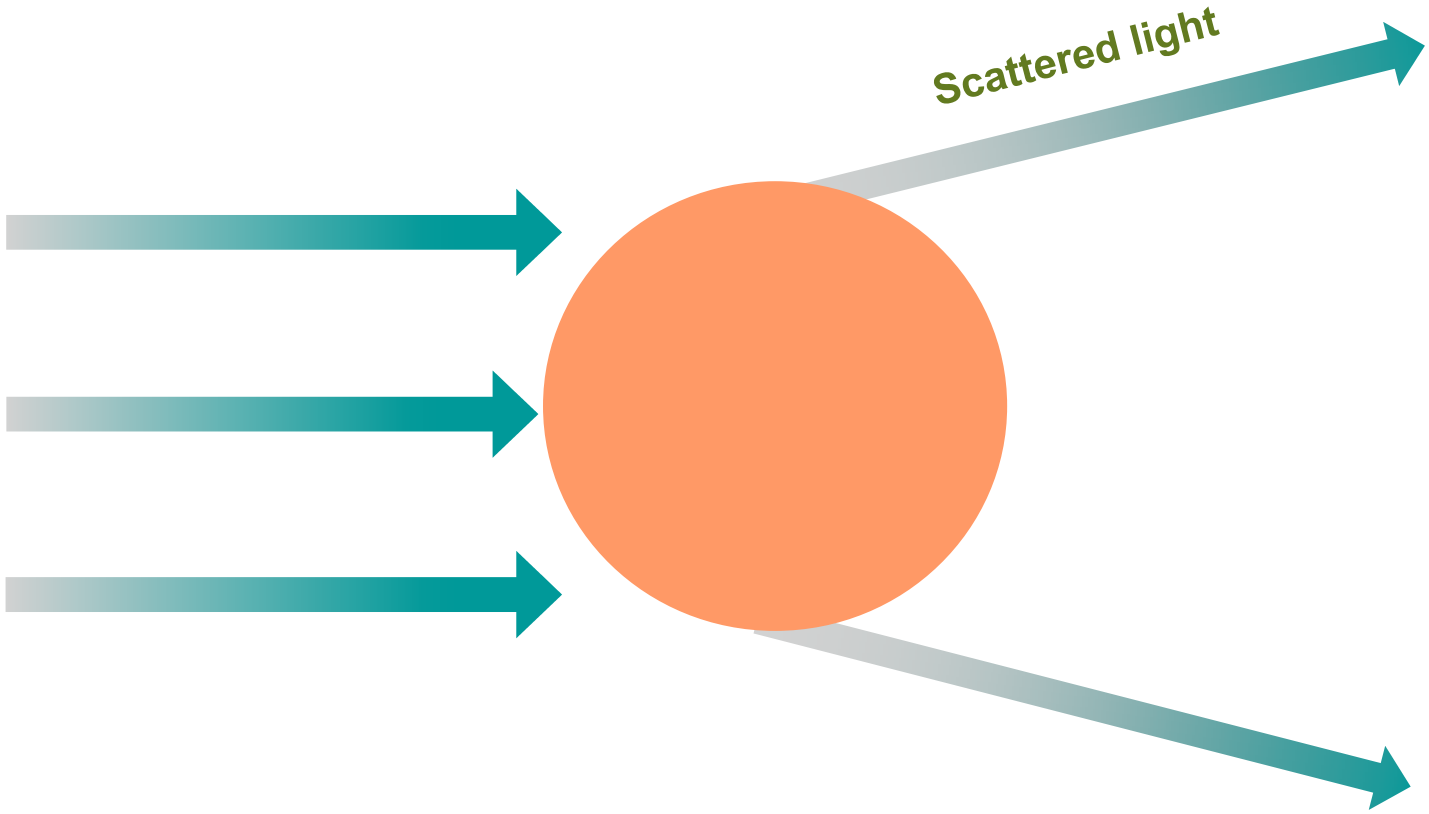


# How the size distribution is calculated?



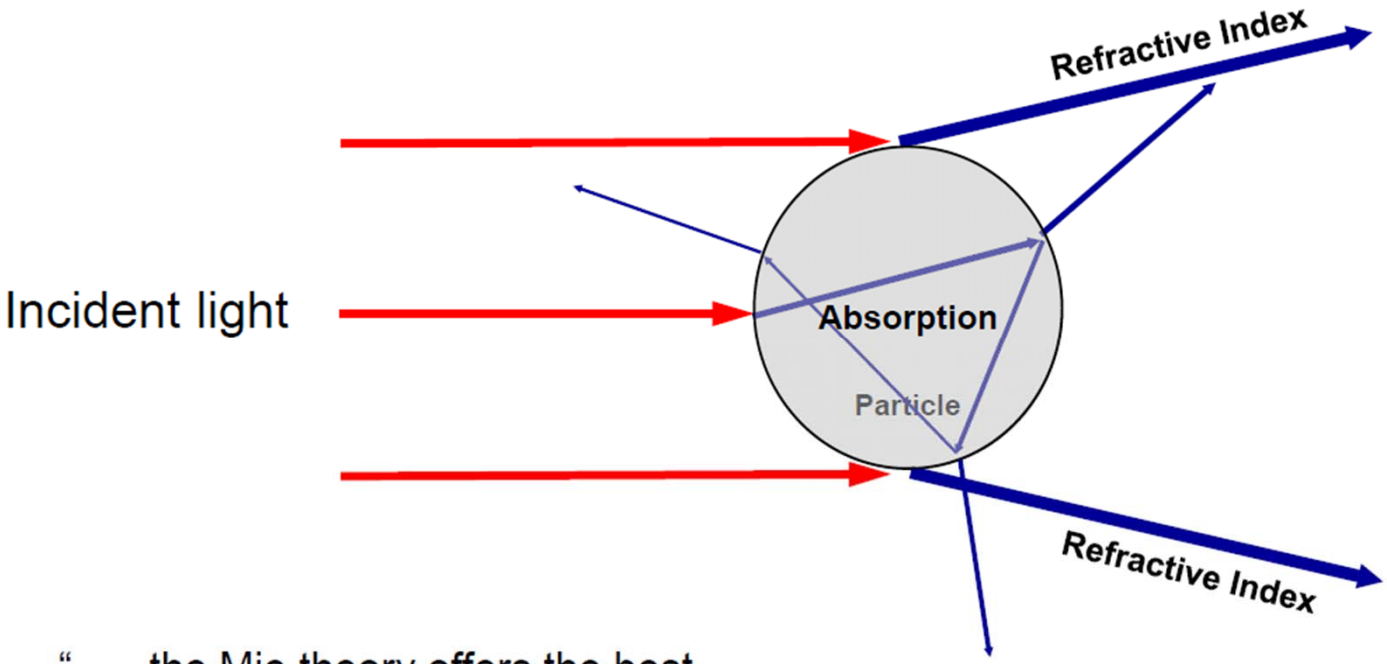
# Scattering models

## Fraunhofer approximation



# Scattering data analysis

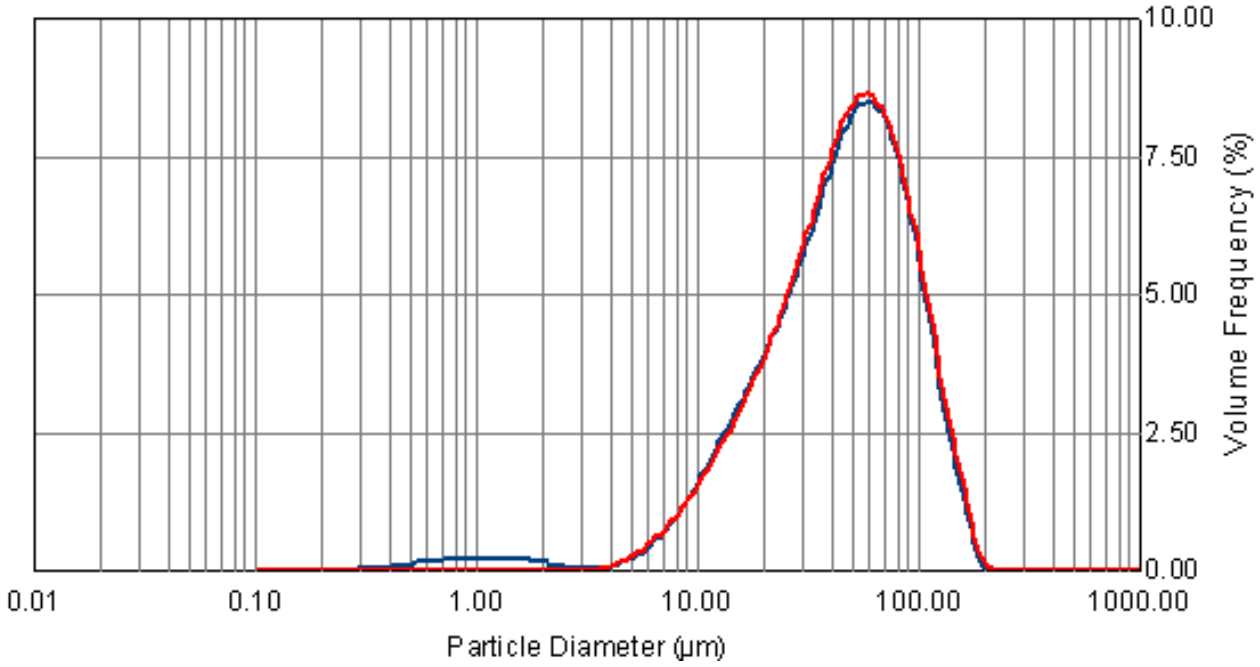
## Mie Theory




"….. the Mie theory offers the best general solution."

ISO 13320-1

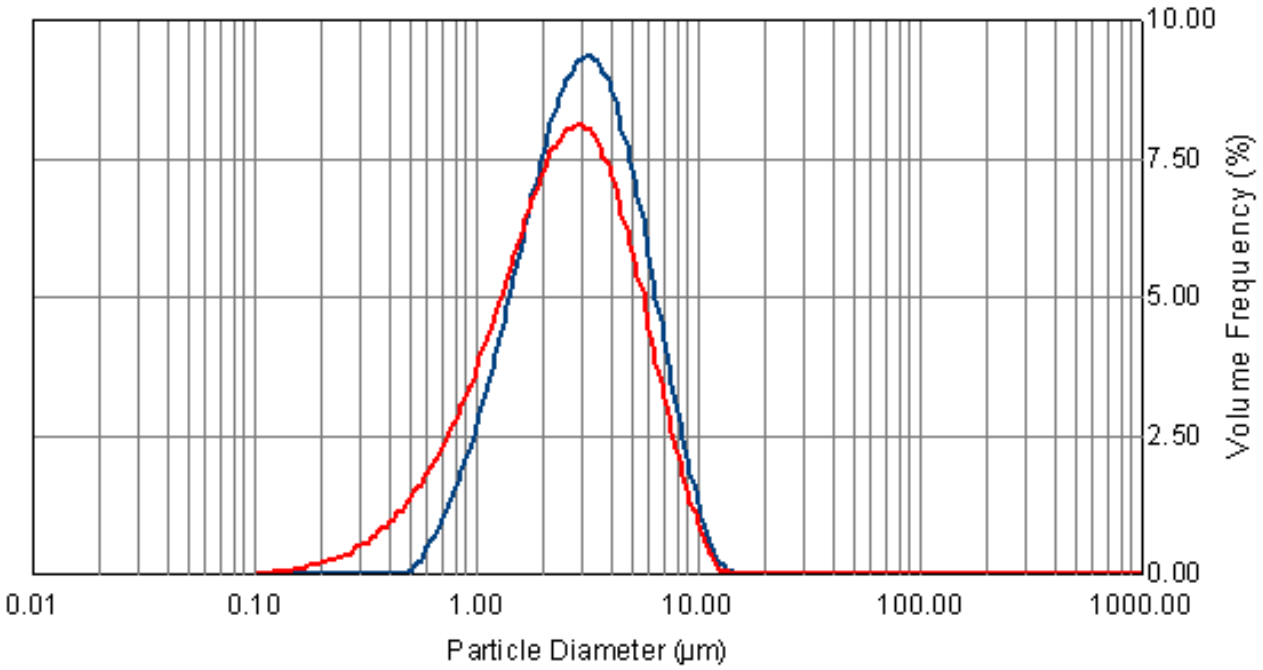
# Scattering Data Analysis
# Using different optical models




Blue Fraunhoffer

Red Mie

# Scattering Data Analysis
# Using different optical models

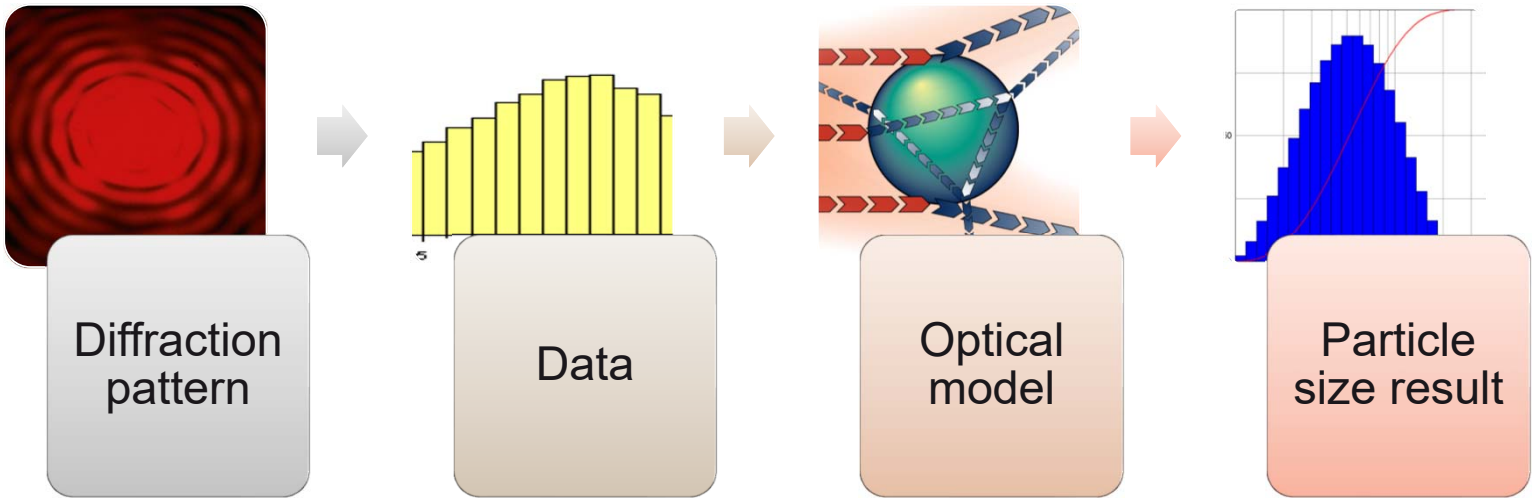



Blue Mie

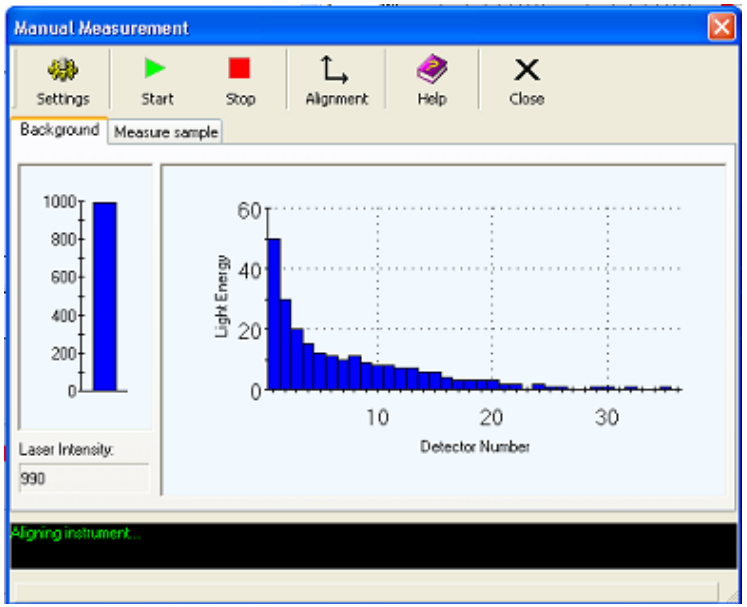
Red Fraunhoffer

# Measuring sprays

# Particle size by Spraytec

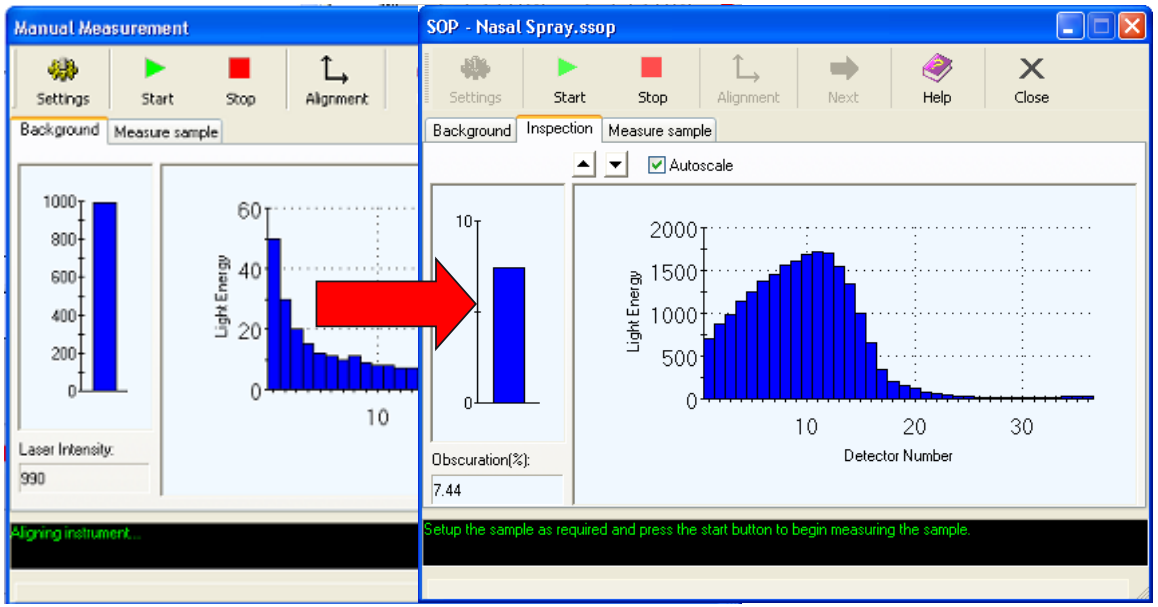


# Spraytec Measurement Process



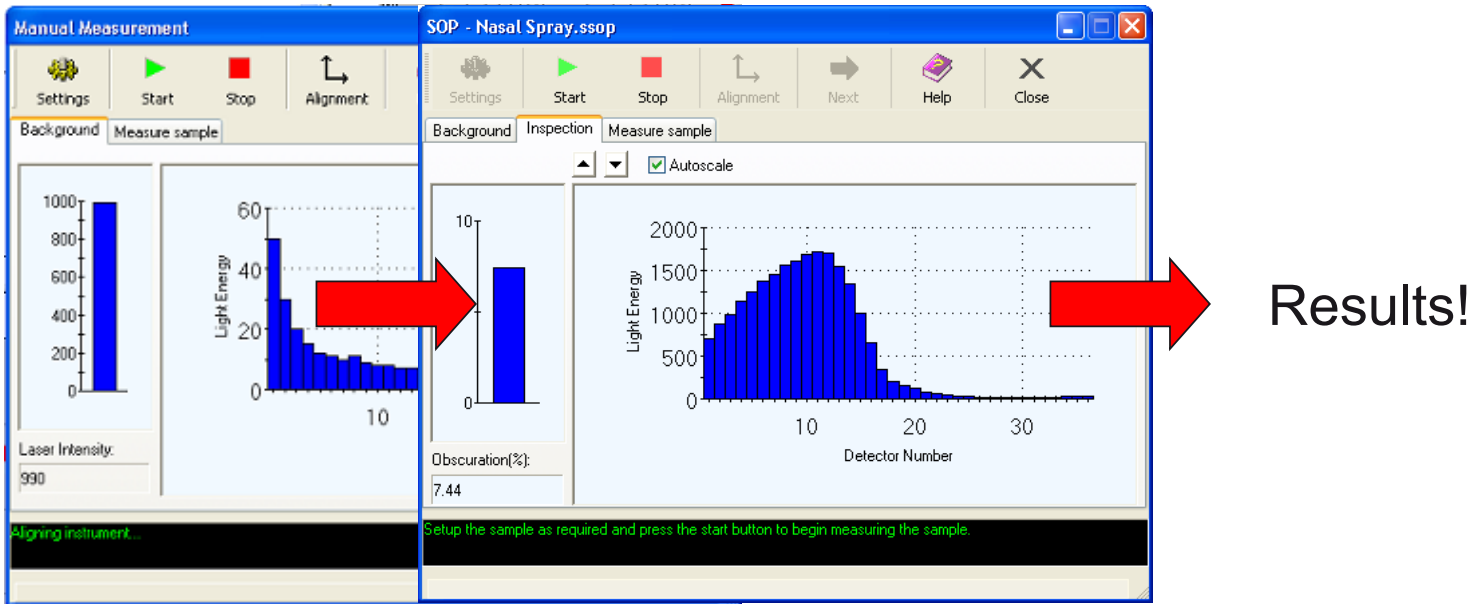

Alignment + Background

# Spraytec Measurement Process




Measurement

# Spraytec Measurement Process



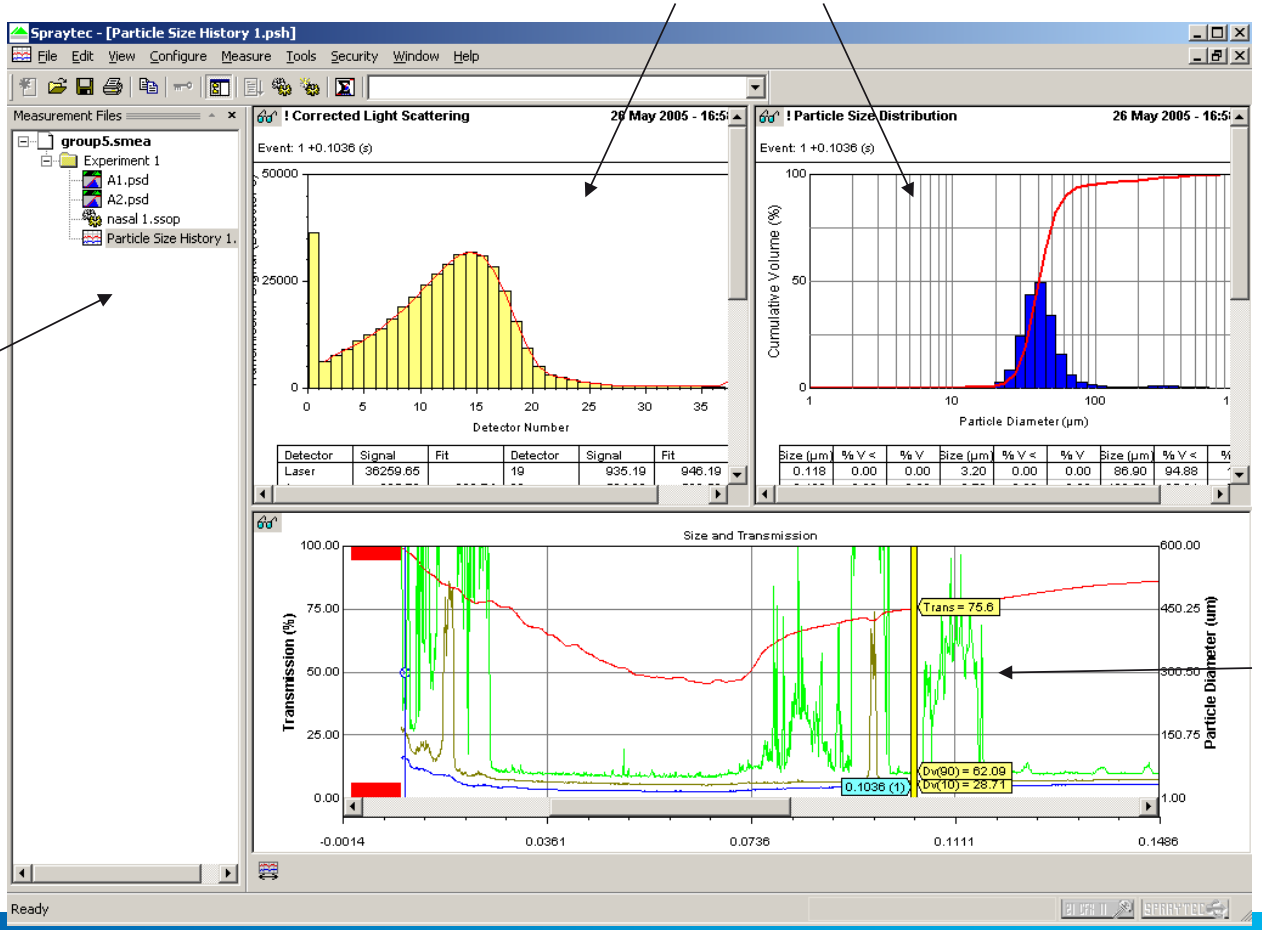

Results!

- Measurement manager ensures each measurement step occurs in the correct order, improving result reliability

# Spraytec Result Interpretation

Record Views

File Viewer

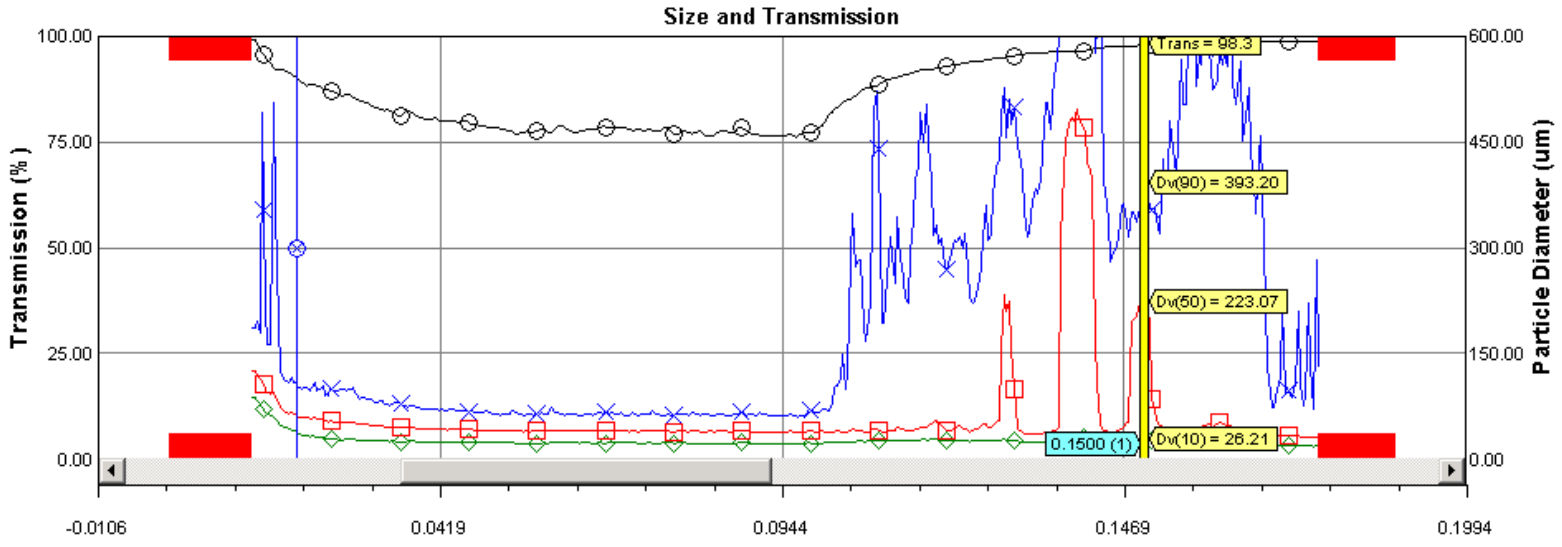



Size History Display

# Spraytec Result Interpretation

## Size History

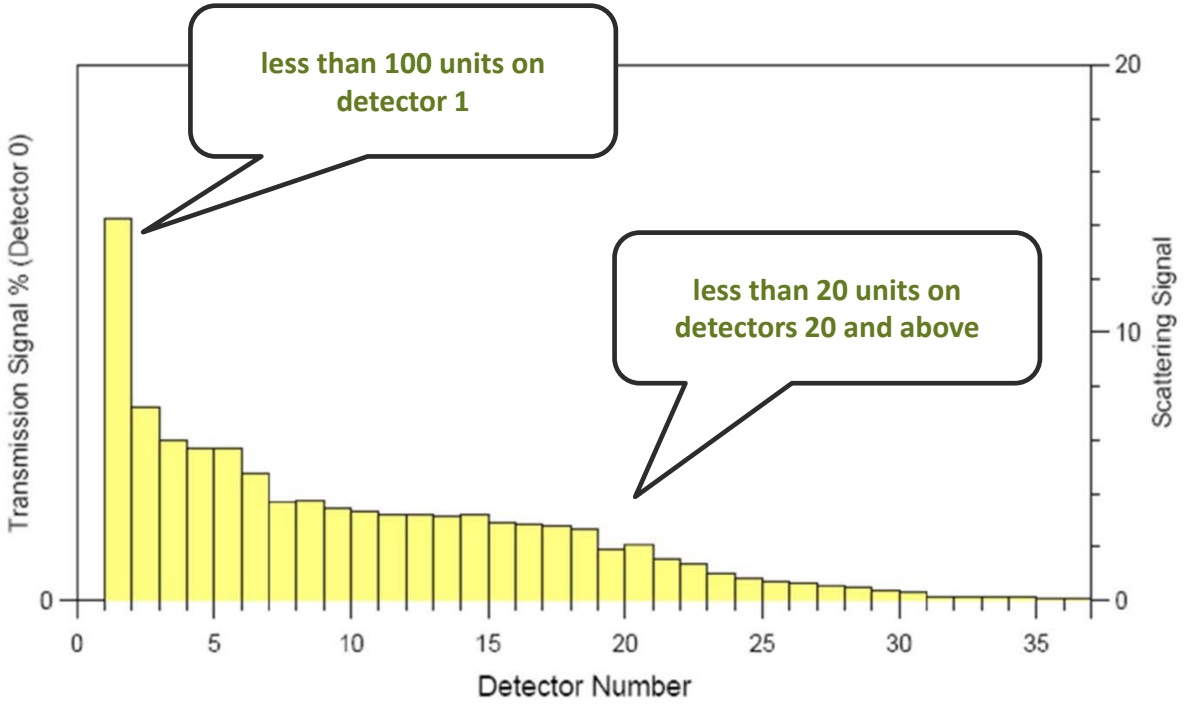
- Frame-by-frame event analysis
- Drag-and-drop result selection
- Zoom facility to examine changes over different time periods
- Over plotting of results at different time points
- Display of measurement triggers and data groups



# Background

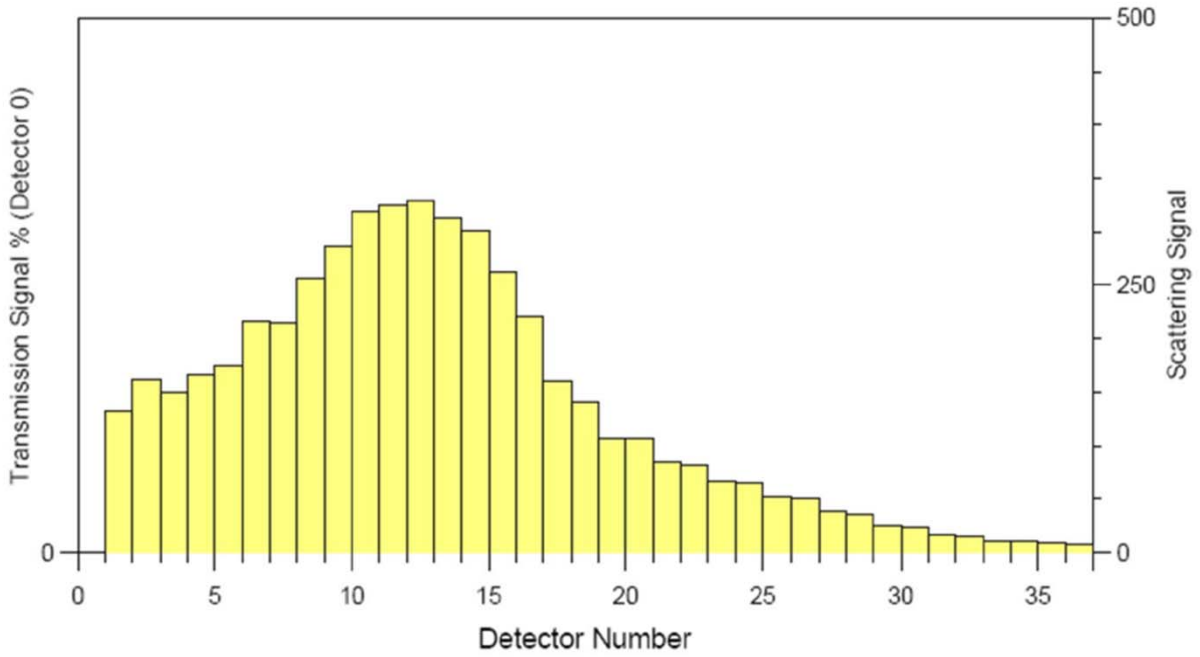
- Background signal should decrease across increasing detector numbers

- As the light energy from the laser decreases with increasing angle



# Background quality

- Droplet deposition on the windows
  - » Unfortunately sprays are messy, and not always easy to control so droplets can deposit on the windows.

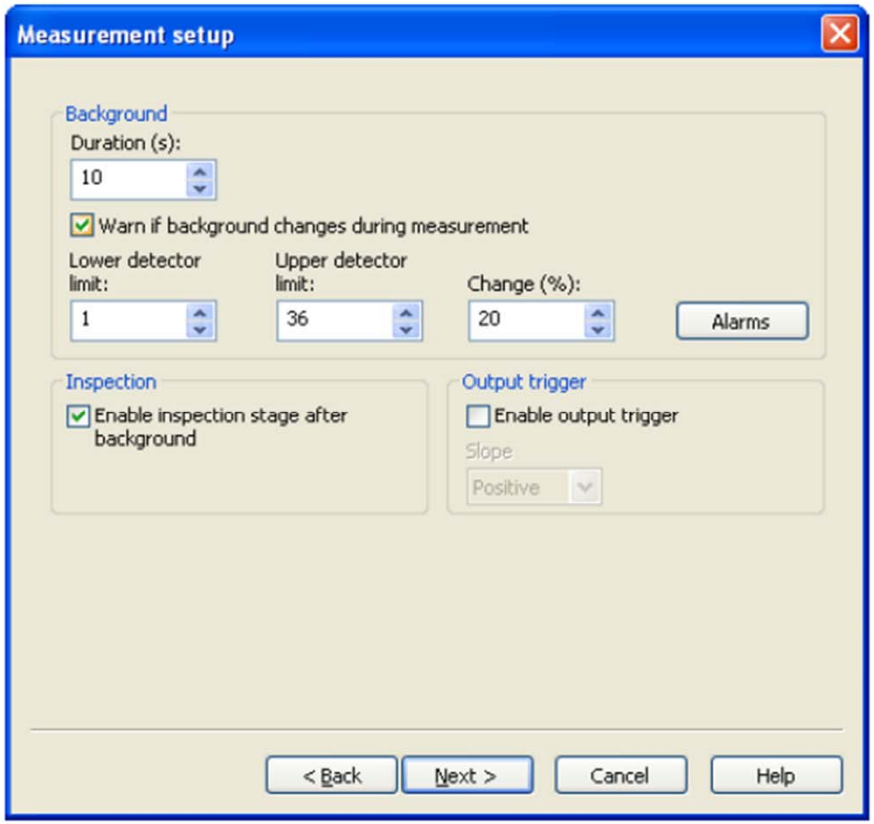


# Preventing deposition on the windows

- An air purge can be used for particularly messy sprays.
- Otherwise, a background can also be measured after each measurement.
- An accpetable % variation of the background level can then be set.
- If this % change is exceeded then a warning to clean the windows will be displayed to the user.

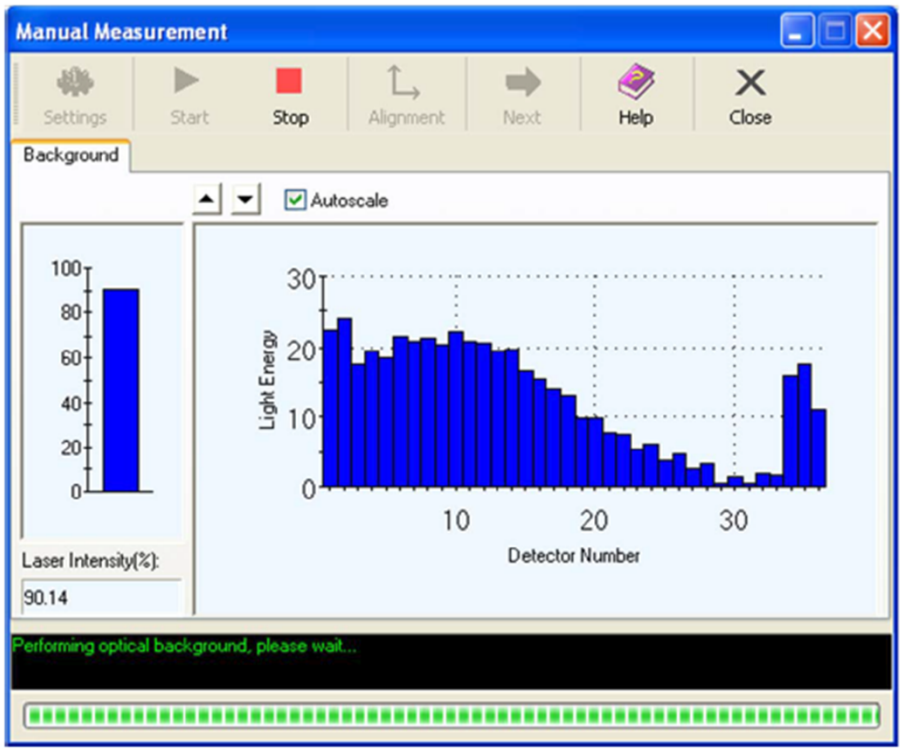
# Background warnings

- The background warnings can be set up in the SOP on the Measurement setup page



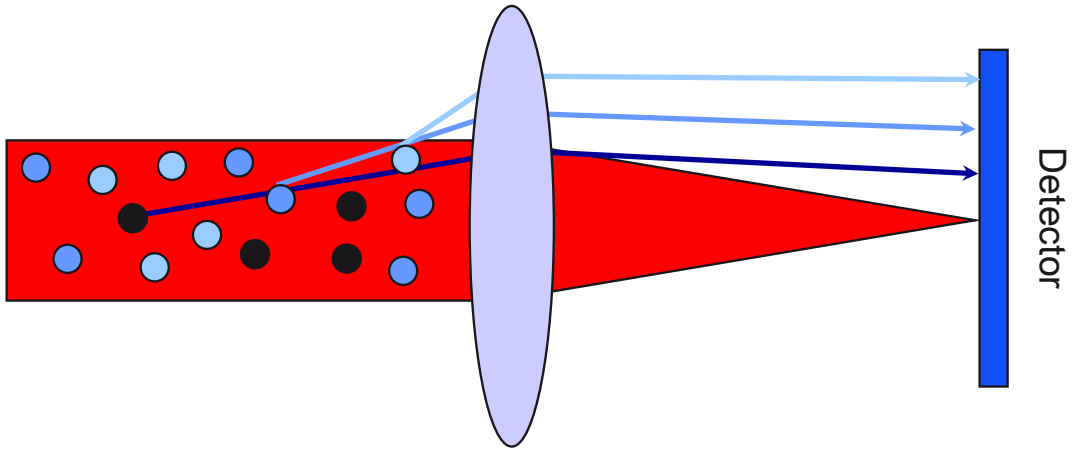
# Ambient light problems

- Background measurements can also be contaminated by ambient light
- This is seen as fluctuations on the outer channels and can cause problems when signal levels are low.
- Check location of the instrument: nearby window? Other light source?



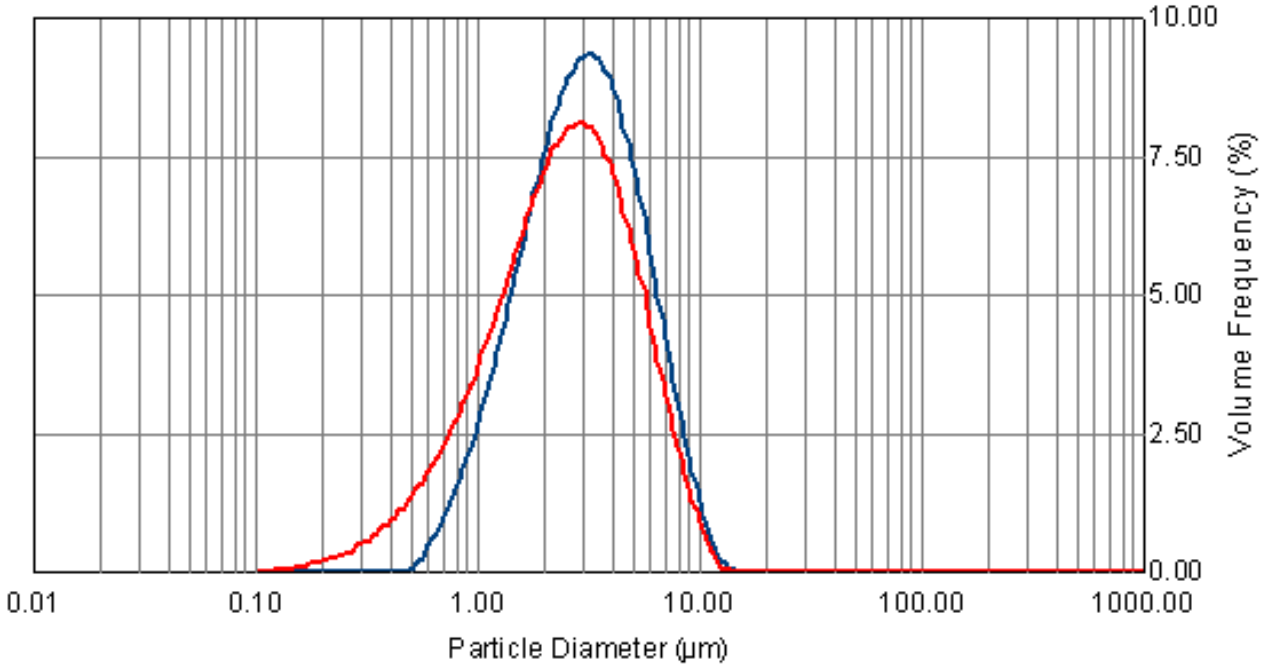
# Spraytec Multiple Scattering

- Multiple scattering causes the measured scattering to move to higher angles, yielding too fine particle size.
- In the Spraytec software it is possible to correct for this.



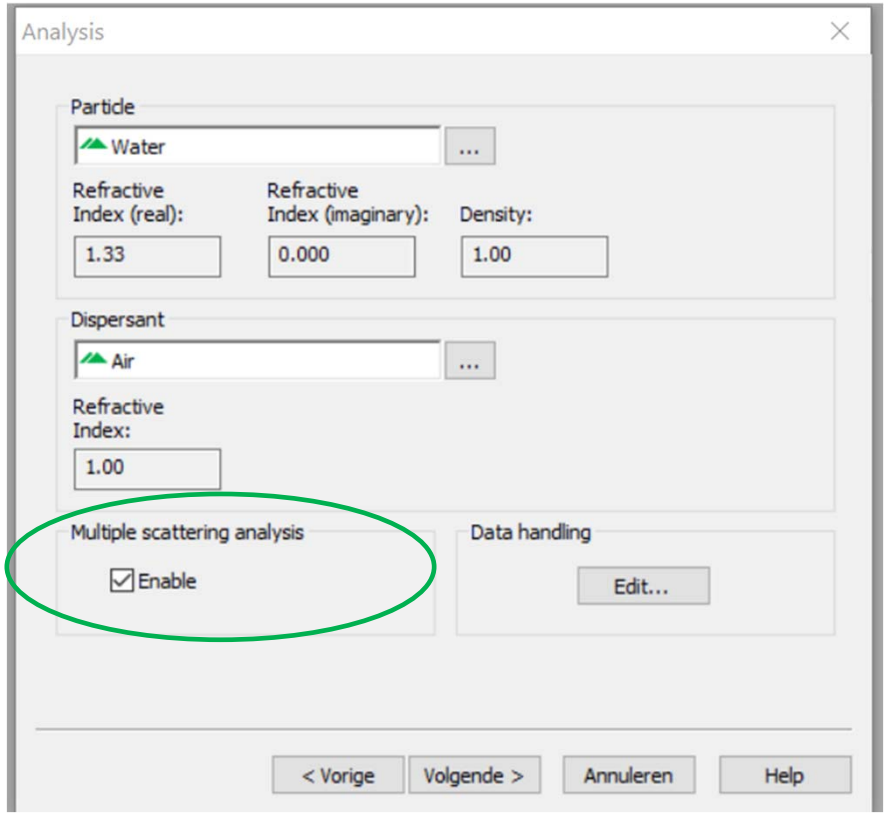
# Spraytec Multiple Scattering

- Example : higher concentration measured and multiple scatter occur
- -> extra tail of small particles (red)



# Spraytec Multiple Scattering

- In the Spraytec software it is possible to correct for this.



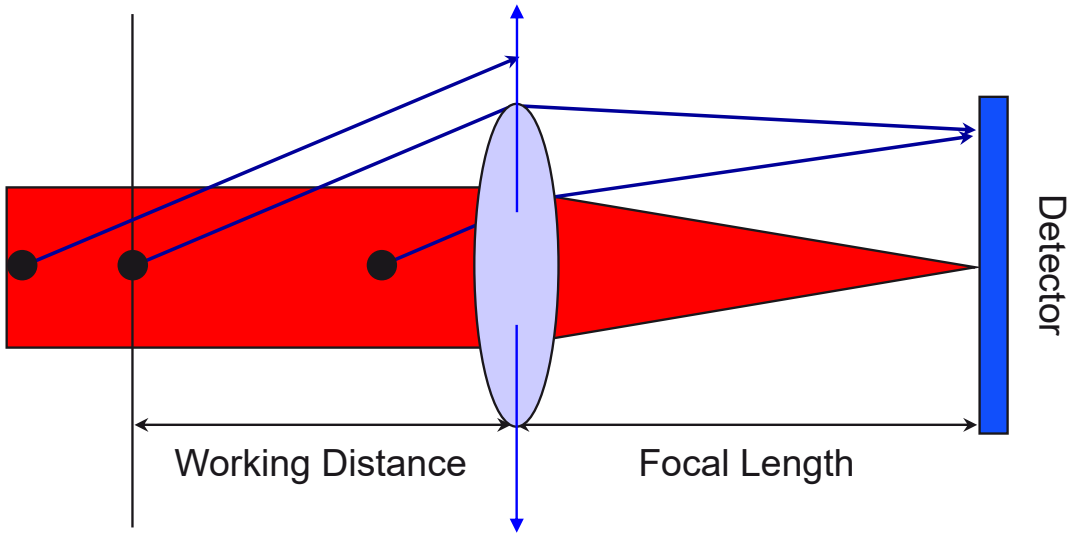
# Spraytec Lens Operation

## Vignetting

- High angle scattering data can be lost if the spray is positioned too far away from the detector lens.
- The maximum distance at which a spray can be measured is known as the working distance.
- This is dependent on the particle size.
  - 150mm for 0.5 micron particles
  - Over 1000mm for 5 micron particles
- Loss of high angle scattering can cause the measured particle size to increase, or the distribution to narrow.

# Spraytec Lens Operation

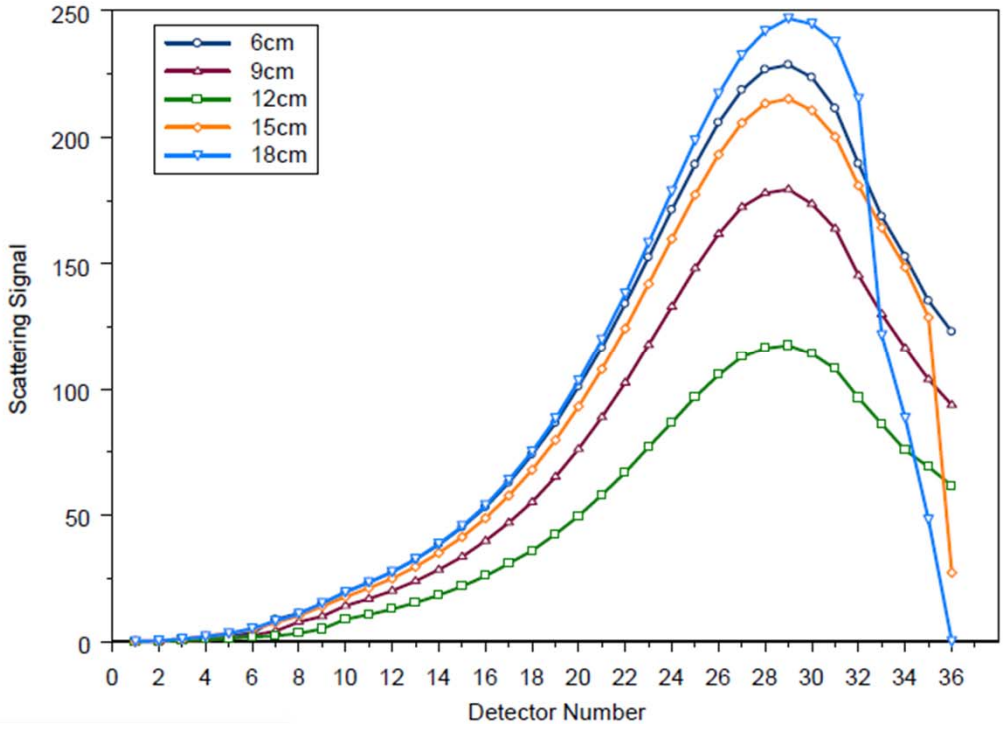
## Vignetting




Working Distance depends on the particle size (scattering angle) and the lens diameter

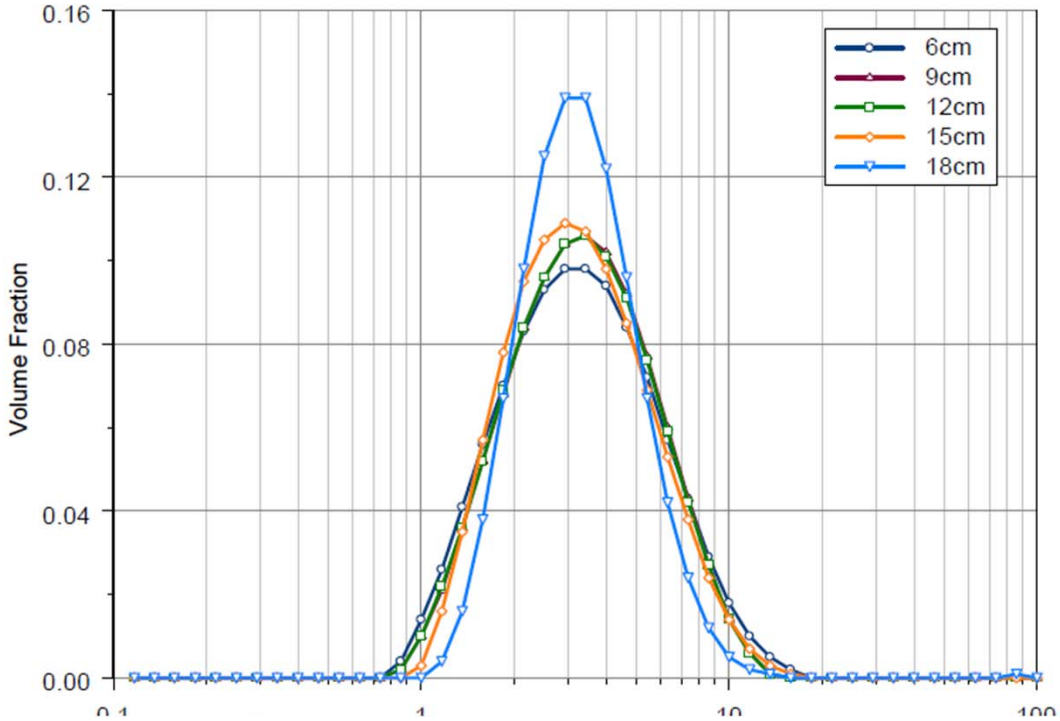
# Vignetting: Inspecting the scattering data

- Scattering data from a spray affected by vignetting
- The data can be reanalysed without the affected data channels

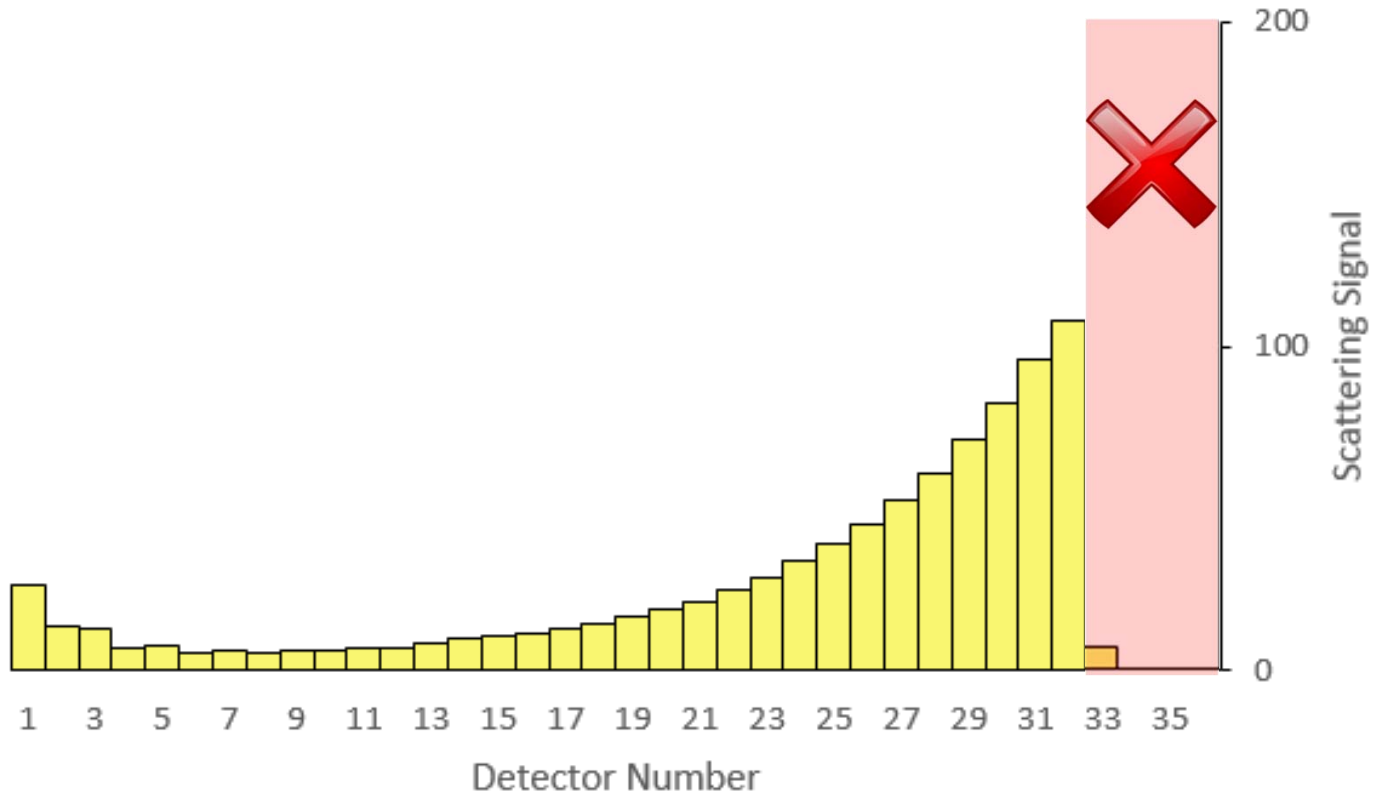


# Vignetting

- This graph shows the particle size distribution for the same spray measured at increasing distance from the detector.
- Vignetting begins to occur at distances over 15cm.



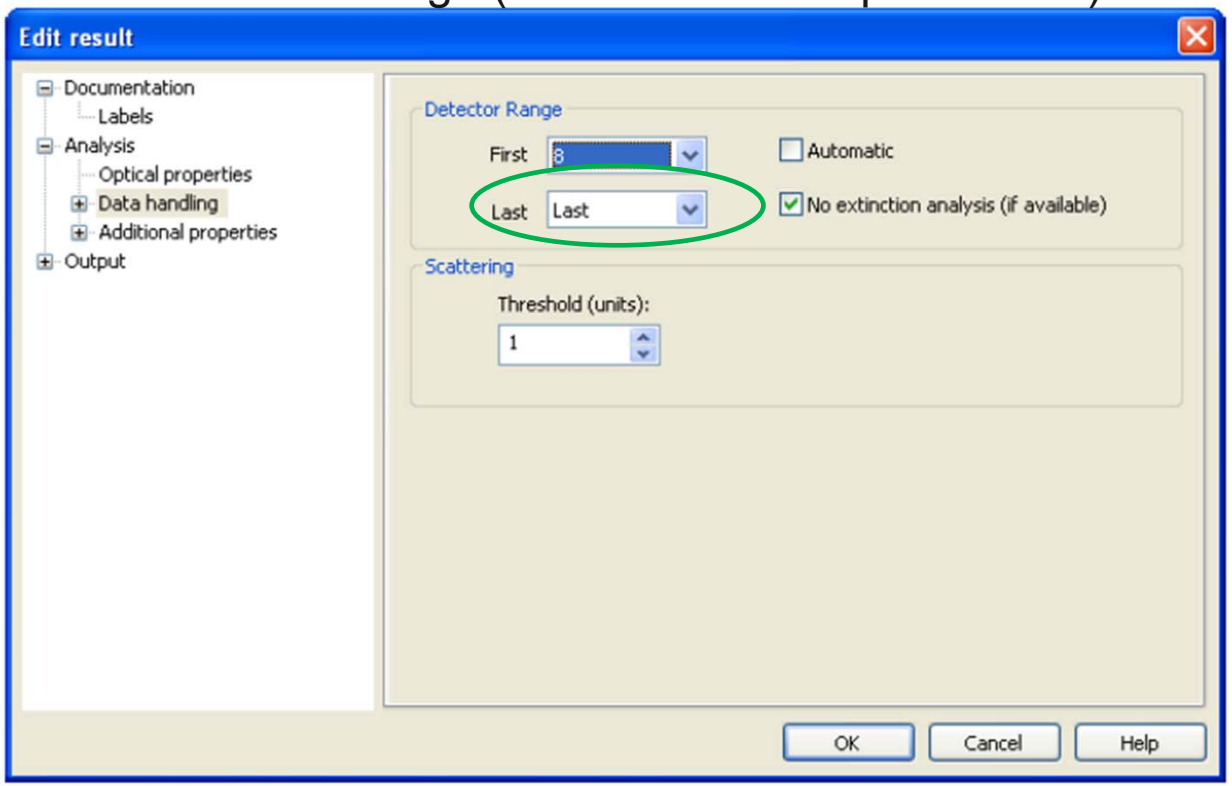
# Spray position and vignetting



# Vignetting – remove data channels

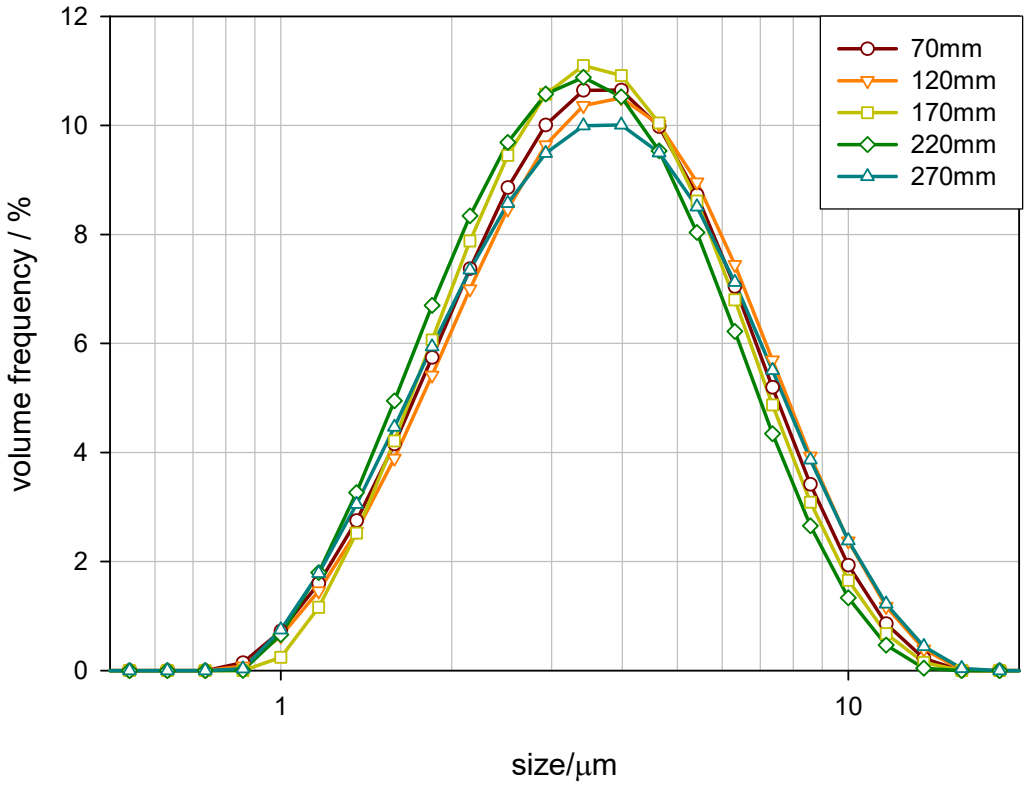
Removing data channels

- Then the data can be reanalysed using the reduced detector range
- Edit records and then alter the detector range (can also be set up in a SOP)



# Vignetting: Remove data higher detectors

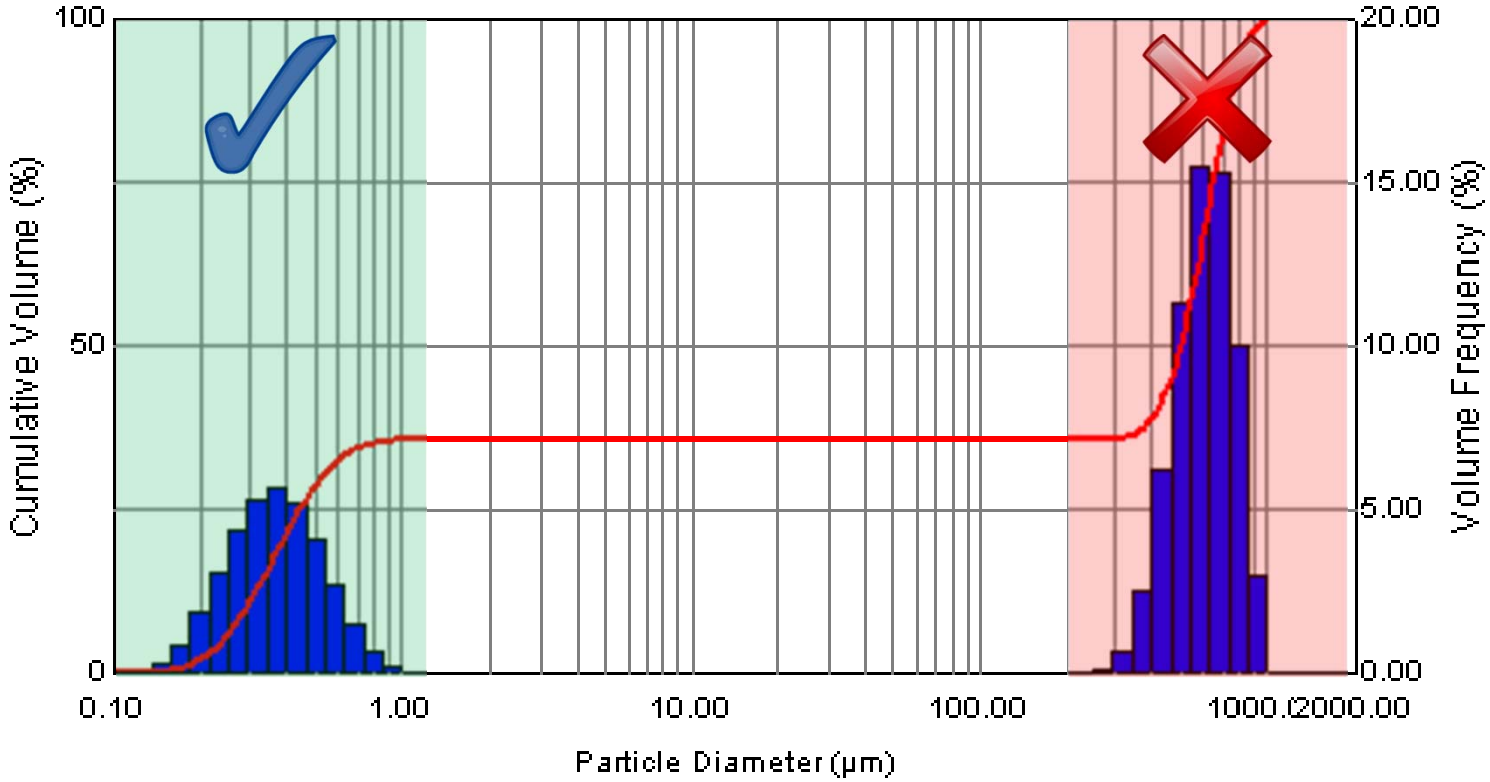
- Remove data higher detectors
  - » Measurement range limited



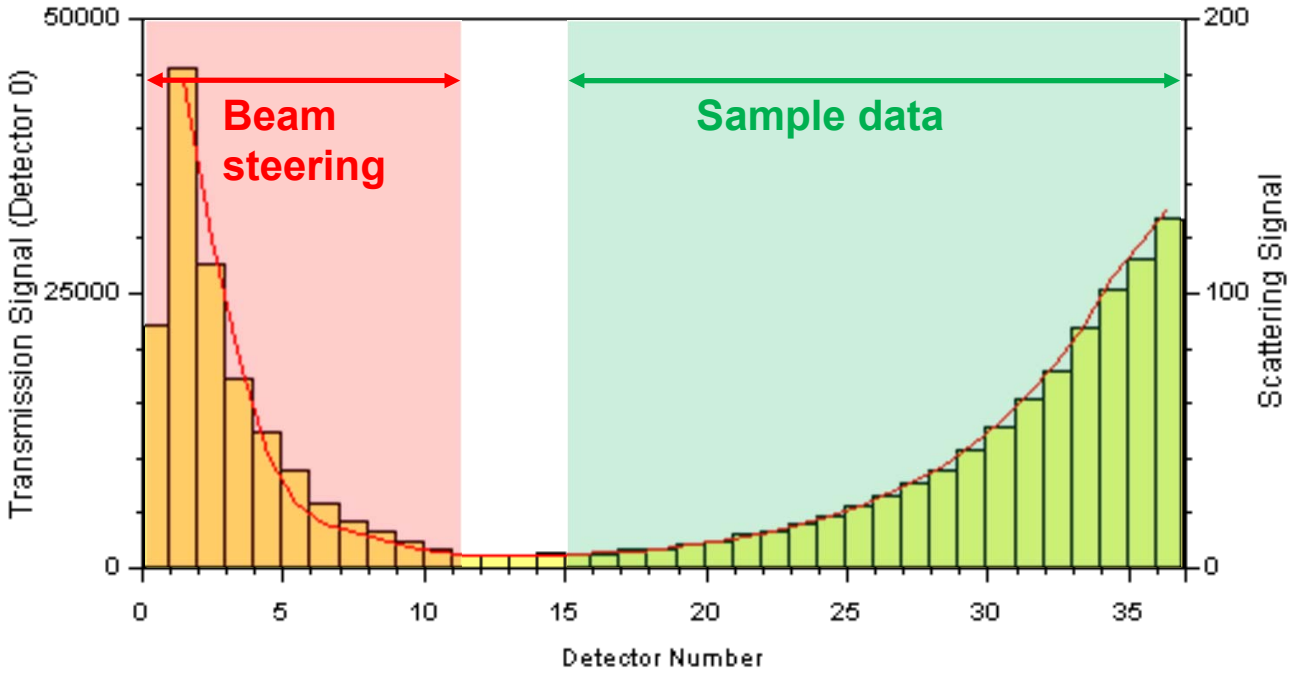
# Beam steering: RI change and beam steering

f.e. Sprays contain volatile components used as propellants.

Unexpected peak large particles.



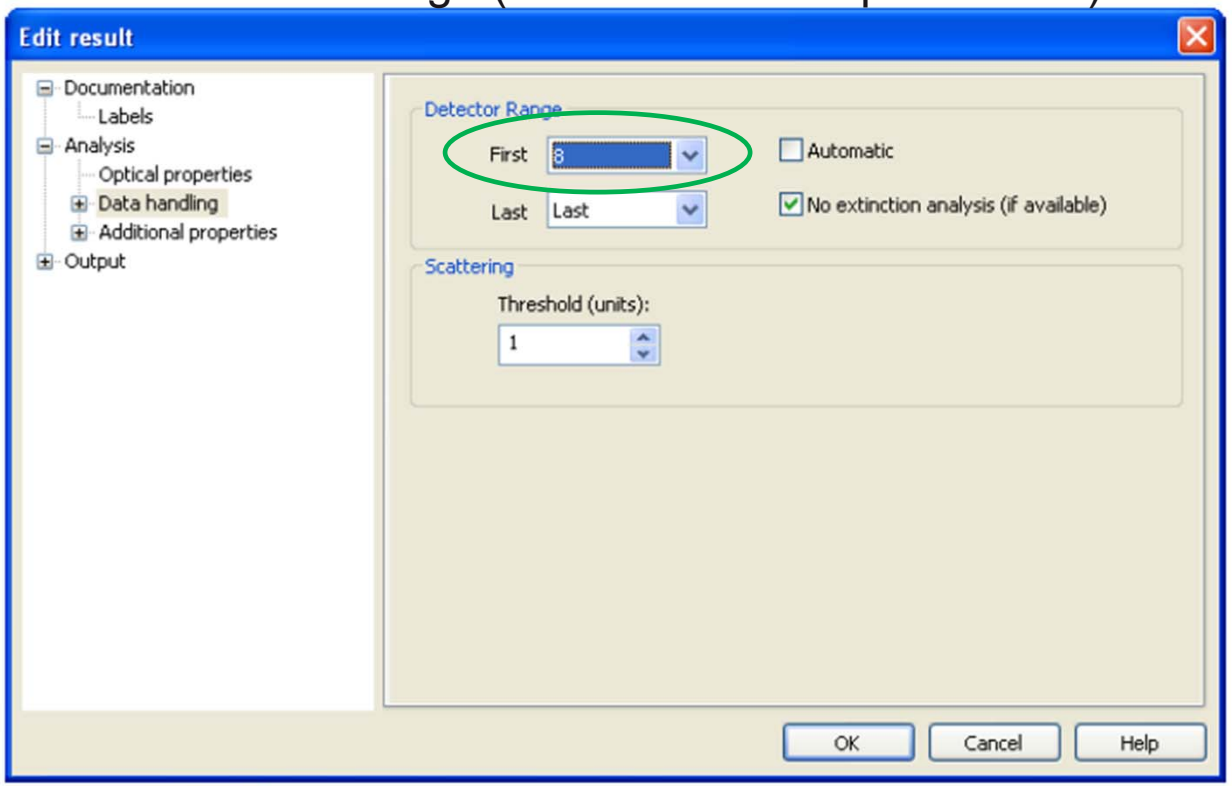
# Beam Steering



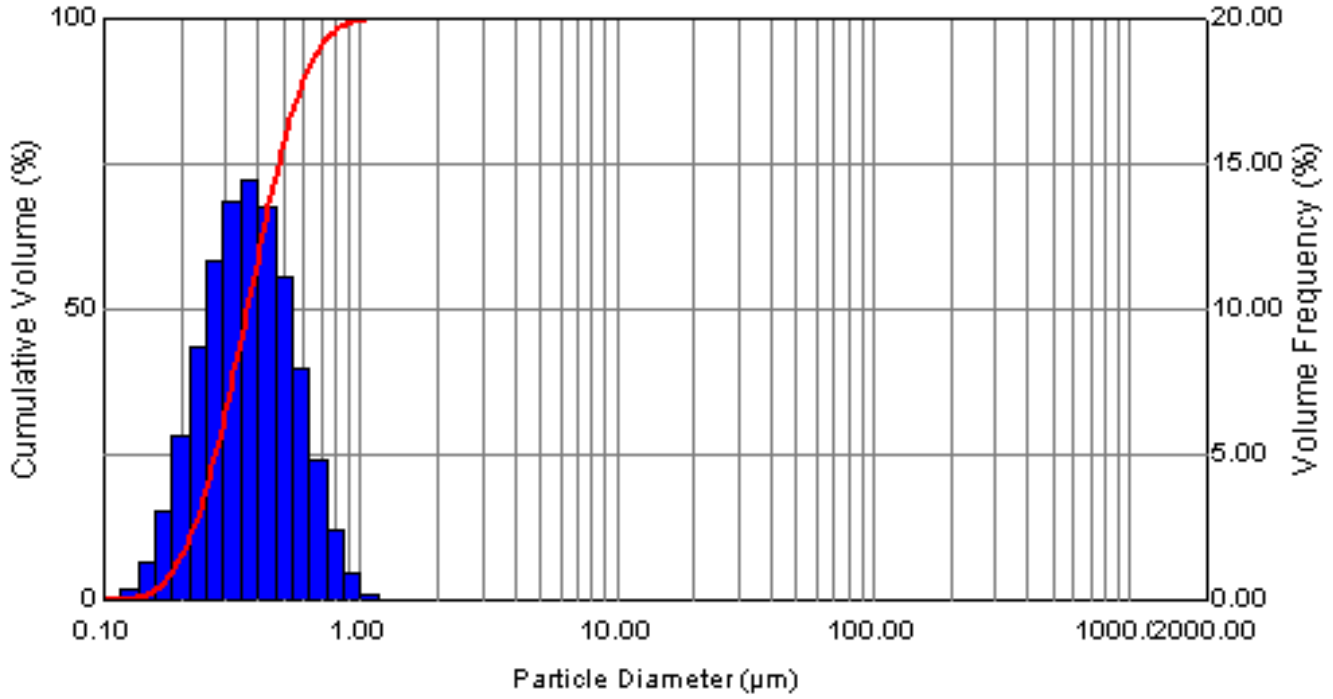
# Beam Steering

Removing data channels

- Then the data can be reanalysed using the reduced detector range
- Edit records and then alter the detector range (can also be set up in a SOP)



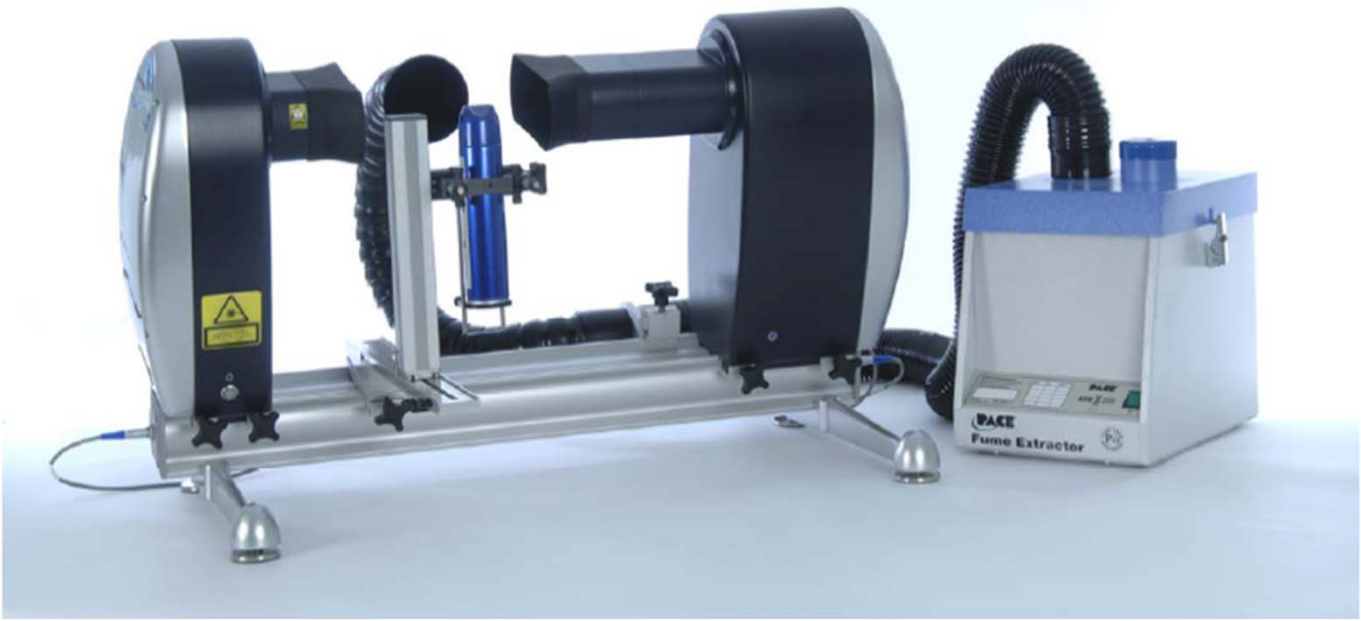
# Beam Steering



# Velocity Bias

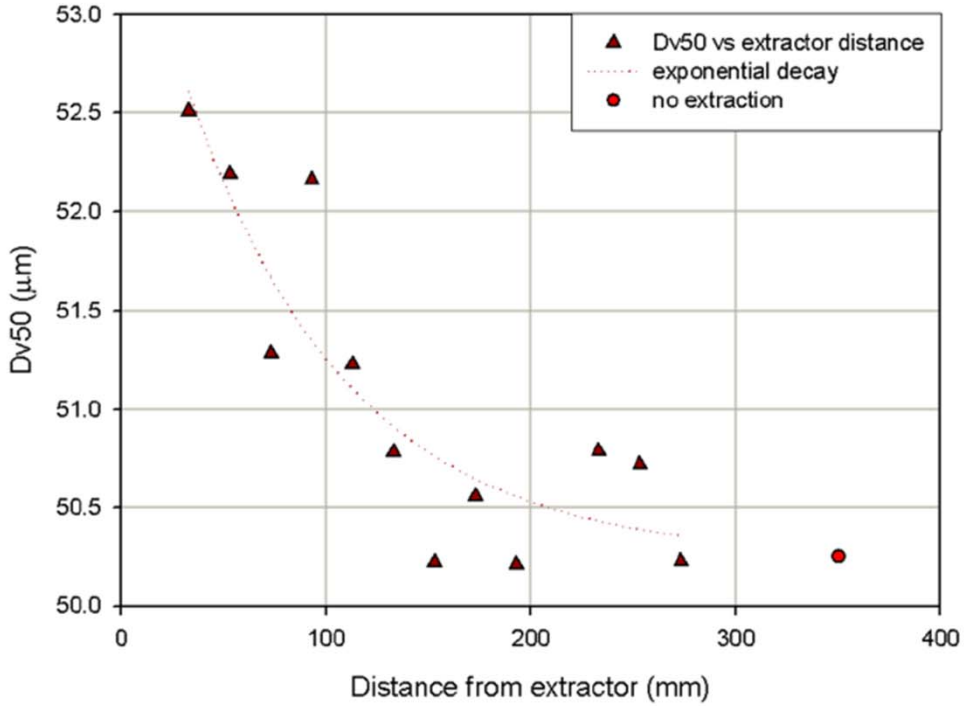
What happens if the extraction system is not effective:

- An extraction system is needed to ensure that all droplets travel through the laser beam at the same velocity.
- Without extraction the fine particles decelerate more quickly and are over sampled.
- An inefficient extraction system can cause a reduction in the measured particle size.



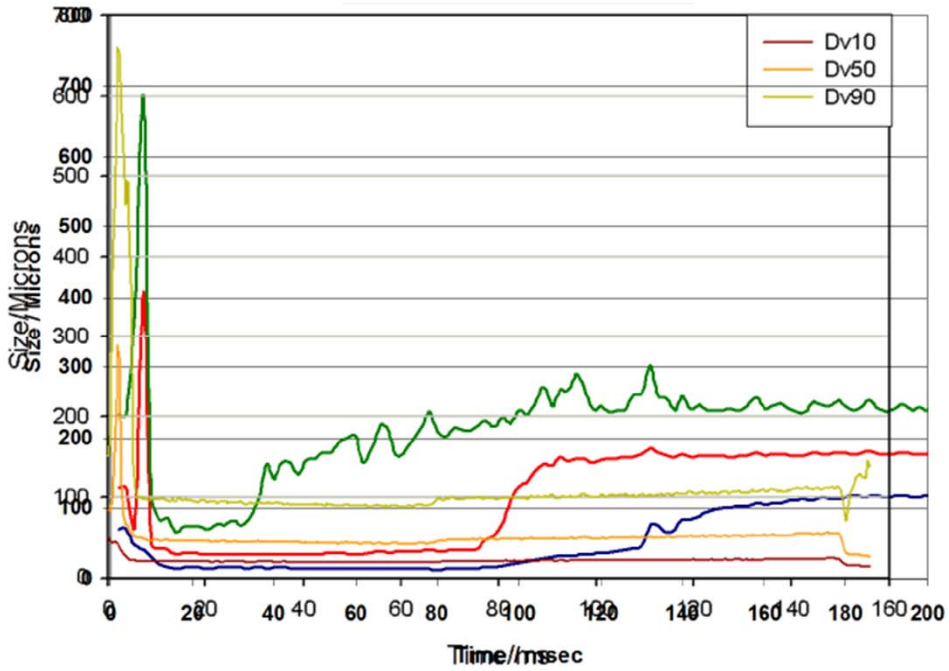
# Velocity Bias

- Effect on the measured size
- Efficiency of the extractor is reduced with distance and the particle size decreases.



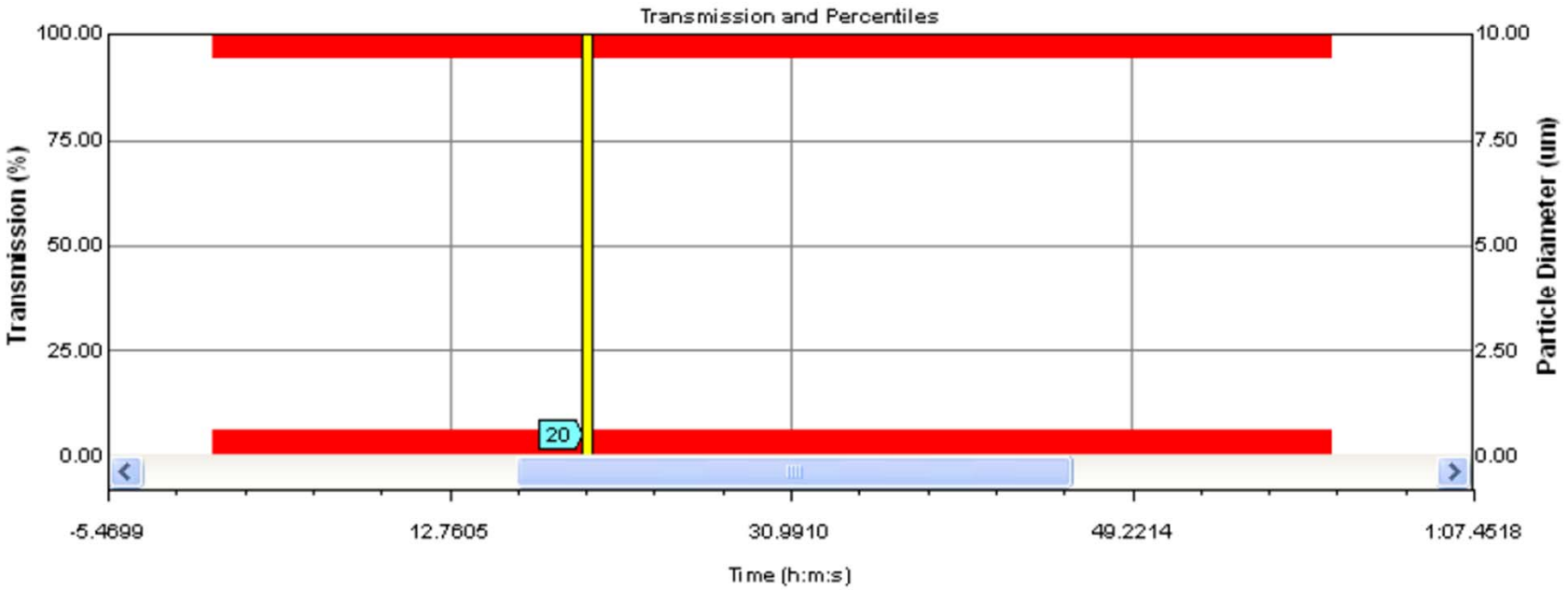
# Velocity Bias

- Effect on the profile
- If the extraction is not sufficient droplets may also fall back through the beam, affecting the stable phase of the transmission profile



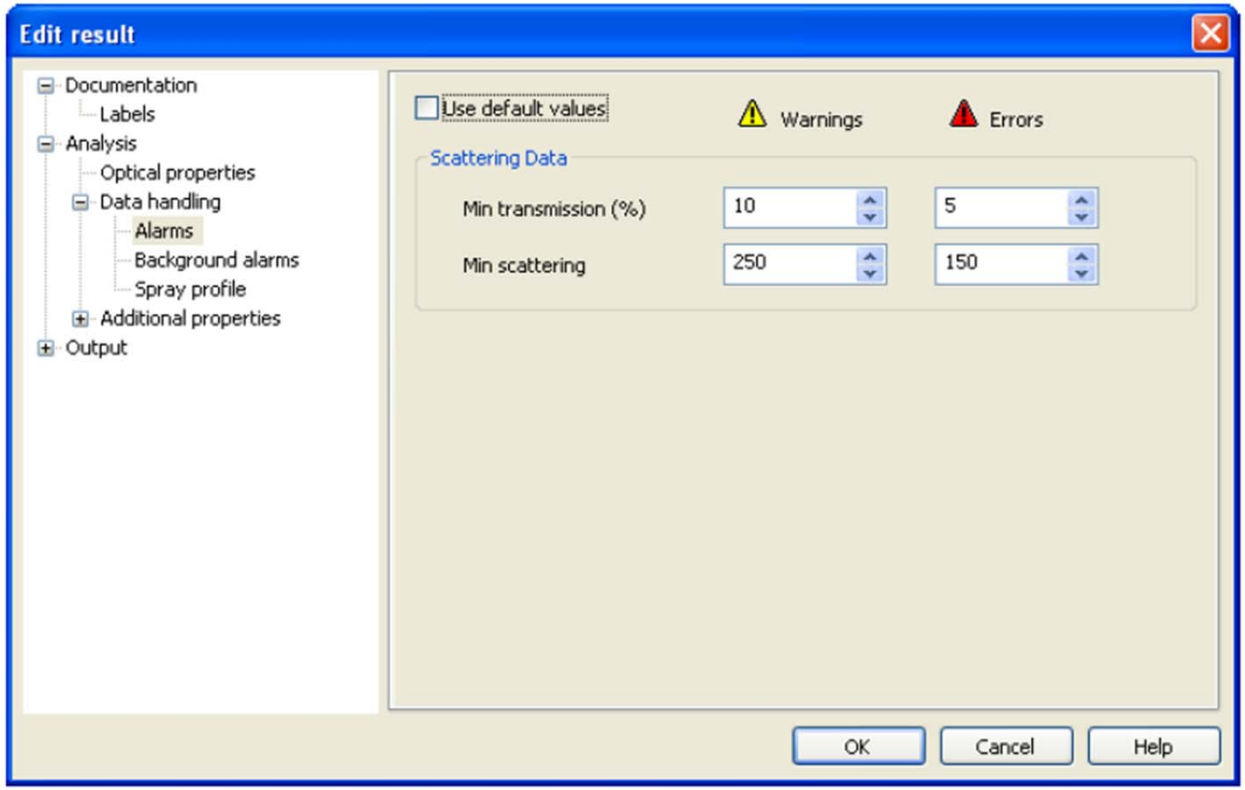
# Measurement at low and high concentrations

- Seeing red?
- If you have measured a spray and you see no results, only red bars, you may have to adjust the warning levels.



# Measurement at low and high concentrations

- Warning and Error levels.
- These can be altered in case you have a spray with a particularly low or high concentration

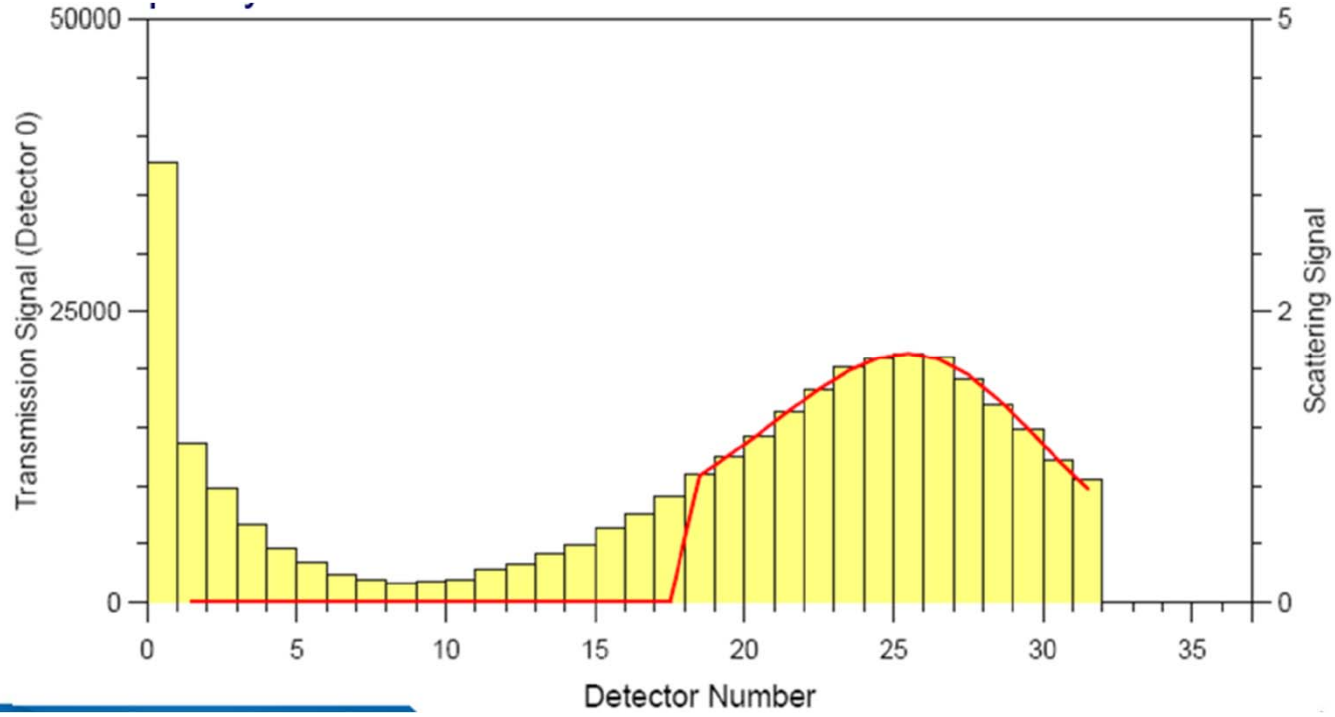


# Measurement at low and high concentrations

- Applying the new levels
- By setting the warning and error levels to zero, you will be able to see the data
- From which you can set a more appropriate error level to be used in future measurements.

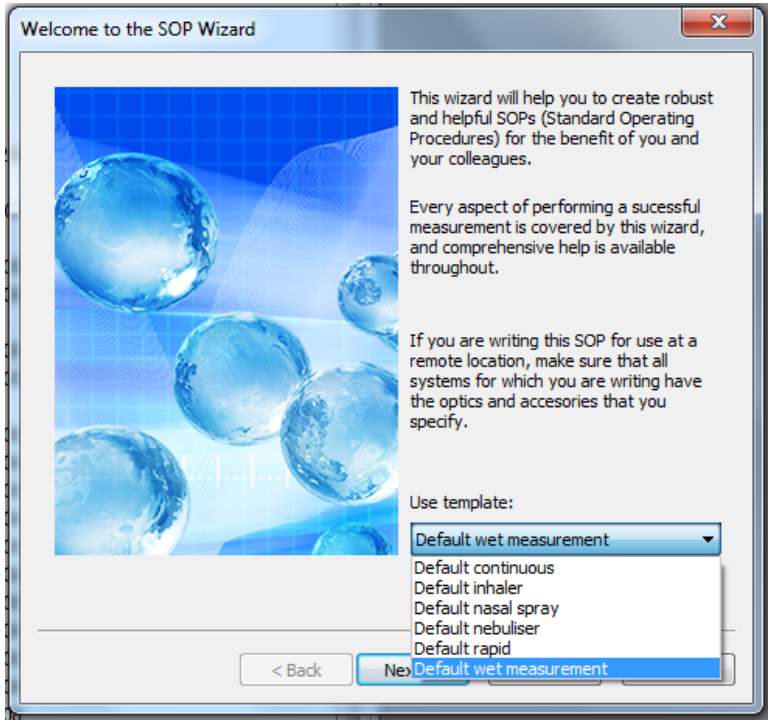
# Measurement at low and high concentrations

- Low signal levels
- If you are measuring at low signal levels, then it is also important to check the signal threshold level.
- Any data below this threshold will not be analysed this will affect the quality of the fit.



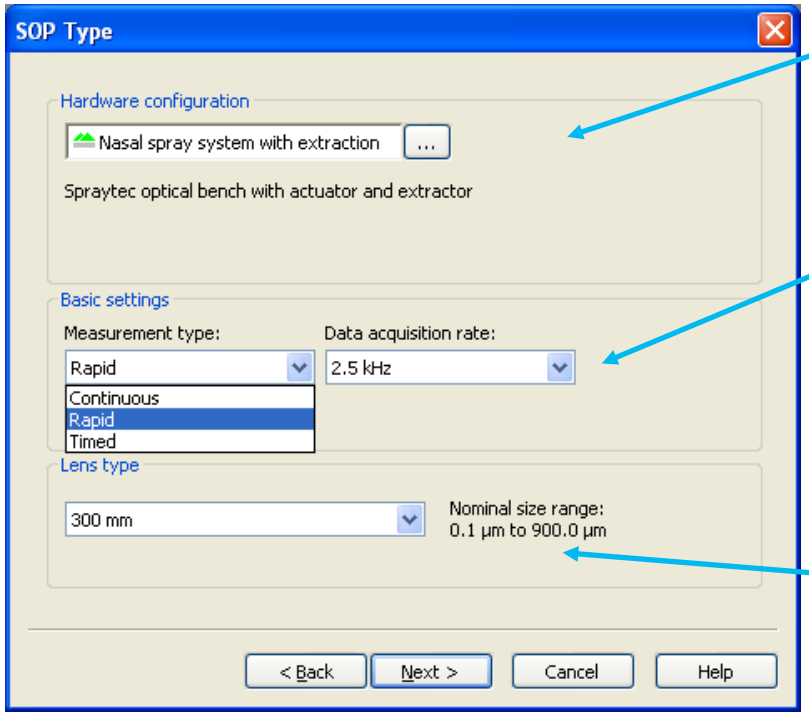
# METHOD DEFINITION AT THE INSTRUMENT

# Spraytec
# Method Definition



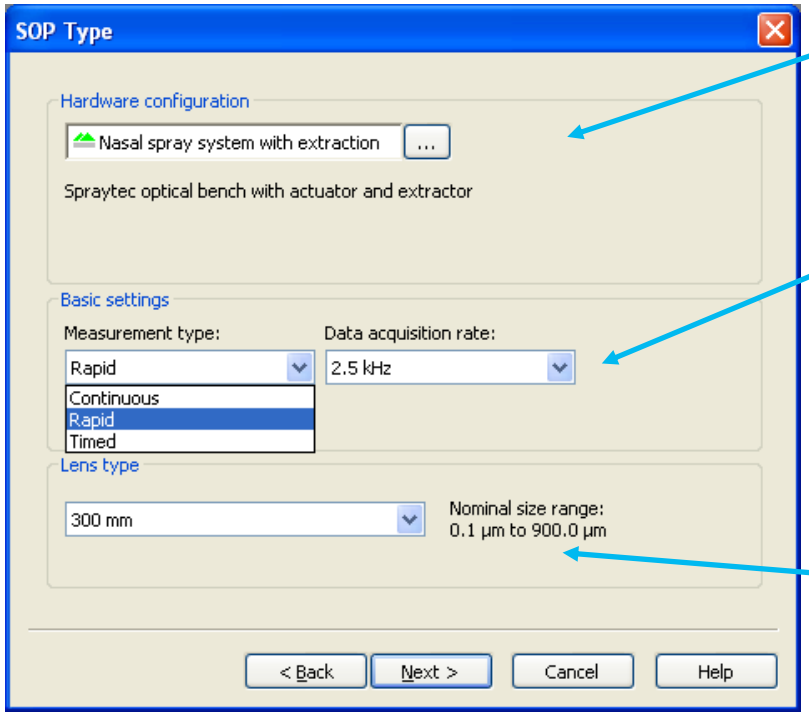

- SOP Wizard
  - » Similar to the Mastersizer 2000
- Guides users through the process of method development
- Automates the measurement process
- Template SOPs provided for different spray types.

# Spraytec SOP Settings
# SOP Type




- Hardware configuration
  - » Includes accessories
- Basic measurement settings:
  - Continuous mode
  - Rapid mode
  - Timed mode
- Lens Range
  - 300mm lens
  - 750mm lens

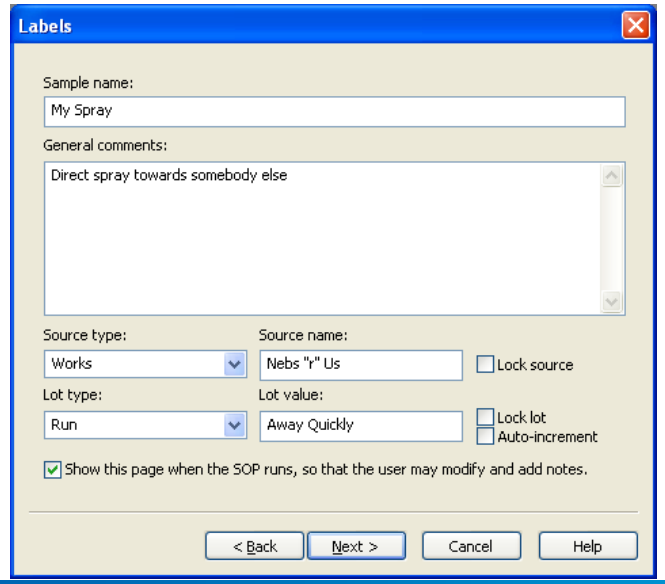
# Spraytec SOP Settings
# SOP Type

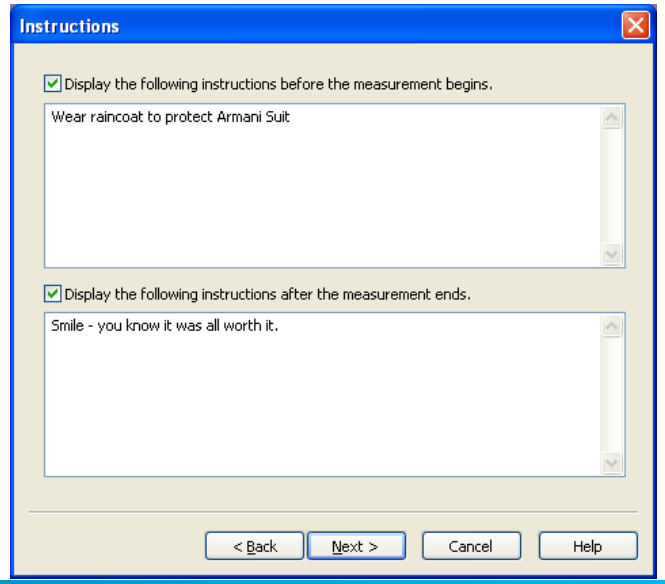



- Hardware configuration
  - » Includes accessories
- Basic measurement settings:
  - Continuous mode
  - Rapid mode
  - Timed mode
- Lens Range
  - 300mm lens
  - 750mm lens

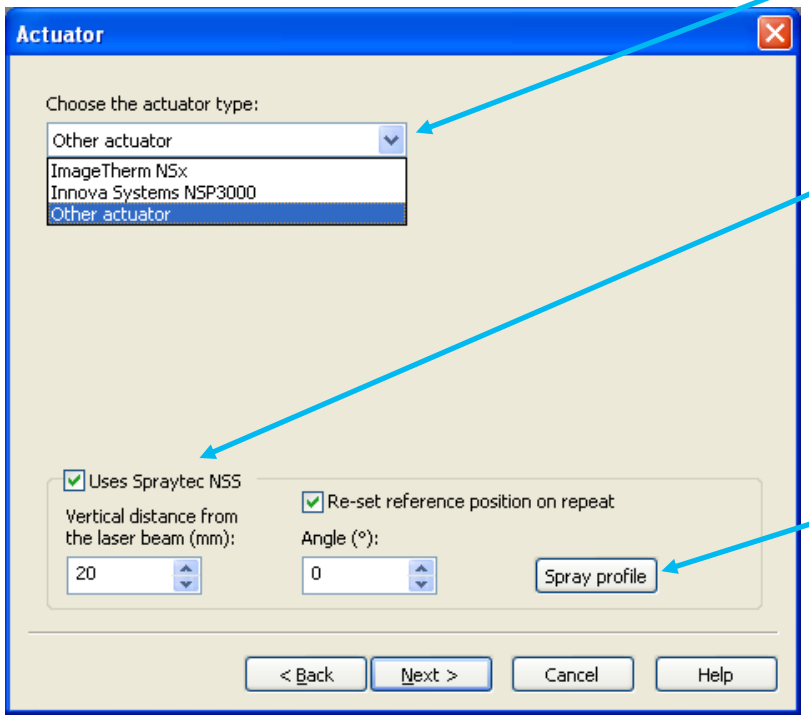
# Spraytec SOP Settings
# Labels and Instructions

- Similar functionality to the Mastersizer 2000
- Provides default sample details
- Prompts the user to carry out specific actions as part of running an SOP



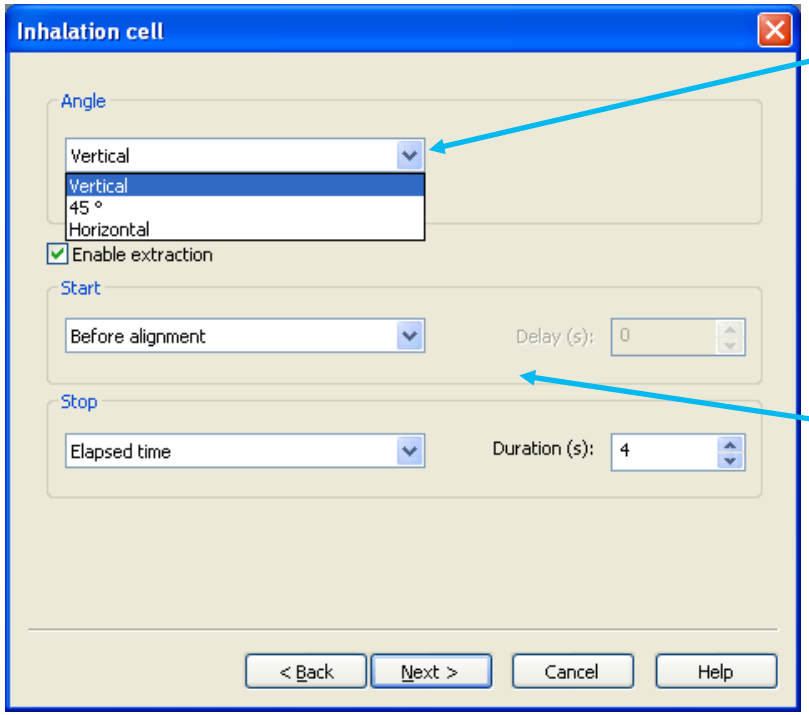



# Actuator Settings




- Actuator type
  - » InnovaSystems or Proveris
- Spraytec NSS settings
  - Distance and angle
  - Requirements for reference setting
- Spray profile
  - Aids the concentration calculation
  - Leave as default unless Cv is important to you…

# Inhalation Cell




## Cell Angle Setting

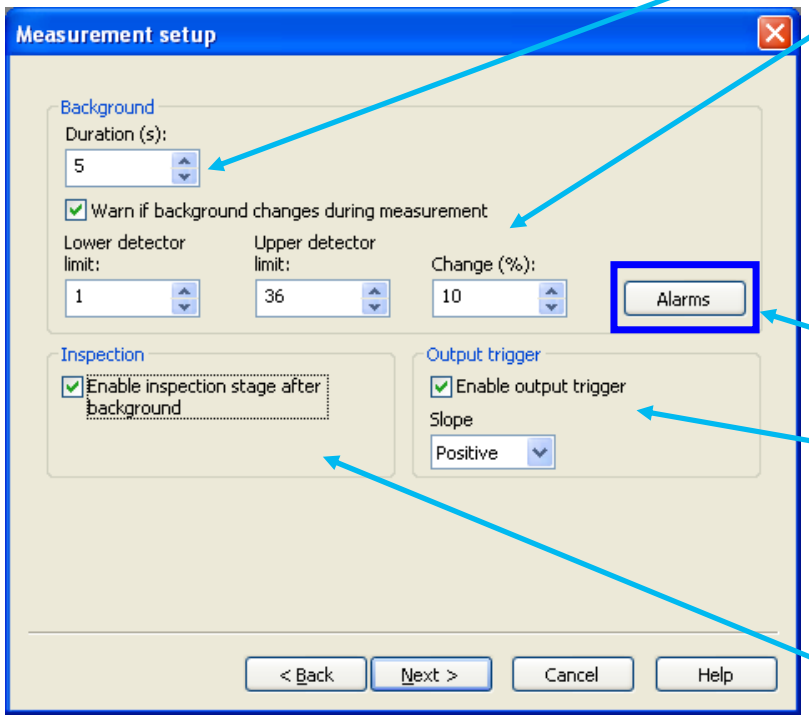
- Set vertical, 45 degrees or horizontal
- This is not verified during the measurement

## Extraction Settings

- Controls the primary pump
- Switch on: At alignment
- Switch off: At end of SOP

# Spraytec SOP Settings

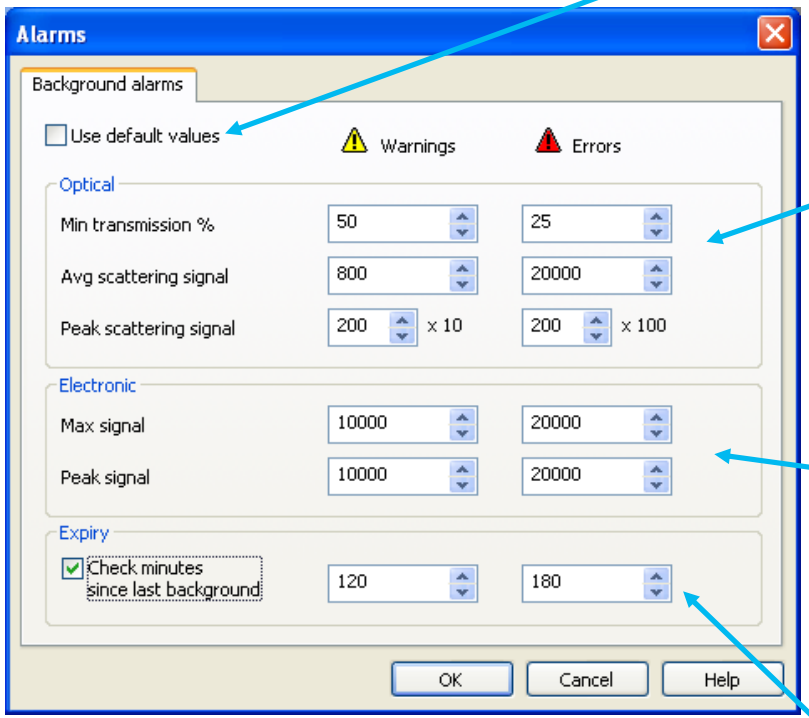
## Measurement Setup




- Background duration
- Background drift warning
  - Enables background check after measurement
  - Determine %age draft across the selected range of detectors
- Alarm settings
- **Enable Output trigger**
  - **Synchronise other devices with the measurement start**
- Enable Inspection Stage
  - Pauses the measurement after the background measurement

# Spraytec SOP Settings

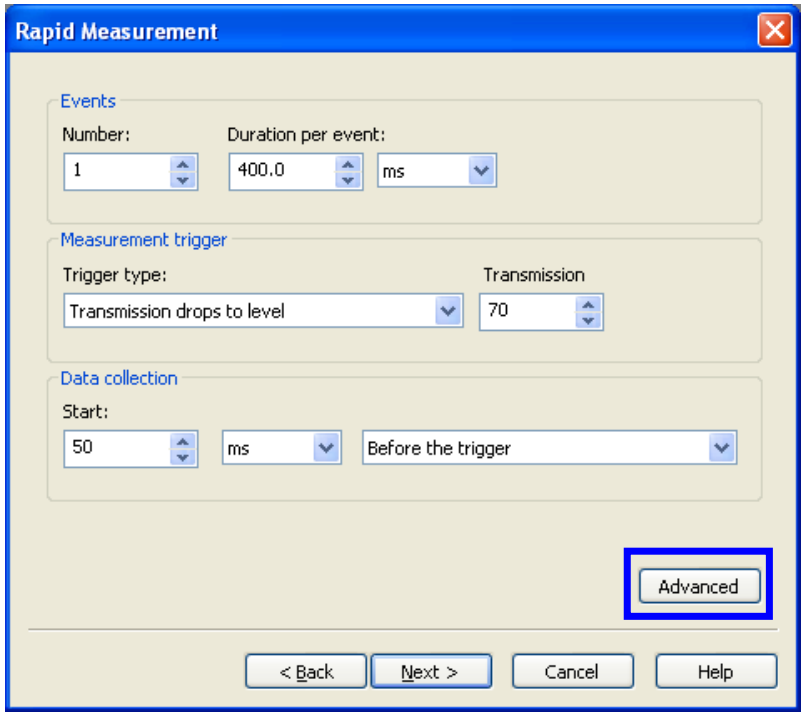
## Measurement Setup: Alarms




- Set Default values
  - Will ensure measures occur apart from if a significant error occurs
- Tests for the optical background
  - Minimum transmission signal
  - Average scattering
  - Peak scattering signal
- Tests for the electronic background
  - Average scattering
  - Peak scattering signal
- Background expiry time

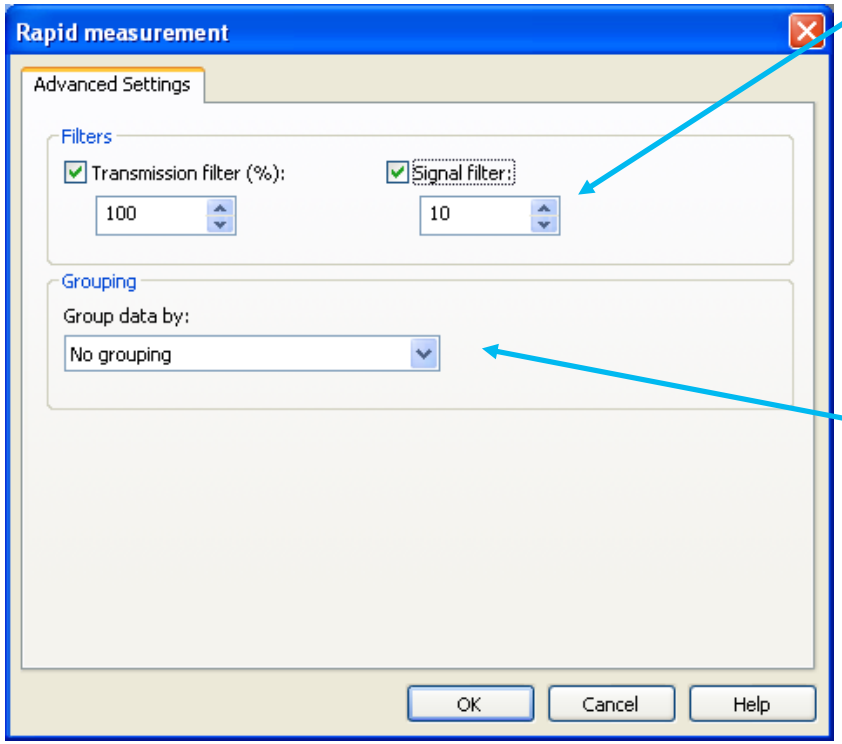
# Spraytec Measurement Triggering

## Rapid mode




- **Triggering based on:**
  - » Manual mouse click
  - » Transmission level
  - » Scattering level
  - » External Signal
    - TTL trigger
    - Switch trigger
- **Can collect data from before the trigger event**
  - » Max buffer size of 3 sec
- **External trigger can also be used to group data**
  - » Useful when multiple events occur within one measurement

# Rapid measurement Advanced Settings




Filters

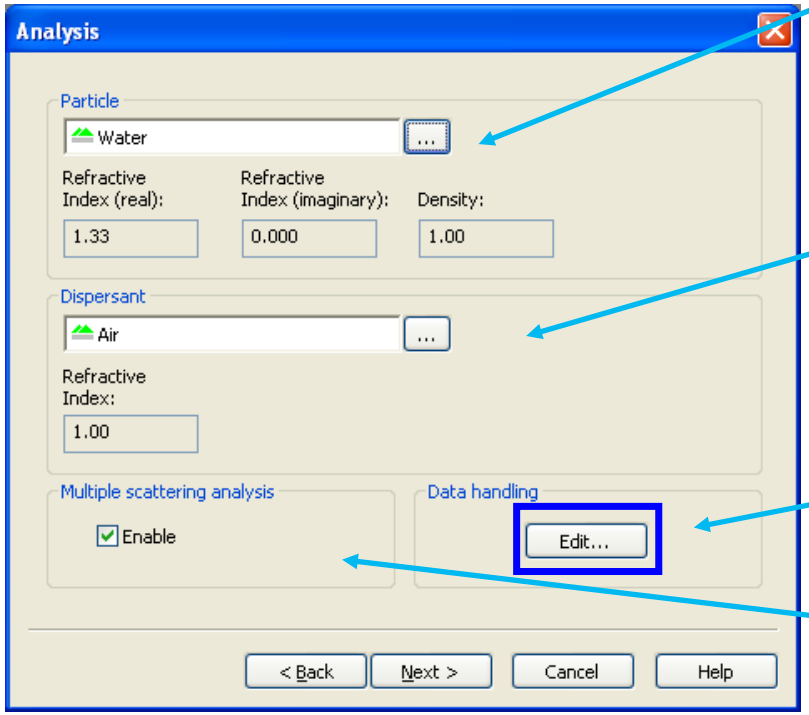
- Transmission: Removes all data above a specified transmission level
- Signal: Removes all data below a specified average signal level

**Can put data into groups based on an external trigger**

- Only used for rapid, repeating, pulsed spray events

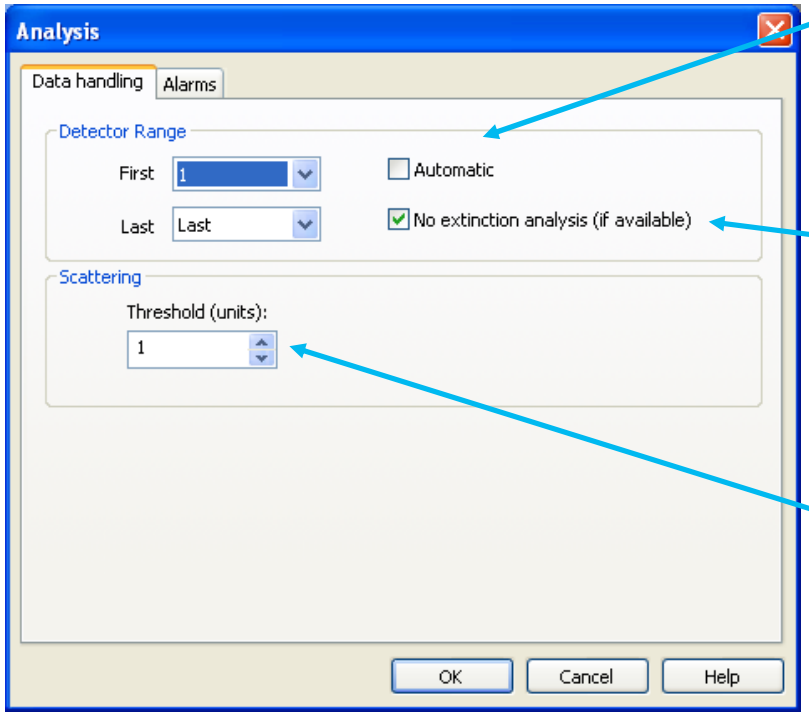
# Spraytec SOP Settings

## Analysis Options




- Particle Properties
  - Refractive Index
  - Absorption
- Dispersant Properties
  - Refractive Index
  - Normally set to Air
- Data handling options
- Multiple scattering analysis
  - Switched on as default
  - Should be disabled for nasal sprays

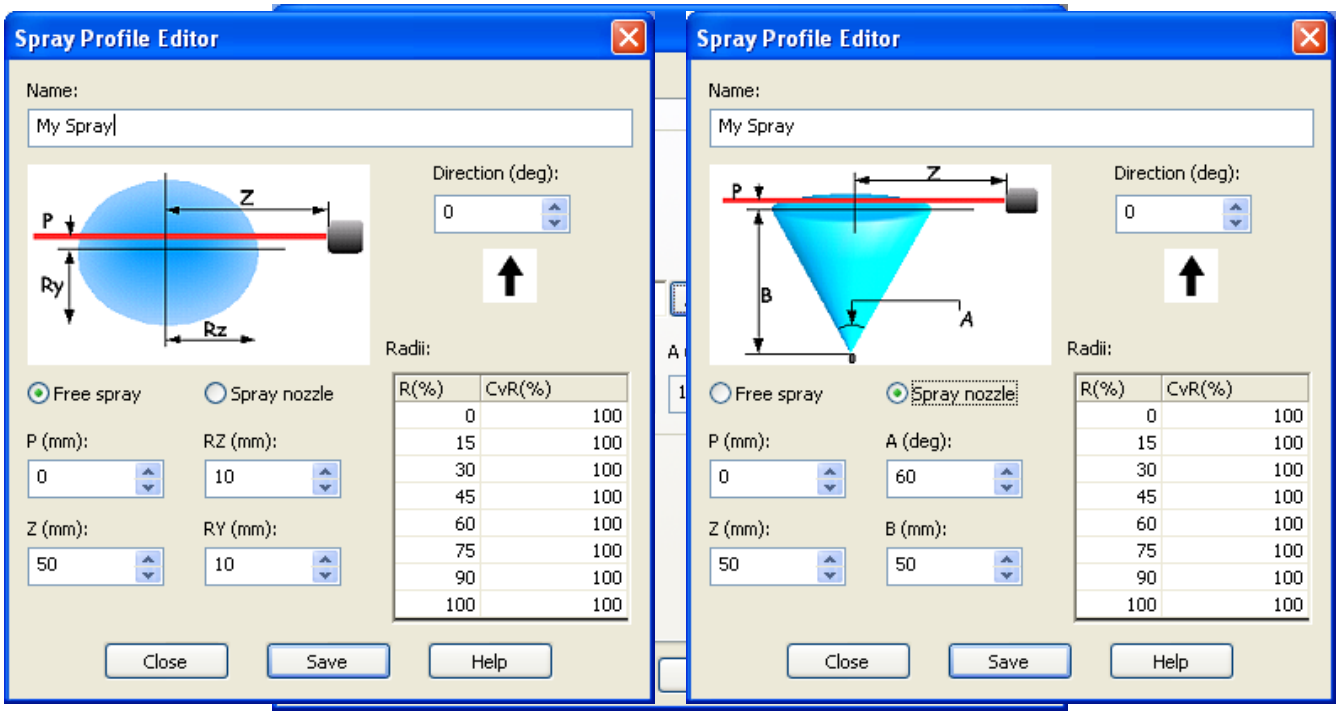
## Analysis Options: Data Handling




- Detector range for the analysis
  - Allows data to be removed
  - Can apply first ring kill using an automatic algorithm
- As default, the extinction analysis is turned off
  - Requires an accurate path length to work…
- Scattering Threshold
  - Data required before a detector channel is included in the analysis
  - Normally set at 0 or 1

# Spraytec SOPs  Analysis Options

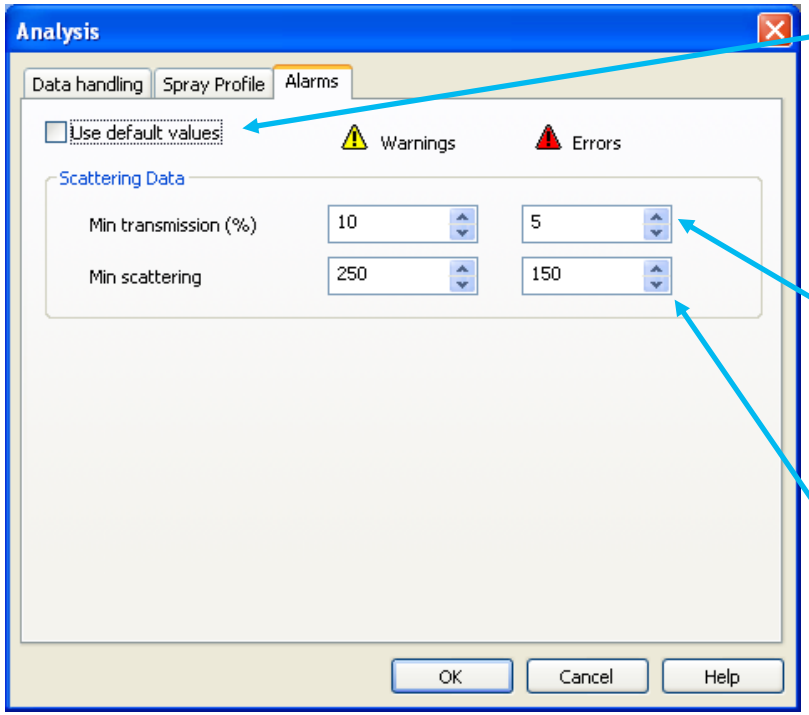
## Data Handling : Spray Profile




- Input path length or spray profile information
  - » Important for concentration calculations and extinction analysis

# Spraytec SOPs Analysis Options

## Data Handling : Analysis Alarms




### Set Default values

- Will ensure measures occur unless a significant error occurs

### Minimum transmission alarm

- Stops size calculation if the spray is too concentrated

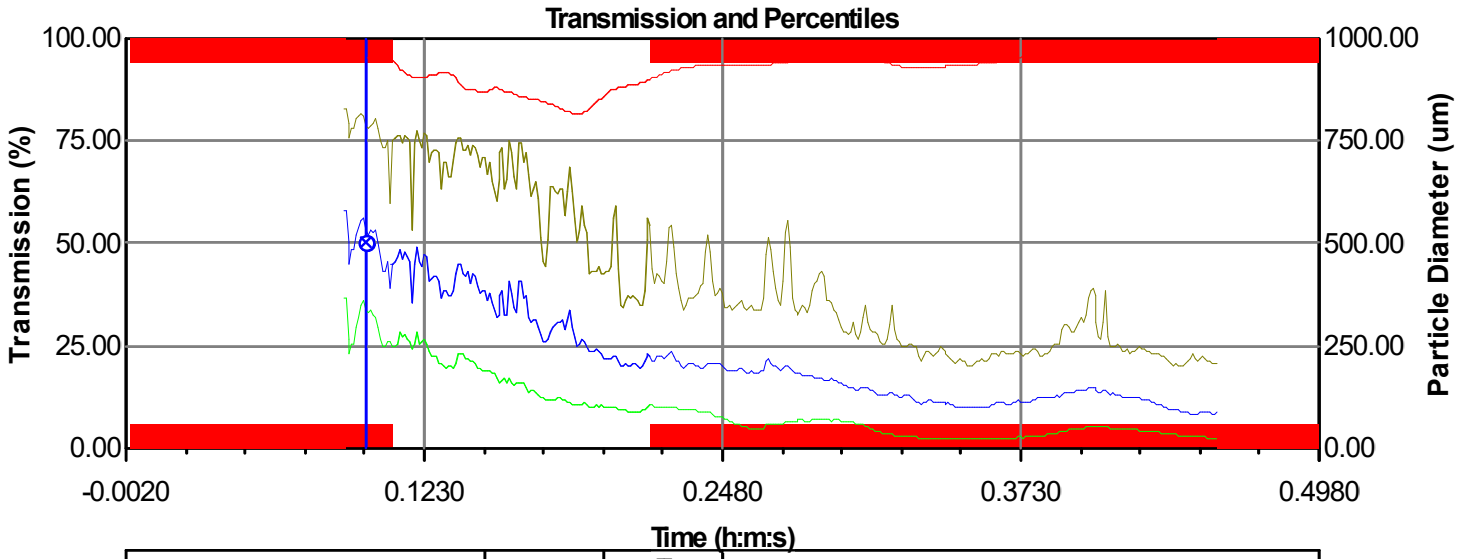
### Minimum scattering alarm

- Stops size calculations if the spray is too dilute

# Spraytec SOPs Analysis Options

## Data Handling : Analysis Alarms

Sample : Placebo nasal dpi
Event: 1 +0.0010 (s)

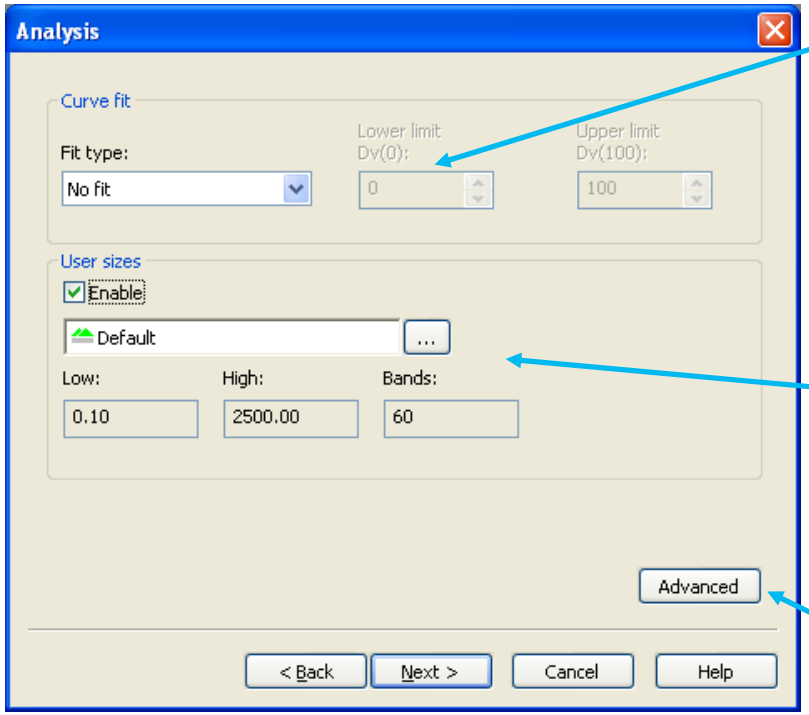



| Title | Legend | I | Correction Equation |
|---|---|---|---|
| Trans (%) | | – | – |
| Dv(10) (µm) | | – | – |
| Dv(50) (µm) | | – | – |
| Dv(90) (µm) | | – | – |

demo 31st aug06.smea\Experiment 1\Placebo nasal dpi 1.psh

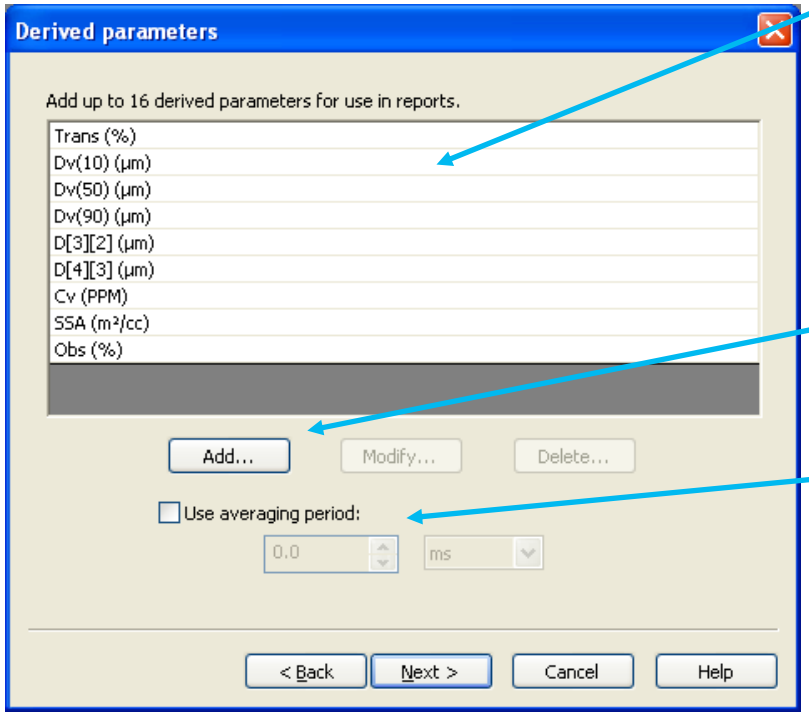
# Spraytec SOPs Analysis

## Additional Parameters




- Use 2-parameter curve fit
  - Rosin Rammler model
  - Log-Normal model
  - Need to specify percentile range for the curve fit
- Change User sizes
  - Size range
  - Linear or log spacing
- Advanced Options
  - Allows the default size range of the analysis to be changed

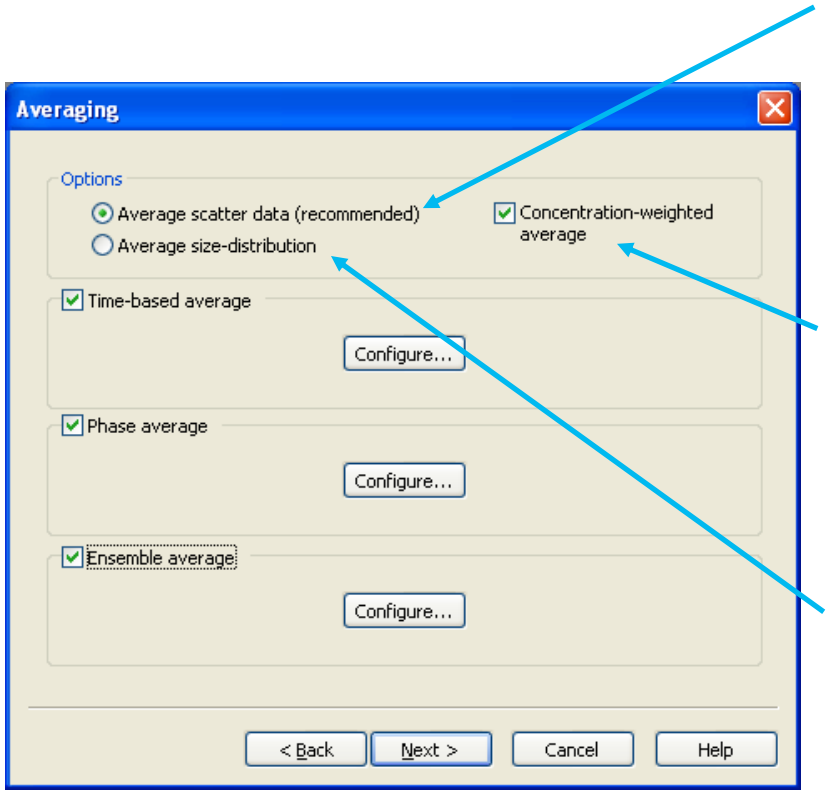
# Spraytec SOPs Derived Parameters




- List of parameters which will be calculated as part of a measurement
  - Can define a maximum of 16
- Add new parameters here….
- Can set an averaging period for each parameter
  - Important if you decide to display the average or StDev on the size history display.

# Spraytec SOPs Rapid Measurement

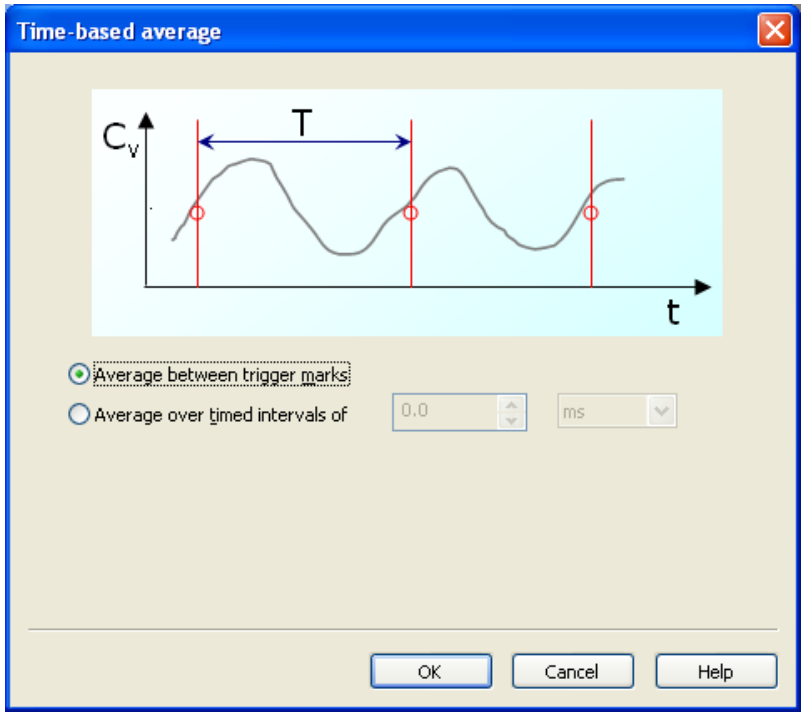
## Averaging




- Data-based average
  - » Calculated by averaging the scattering data over a specific time period. A new size distribution is then calculated for this average data set
- Concentration weighting
  - » When enabled, corrects for changes in the particle concentration when calculating an average
- Result-based average
  - » Calculated by averaging the size distribution size band data over a specific time period, producing an average size distribution

# Spraytec SOPs Rapid Measurement

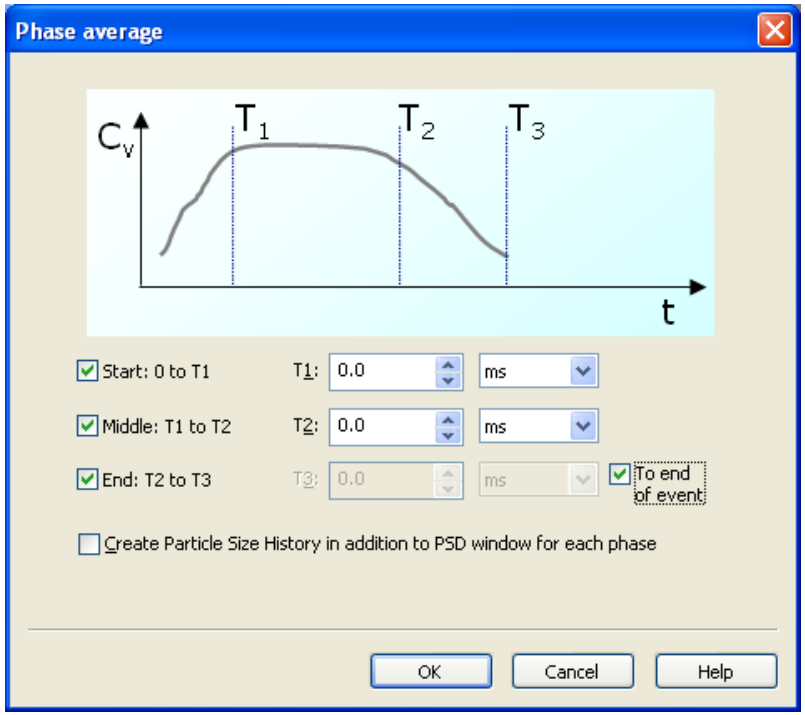
## Time-based Averaging




- Averages the data over fixed time periods
- Time period specified by
  - » External trigger events
  - » Specified time interval
- Produces a new Particle Size History containing the average results from each time period

# Spraytec SOPs Rapid Measurement

## Phase Averaging

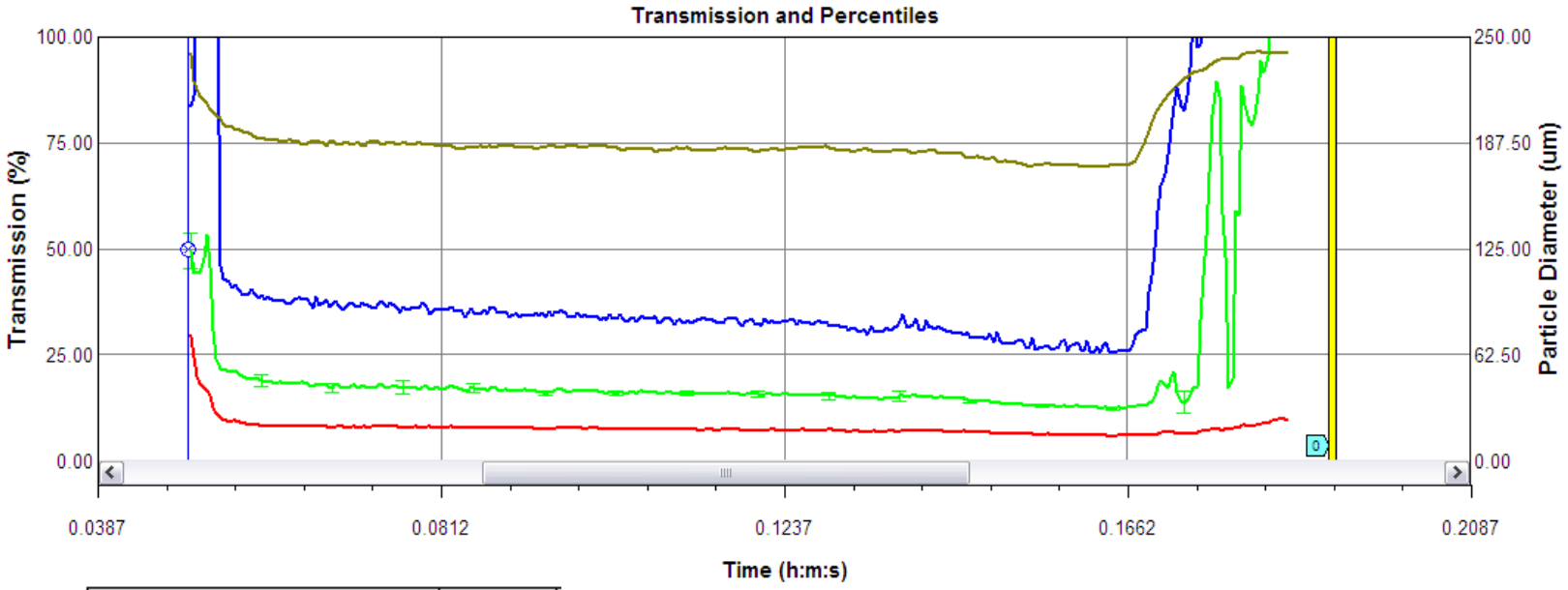



- Averages the data across a maximum of 3 separate “phases” with an event
  - » Start / Formation Phase
  - » Middle / Fully Developed Phase
  - » End / Dissipation Phase
- First phase starts at the beginning of the event
- Produces average size distributions for each phase and a new PSH if required

- Meets the FDA's guidance for nasal spray testing

# Nasal sprays

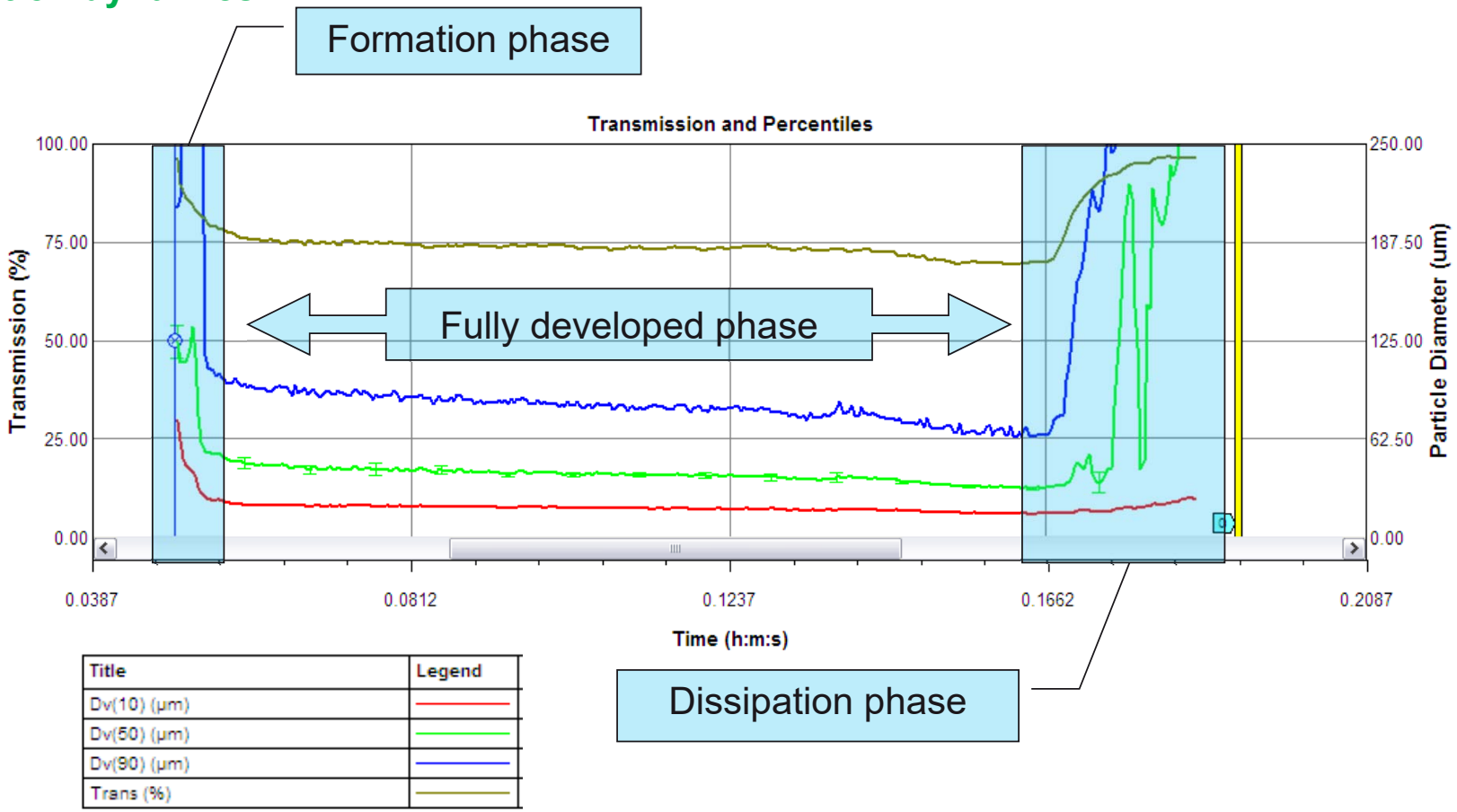
## Atomisation dynamics




| Title | Legend |
|---|---|
| Dv(10) (µm) | |
| Dv(50) (µm) | |
| Dv(90) (µm) | |
| Trans (%) | |

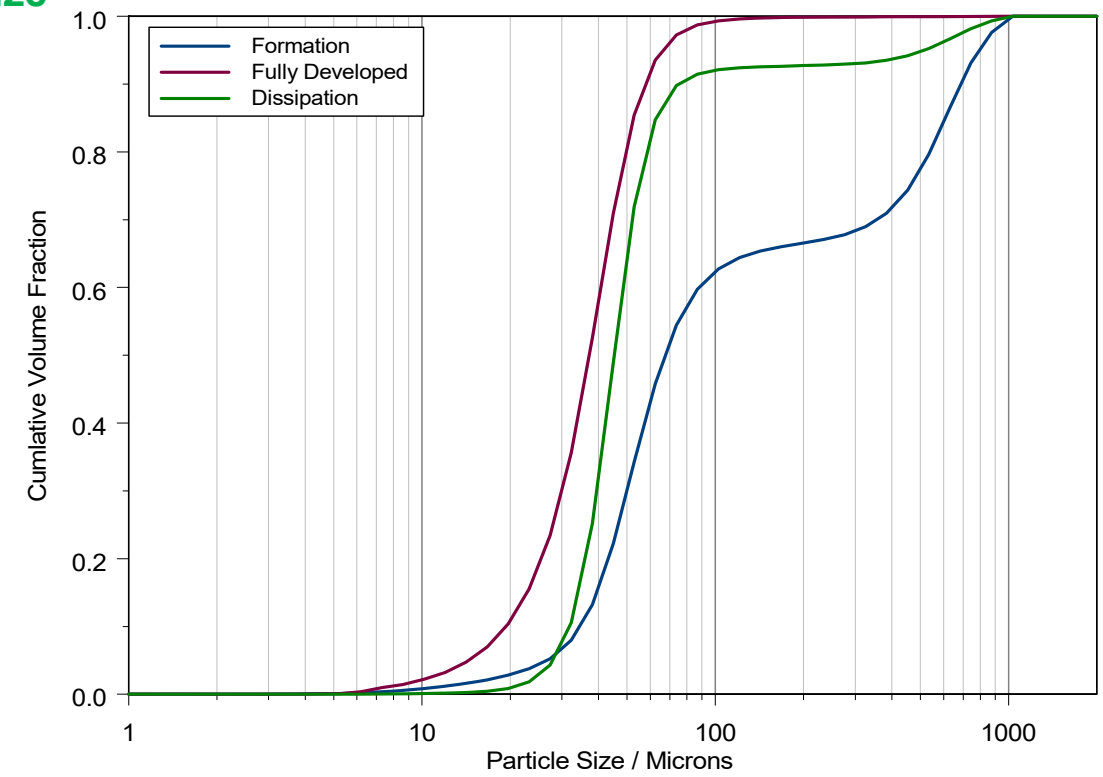
# Nasal sprays

## Atomisation dynamics



# Nasal sprays

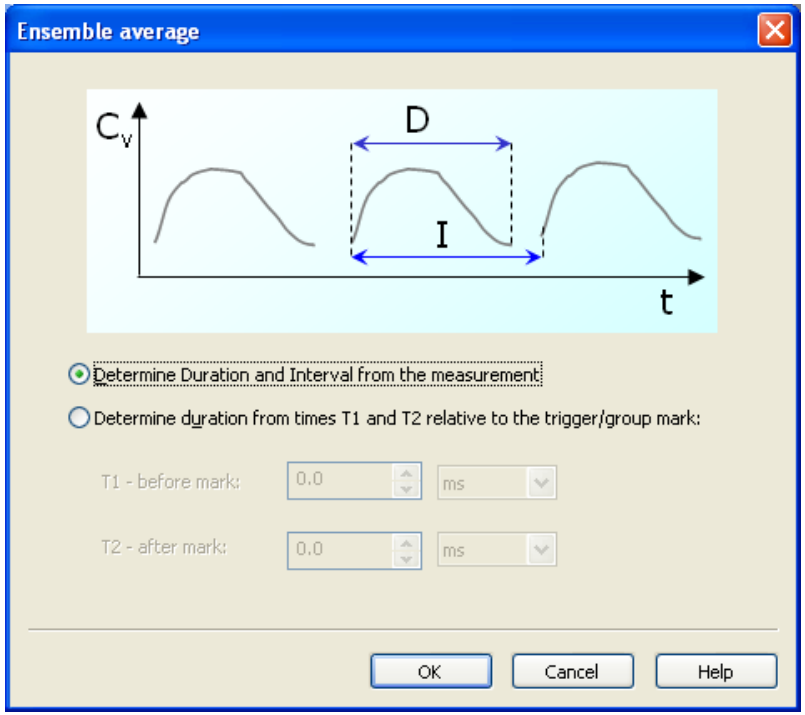
## Delivered particle size




| Phase | Dv10 / µm | Dv50 / µm | Dv90 / µm |
|---|---|---|---|
| Formation Phase | 34.54 | 67.93 | 690.13 |
| Fully Developed Phase | 19.33 | 37.2 | 58.31 |
| Dissipation Phase | 31.83 | 45.27 | 75.36 |

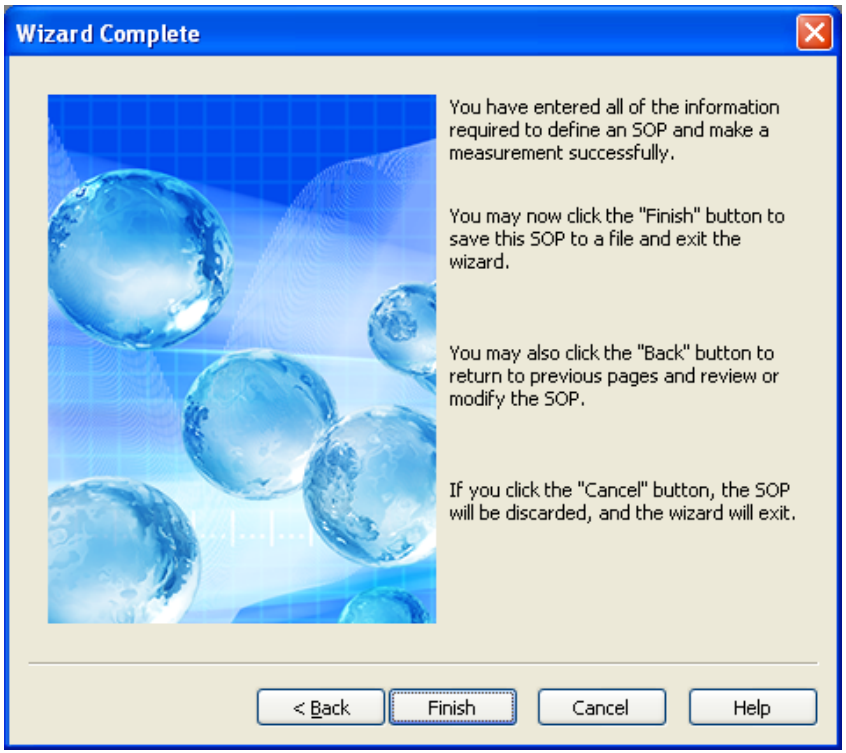
# Spraytec SOPs Rapid Measurement

## Ensemble Averaging




- Use to calculate an average event
- Averages the data for the same time point in each event
  - » Start and stop time defined by the trigger position
- Produces an average Particle Size History file

# Spraytec SOPs Wizard Complete!



# Spraytec Inhallation cell

# PHARMACEUTICAL AEROSOLS

## When can we use Laser Diffraction?

- Nebulizers and soft mist inhalers
- Dry powder inhalers (DPIs)
- Meter-dosed inhalers (MDIs)
- Nasal sprays
- What might we need?
  - *Inhalation cell*
    - Pump
    - Flow meter
    - Critical flow controller
  - *Nasal spray support*
    - Actuator

# Pharmaceutical Aerosols

## Why use Laser Diffraction?

- Access to Dynamic Information
- Formulation Screening Capabilities
- Measurements under “real” conditions

# STP2300 Spraytec Inhalation cell

- For the measurement of
  - Metered-dose Inhalers
  - Dry-powder inhalers
  - Nebulisers
- Enables measurements in an enclosed cell at a controlled flow rate
- Can be mounted
  - Vertically – measurement in the throat
  - Horizontally – measurement in the mouth
  - 45 degrees – nebulisers
- Compatible with standard inhaler testing equipment (e.g. USP throat, cascade impactor)

# summary regulatory requirements

## for DPI particle size

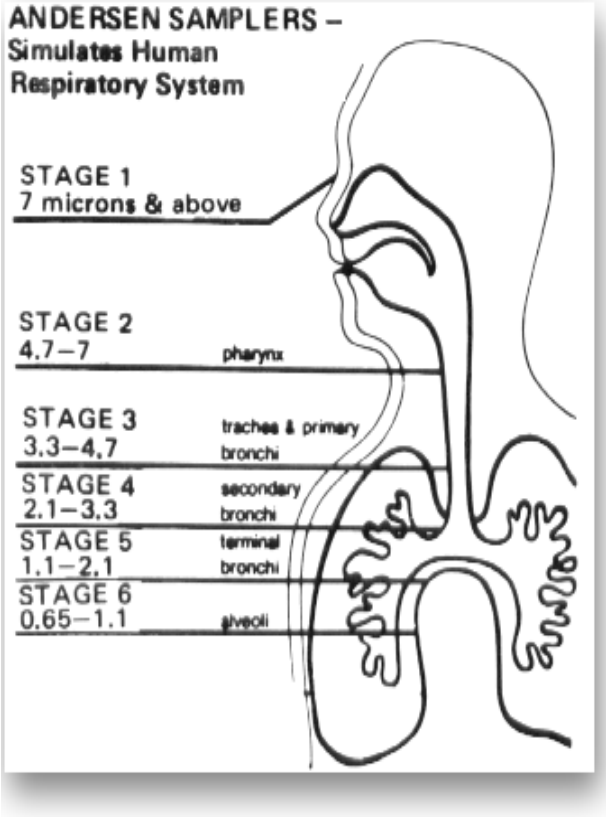
- Each device has a different resistance to air flow.
- Flow rate is defined to give a certain pressure drop of across the device
  - USP requires 4kPa (with max flow rate of 100l/m)
- The inhalation volume is also defined:
  - USP : 4L
  - FDA/Eur. Ph. : 2L
- Critical flow control is required
- Pre separator required for cascade impaction

# STP2310: USP Induction Port

- USP Throat from Copley Scientific
- Generally used with
  - Metered-dosed inhalers
  - Dry-powder inhalers

# Andersen Cascade Impactor ACI

# Andersen Cascade Impactor ACI




# STP2311-(220/110) HCP5 High Capacity Pump

- From Copley Scientific
- Designed for testing inhalers
- Regulated vacuum from 0l/min to 250l/min
  - » Dependent on inhaler device resistance
- Unregulated output of 416l/min
  - » For use with flow controllers(TPK2000) for DPI testing
- Requires a switching box to be synchronised with the Spraytec
- This pump is designed to be used with devices which deliver particles over short time periods – not minutes

# STP2329 TPK2100 critical flow controller

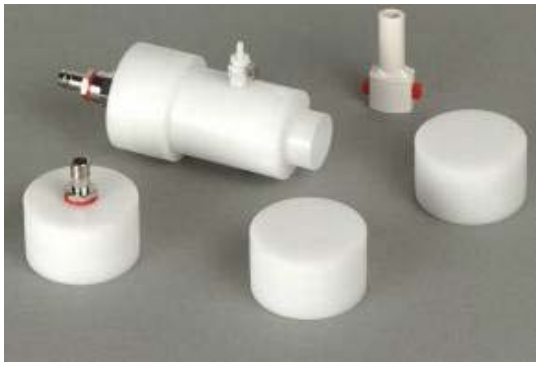
- Flow control valve
  - » Automatically opened using the Spraytec TTL trigger
  - » Control the flow use to activate DPI
    - Desired pressure drop is achieved instantaneously at the start of the measurement
    - Monitors pressure drop across the flow valve to ensure sonic flow is achieved
- Measures pressure drop across an inhaler
  - » Requires STP2305 – dose collection device
  - » 0kPa to 15kPa
- Can log flow data from DFM2000 (STP2314)
- STP2328 Copley Scientific Calibration Kit for the TPK2100 critical flow controller

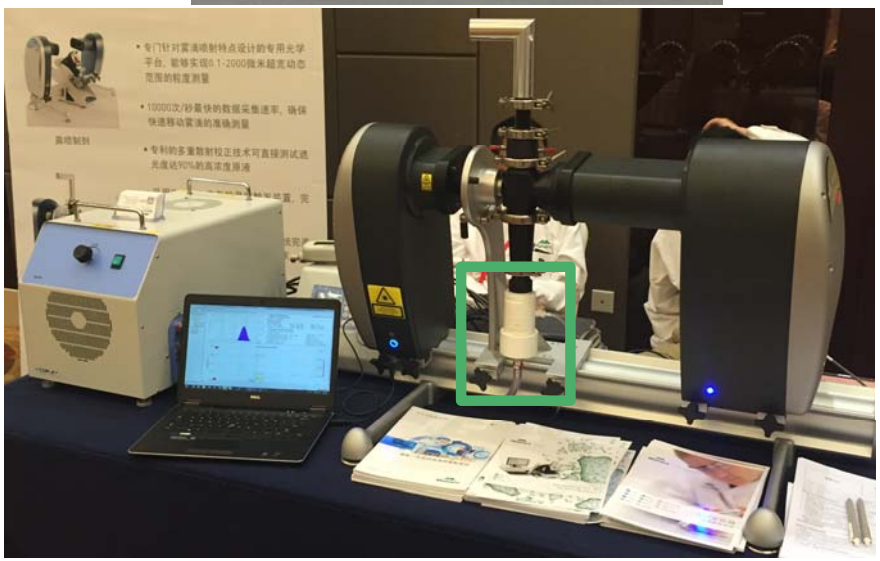
# STP2314 DFM2000 Flow meter

- Measures flow rate produced by the HCP5 pump (STP2311)
- Measurement range
  - » 0l/min to 290l/min (0.1l/min resolution)
- Interfaces with TPK2000 critical flow controller
- Includes an adapter to attach the flow meter to the UPS induction port


# STP2305 Dose Collection Device

- From Copley Scientific
- Collects the dose emitted from an inhaler prior to a vacuum pump
  - » Prevents damage to the pump
- Required during DPI testing with the TPK2000 critical flow controller
  - » Measures pressure drop across the device
- Includes 100 glass filters
  - » And replacement seals

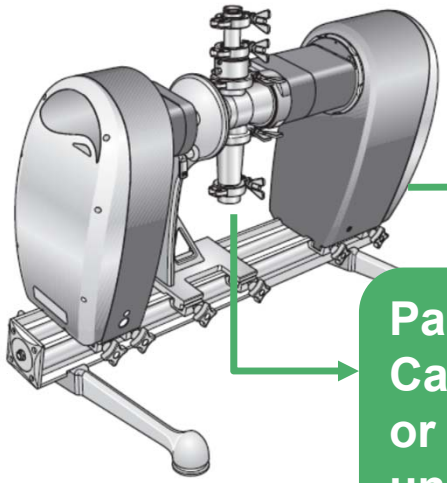




# STP2306 Mouth Piece adapter

- from Copley Scientific
- Connects inhaler to
  - » USP Throat (STP2310)
  - » Dose collection device (STP2305)
  - » Or directly to the inhalation cell
- Requires purchase of moulding tool STP2307
  - » Example inhaler must be supplied with the order

# Metered-dose inhaler set-up



Input:
USP induction port (STP2310) &
Mouthpiece adaptor (STP2306 &2307)

Flow meter
DFM2000
STP2314

Spraytec and inhalation cell:
STP5315

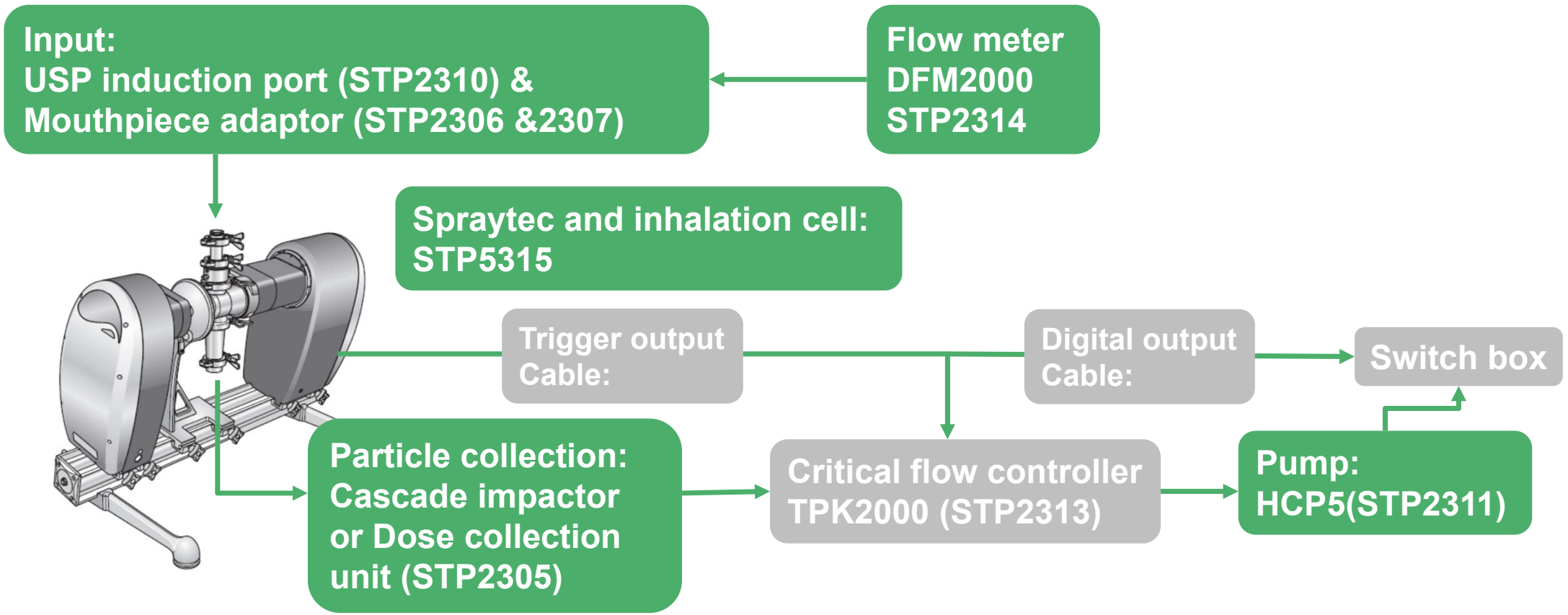
Digital output
Cable

Switch box
STP2400

Particle collection:
Cascade impactor
or Dose collection
unit (STP2305)

Pump:
HCP5(STP2311)

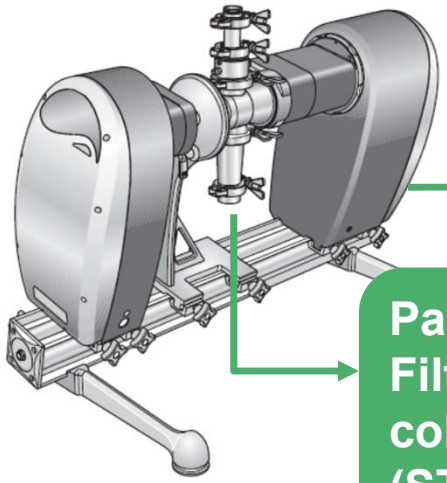
# Dry-powder inhaler set-up



# Nebuliser set-up

**Input:**
**Mouthpiece adaptor (STP2306 &2307)**
**T-piece (customer)**

**Flow meter**
**DFM2000**
**STP2314**



**Spraytec and inhalation cell:**
**STP5315 in horizontal position**

**Digital output**
**Cable**

**Switch box**
**STP2400**

**Particle collection:**
**Filter (STP2309) or**
**collection unit**
**(STP2305)**

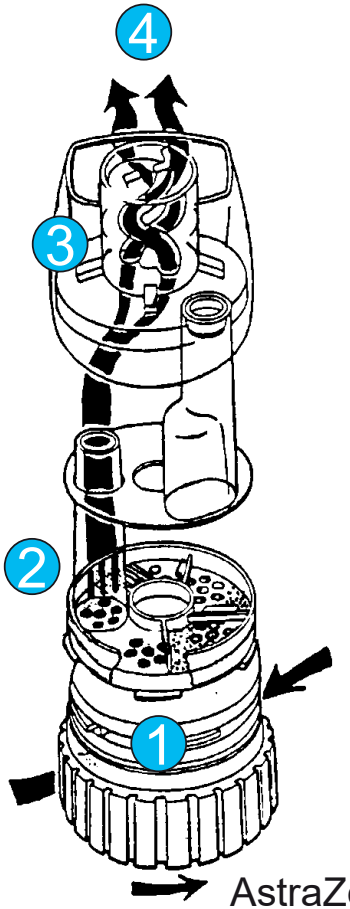
**Pump:**
**HCP5(STP2311)**

# Dry Powder Inhalers

## Principle of operation

- Delivers micronised drug (+ excipient)
  - Drug: 1 -10 microns
  - Excipient: 60 - 200 microns

- Drug Delivery Process:
  1. Powder is metered prior to delivery
  2. Powder is entrained when patient inhales
  3. Shear is applied to disperse agglomerates
  4. Aerosol is delivered to the patient

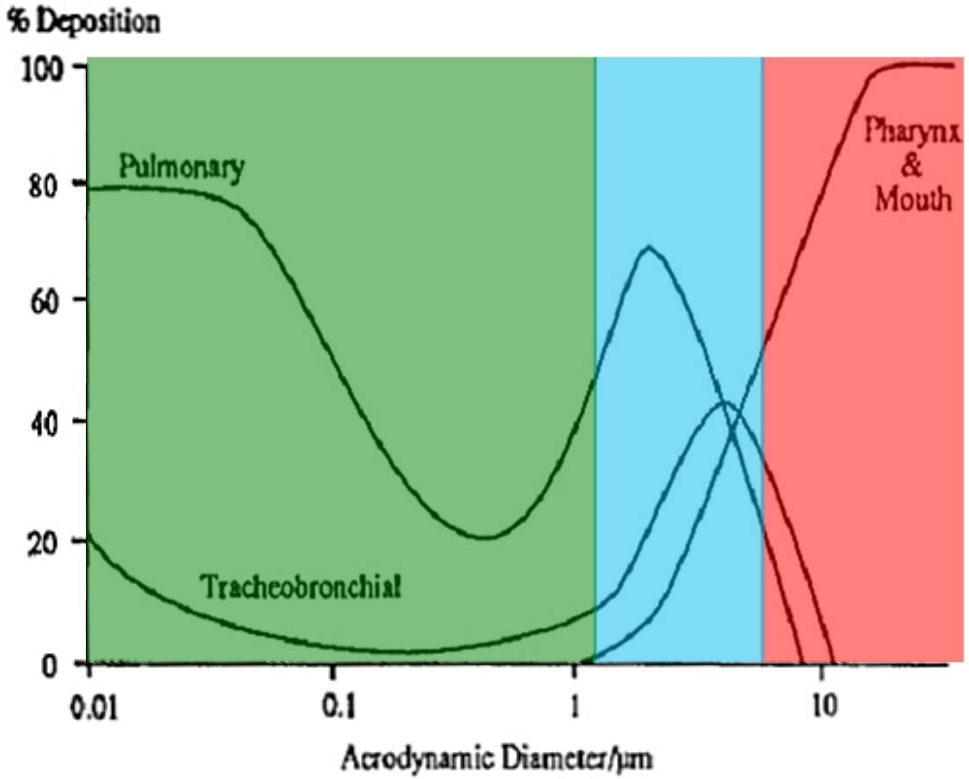



AstraZeneca
Turbuhaler

# Pharmaceutical Aerosols Why?

## Inhaled drug formulations

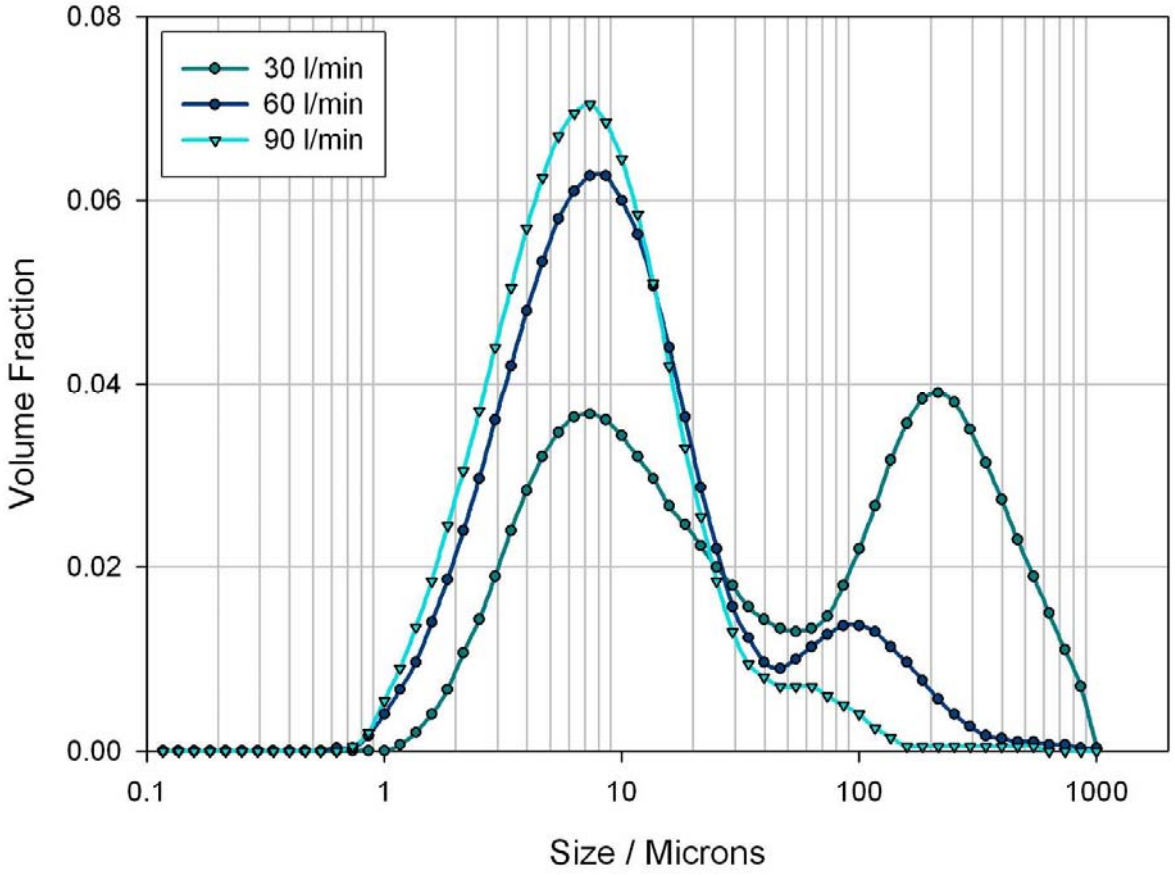
- Throat Deposition
  - » Impaction (>5μm)
- Upper Airways
  - » Sedimentation (1-5μm)
- Lung Deposition
  - » Diffusion (<2μm)




Clive Washington: Particle size analysis in pharmaceutics and other industries: Theory and Practice p179
Ellis Horwood, 1992 ISBN: 0 13 651613 0

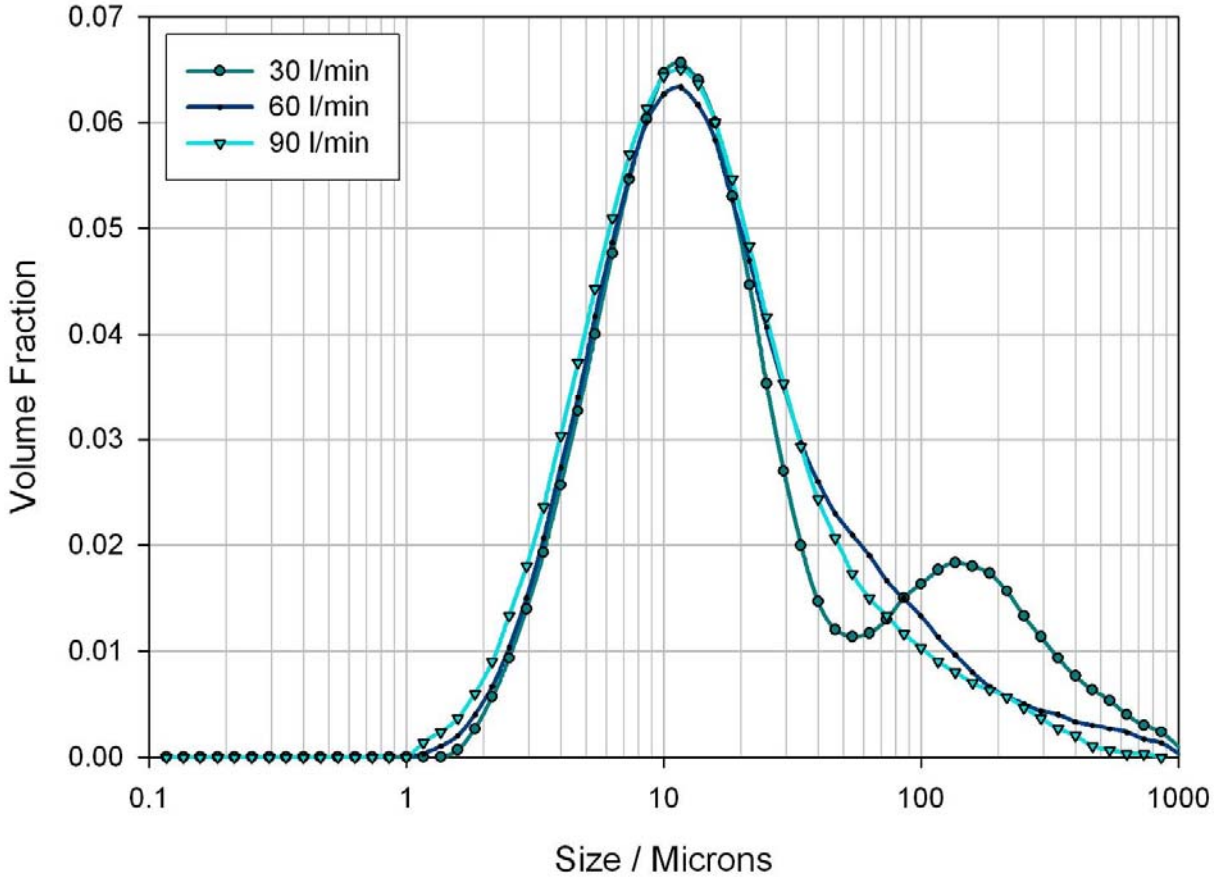
# Particle size flow rate dependence

## Unprocessed lactose powder



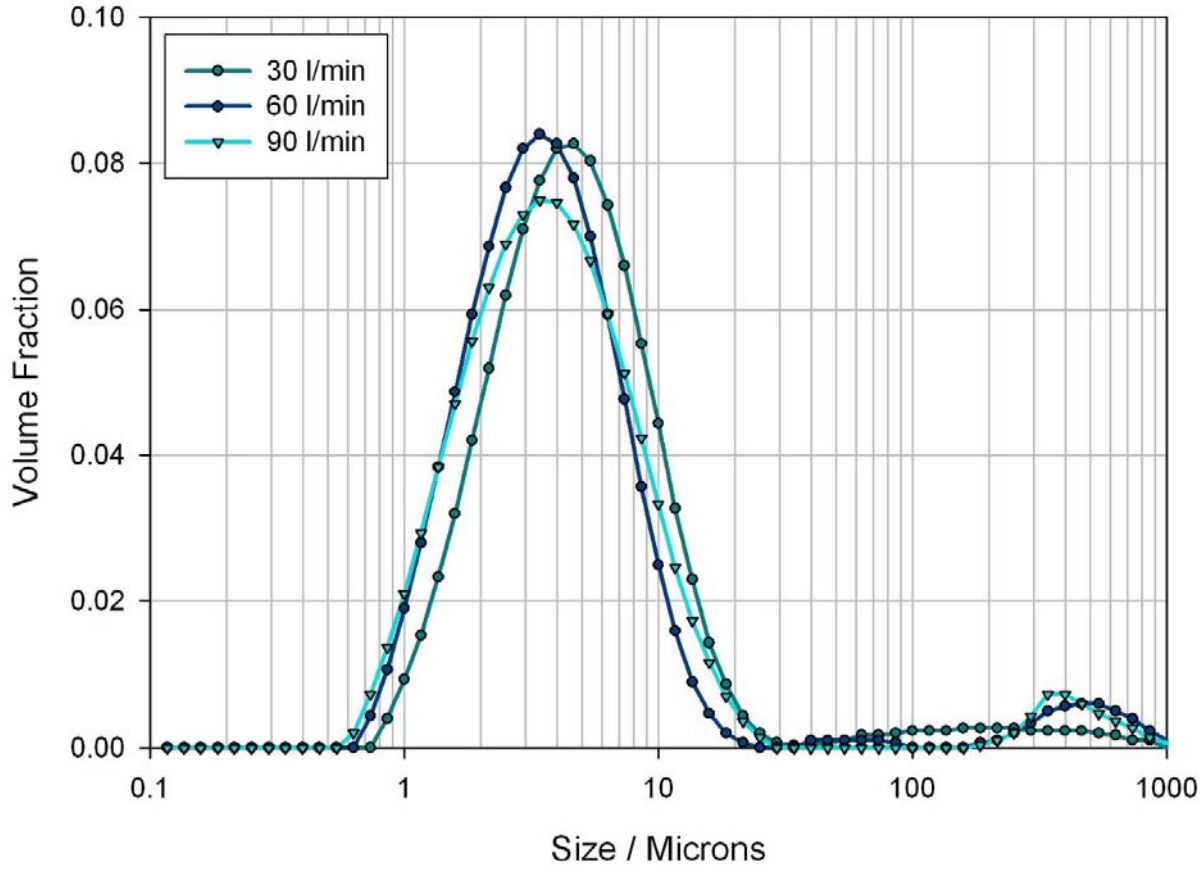
# Particle size flow rate dependence

## Grindomix powder



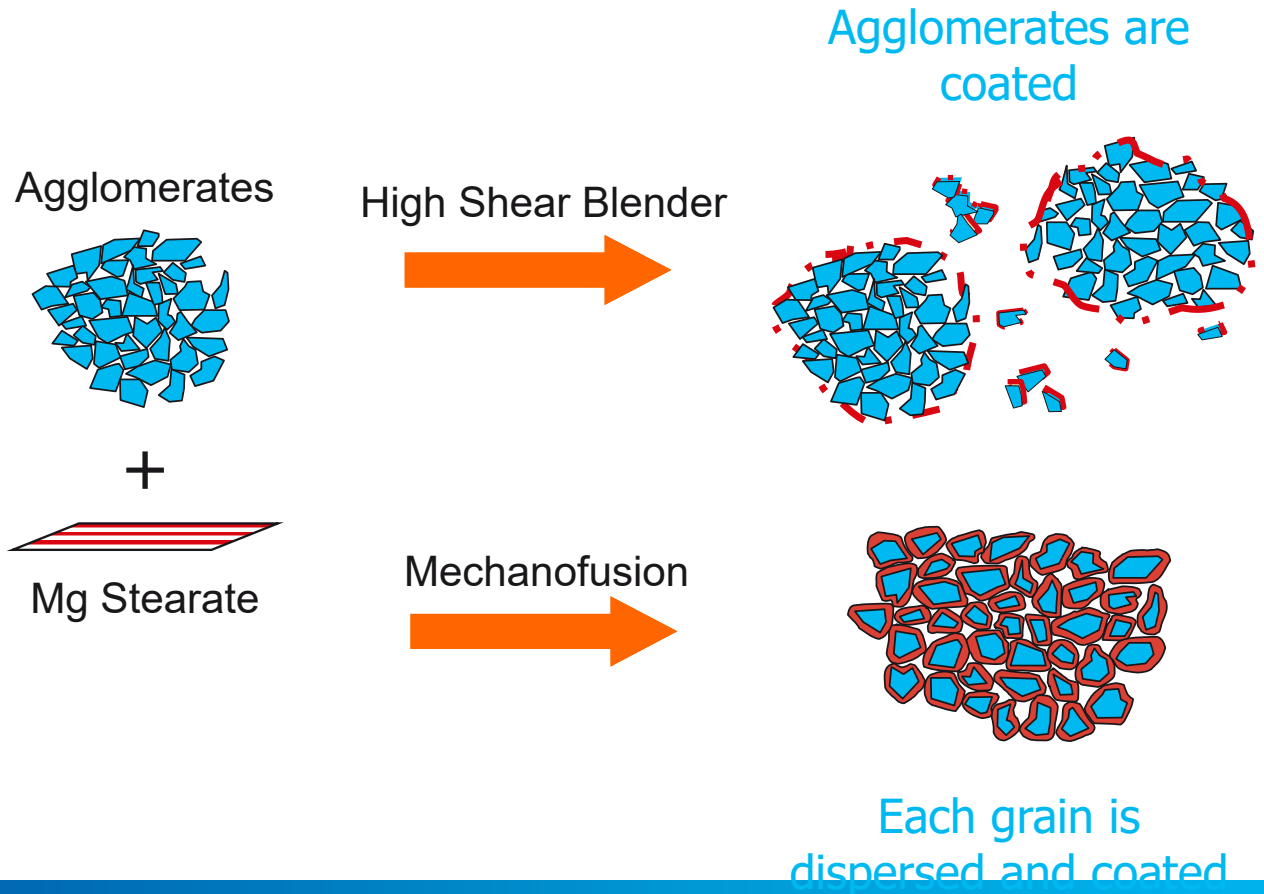
# Particle size flow rate dependence

## Mechofused powder



# Changes to process

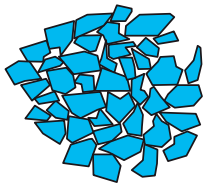
**Changes aerosolisation behaviour…**



# Changes to process

**Changes in aerosolisation behaviour…**

Agglomerates

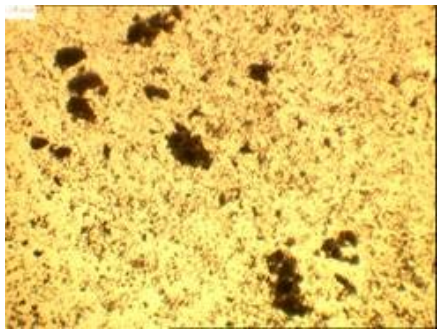


+

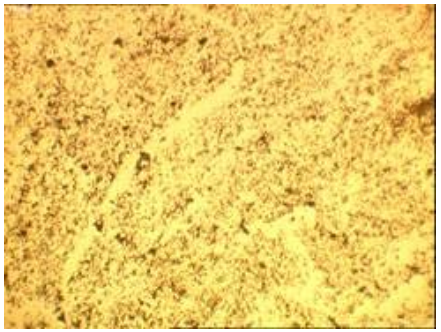
Mg Stearate

High Shear Blender

Agglomerates are coated



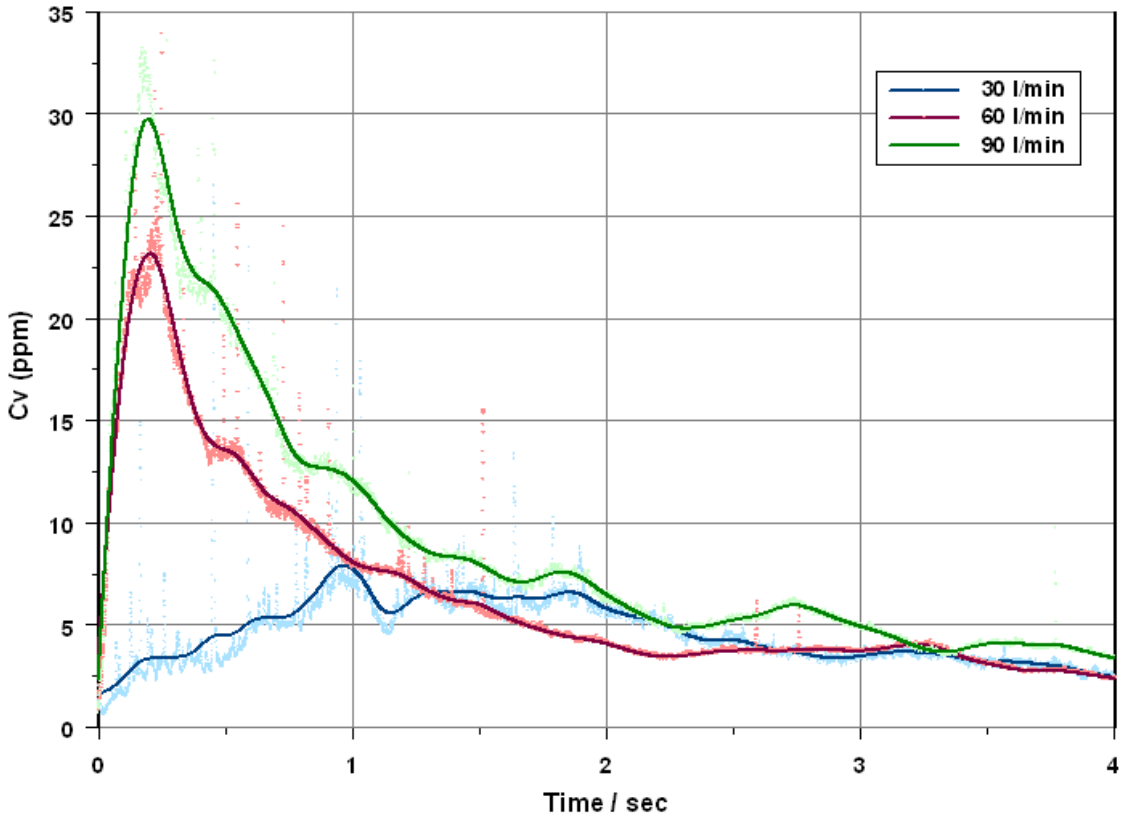
Mechanofusion



Each grain is dispersed and coated

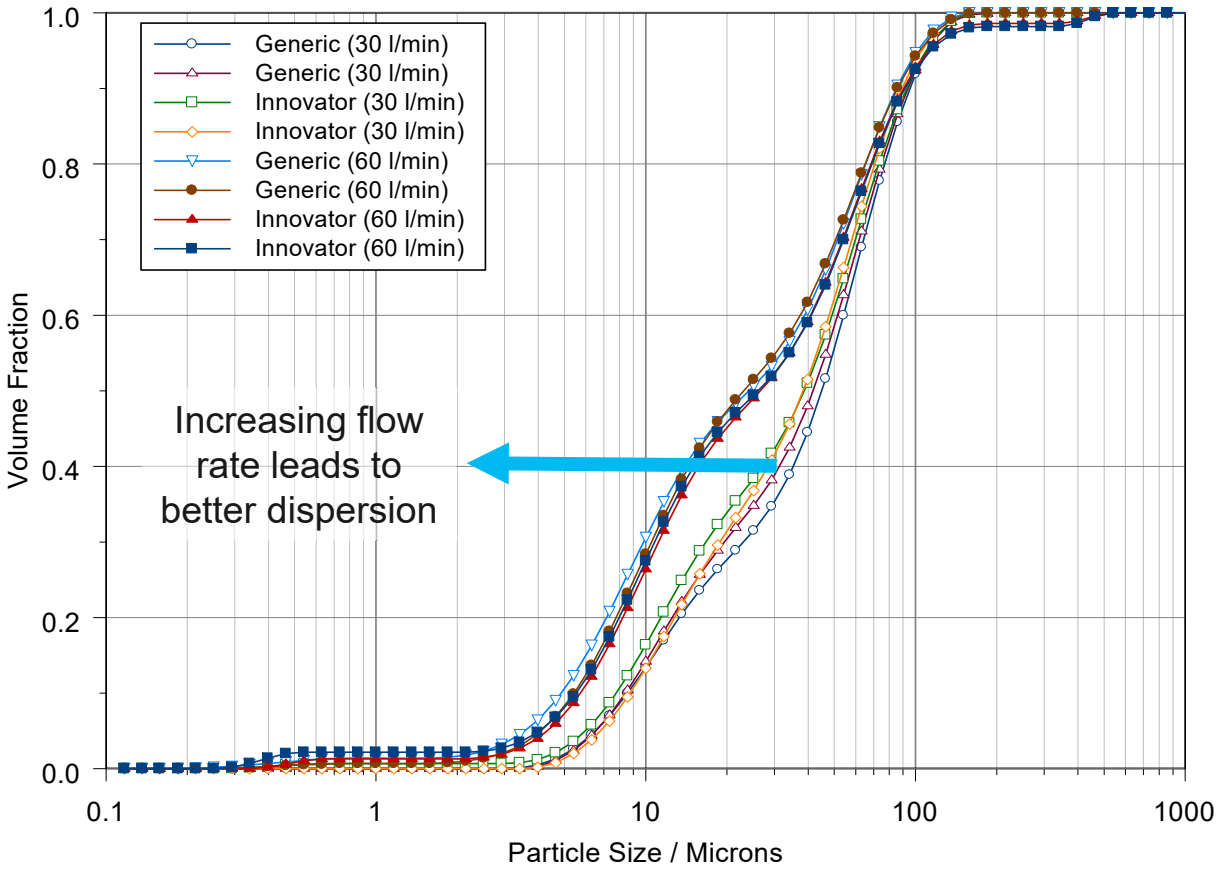
# Cv time dependence

## Mechofused powder



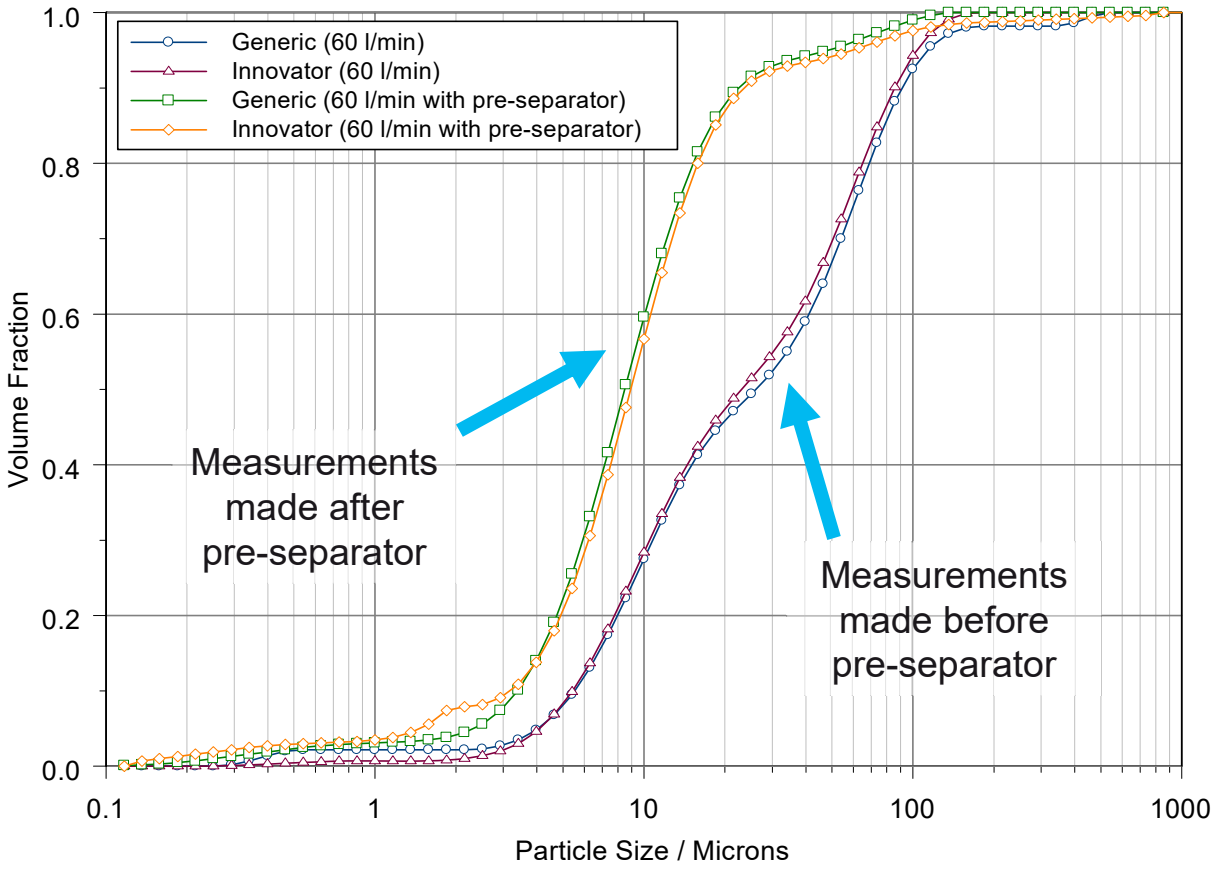
# Dry Powder Inhaler

## Comparing Formulations



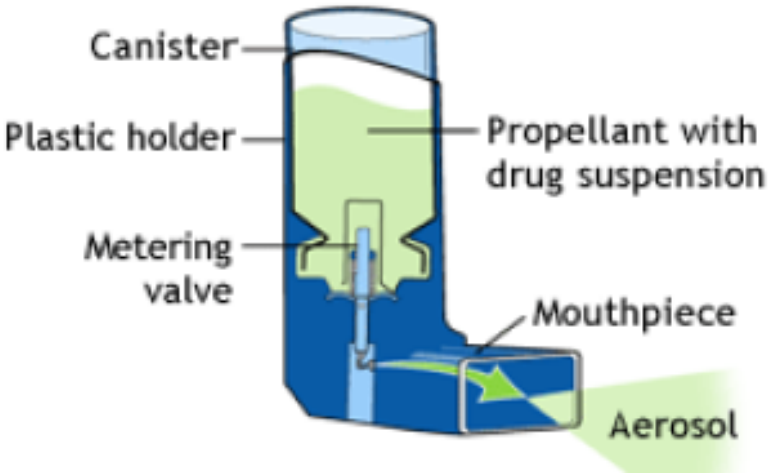
# Dry Powder Inhaler

## Comparing Formulations



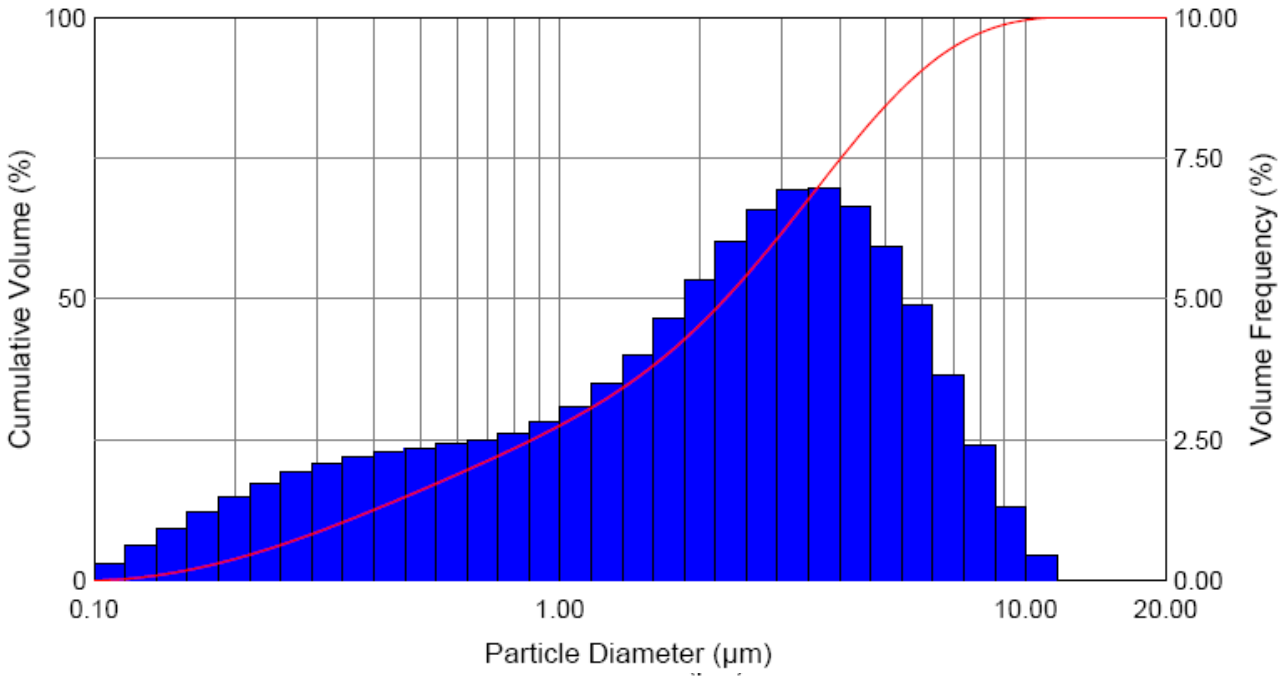
# Metered Dosed Inhalers

- Canister containing drug substance in suspension or solution
- Solvents or surfactants are added to aid solubility or dispersion.
- Solution is metered by the valve.
- Aerosol is produced as the solution is forced through the metering valve by the propellant.



# Example of measurement

- Likely to encounter beam steering due to the propellant.



# summary of regulatory information

## Metered Dose Inhalers

- Flow rate of 28.3l/m for use with ACI
- Pre-separator is not required
- Critical flow apparatus is not required

# Nebuliser Characterisation

## General Overview

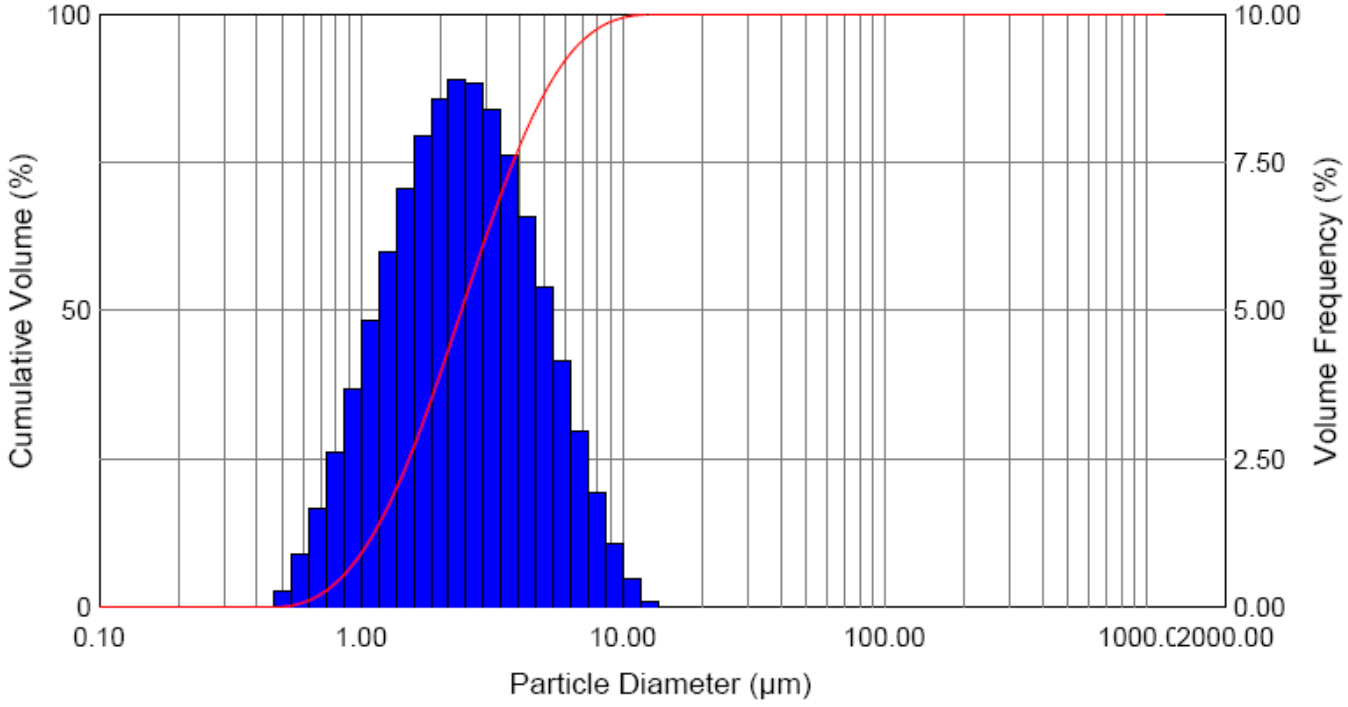
- Drug dissolved in aqueous solution
- Liquid shearing produces droplets
  - » Primary droplets are re-circulated
  - » Satellite droplets are inhaled
- Important parameters include:
  - » Jet and baffle design
  - » Surface tension and viscosity of drug solution
  - » Gas pressure, density and flow rate

Pari LC Jet

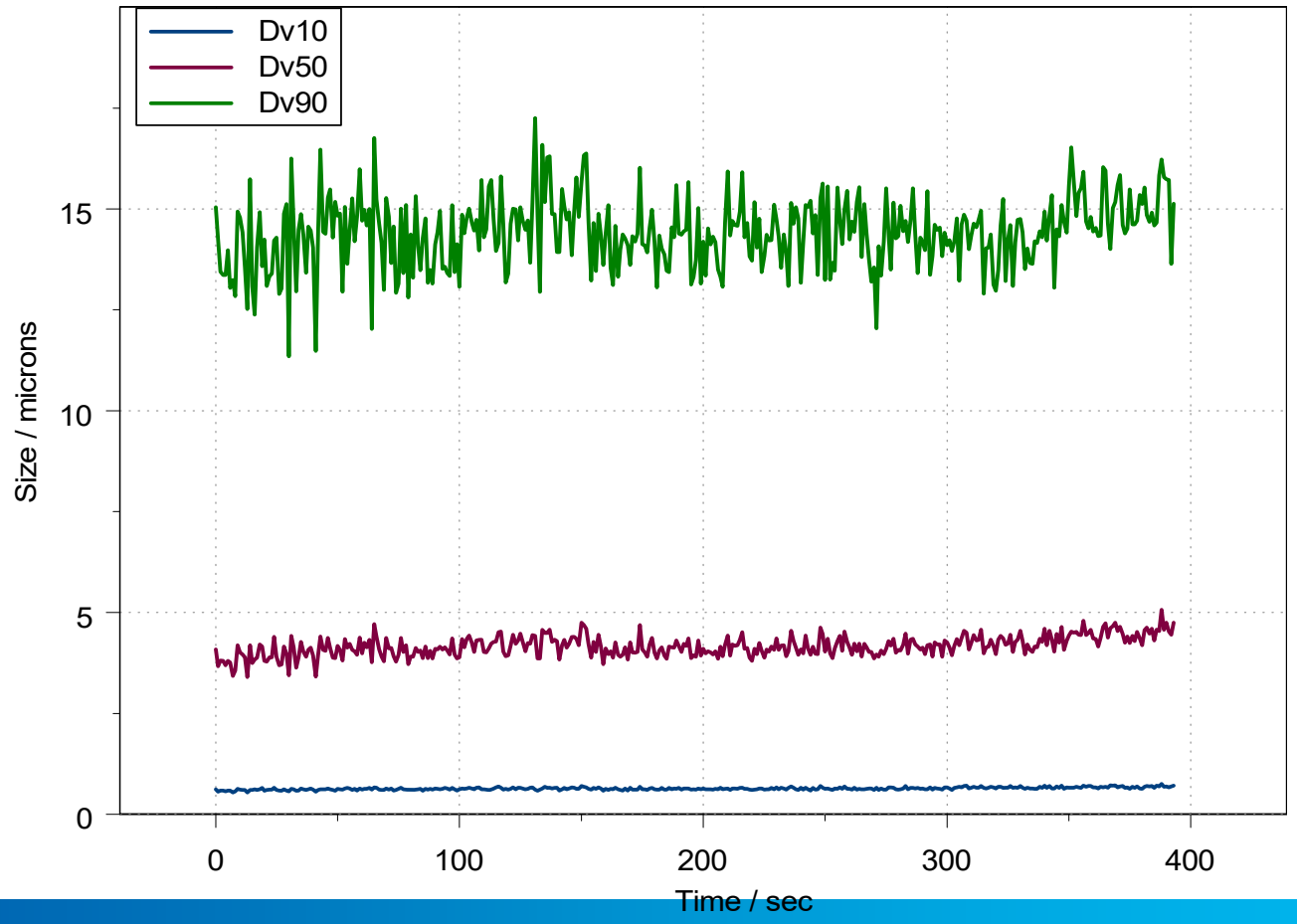
- Good correlation between laser diffraction and impaction results
  - Avoids evaporation problems seen with inertial impactors
  - Rapid characterization

# Particle size distribution

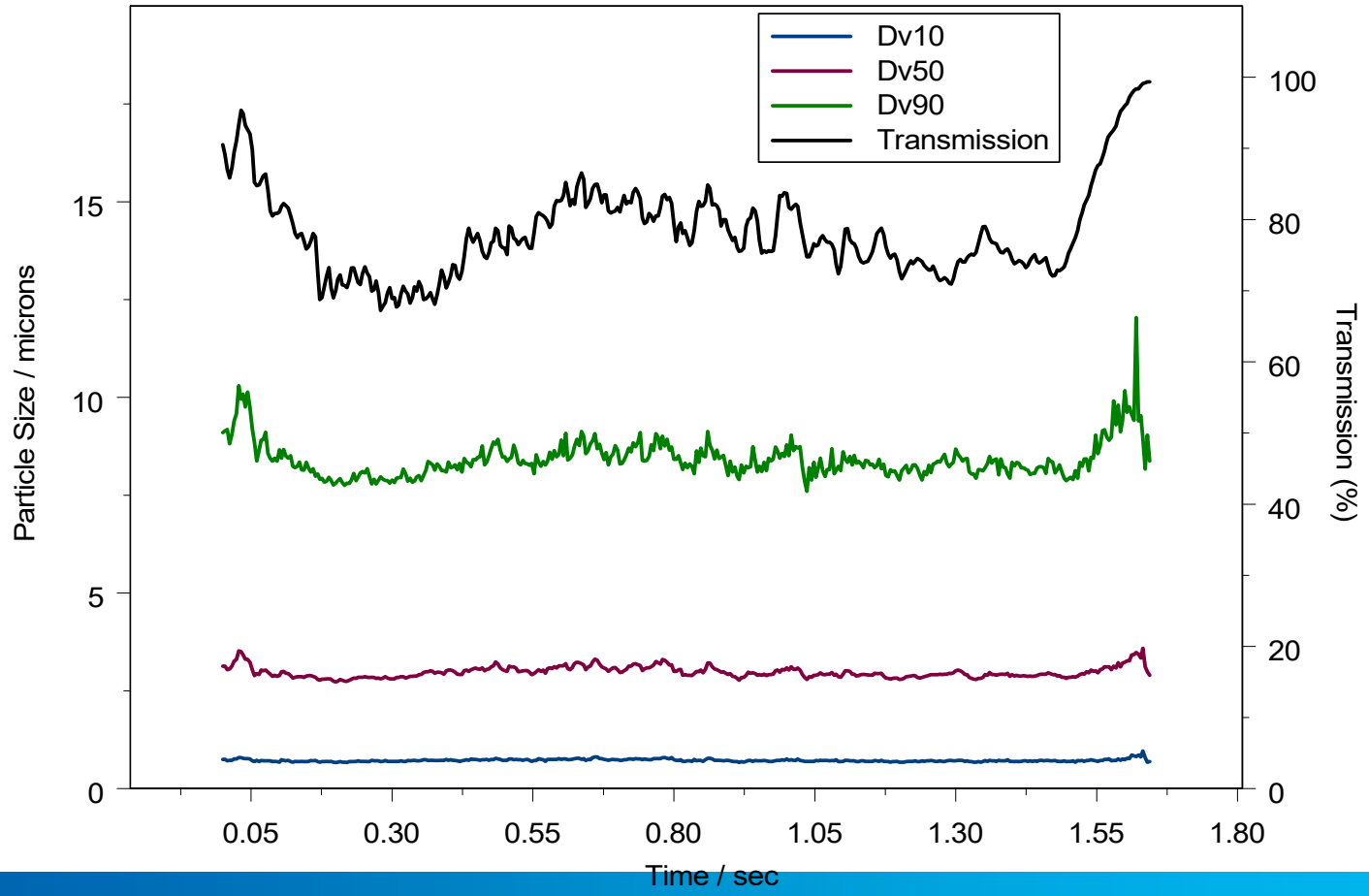
- Beam steering can observed from nebulisers
  - » Due to the evaporation of very fine droplets
  - » Smaller effect than that observed in MDI's



# Nebuliser Characterisation
# 12 l/min driving gas flow rate



# Nebuliser Characterisation
# Measurement During Inhalation



# Spraytec Nasal Spray

# Spraytec Nasal Spray Measurements

- Spraytec NSS Nasal Spray Support
- Vertical Position Control
  - » 0 – 100mm
- Control of angle
  - » 0 – 45 degrees
  - » 5 degree steps
- Position feedback to software


# Regulatory perspective for nasal spray testing

- Device and formulation interaction are critical
  - » Nasal sprays are combination products
  - » Need to ensure reproducible delivery
- Droplet size analysis is used to assess
  - » Quality: Product performance
  - » Safety: Lung penetration
  - » Efficacy: Deposition location

Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

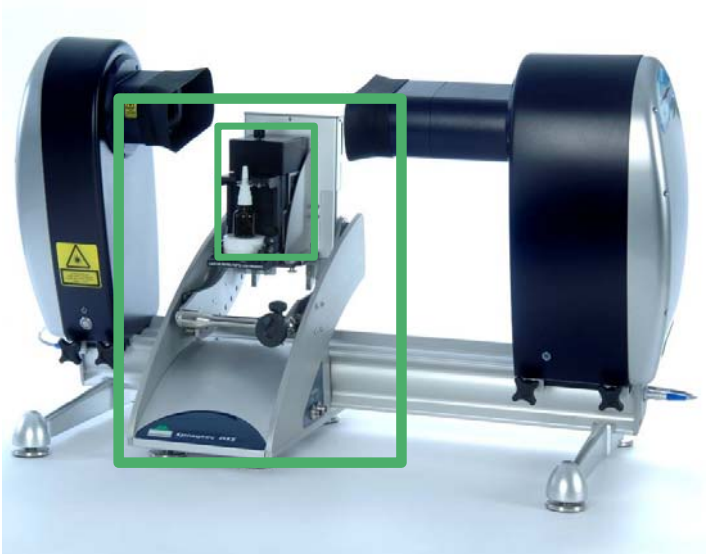
April 2003

# Nasal sprays: regulatory perspective

- Device and formulation interaction are critical
  - » Nasal sprays are combination products
  - » Need to ensure reproducible delivery
- Droplet size analysis is used to assess
  - » Quality: Product performance
  - » Safety: Lung penetration
  - » Efficacy: Deposition location

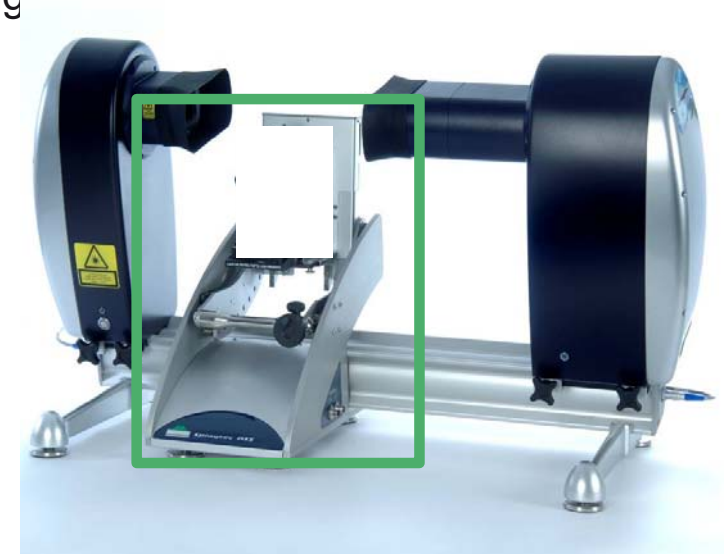
# STP2213 Spraytec NSS nasal spray support

- References a Proveris Vereo or Proveris Solo nasal spray  actuator relative to the measurement zone
  - » Feedback of distance between nozzle and laser beam (0-10cm range)
  - » And angle of actuation (vertical – 45 degree range)
- Measurement distance and angle can be specified in the Spraytec SOP
- Only the Solo actuator (velocity controlled) can be supplied by Malvern



# STP2214 Spraytec NSS nasal spray support

- References an Innova systems NSP3000 Mighty Runt nasal spray actuator relative to the measurement zone
  - » Feedback of distance between nozzle and laser beam (0-10cm rang
  - » And angle of actuation (vertical – 45 degree range)
- Measurement distance and angle can be specified in the Spraytec SOP
- The Mighty Runt (force controlled) must be purchased directly from Innova Systems



# STP2325 Solo for Spraytec nasal spray actuator

- Controls velocity of actuation
  - » Characterises the bottle size
    - Seats bottle before actuation
  - » User inputs
    - Maximum velocity

## For actuation and return

- Hold time
- Delay between actuations
- Trigger mechanism
- » Outputs
  - Force vs time profile
  - Position vs time profile
  - Option to record shot weight

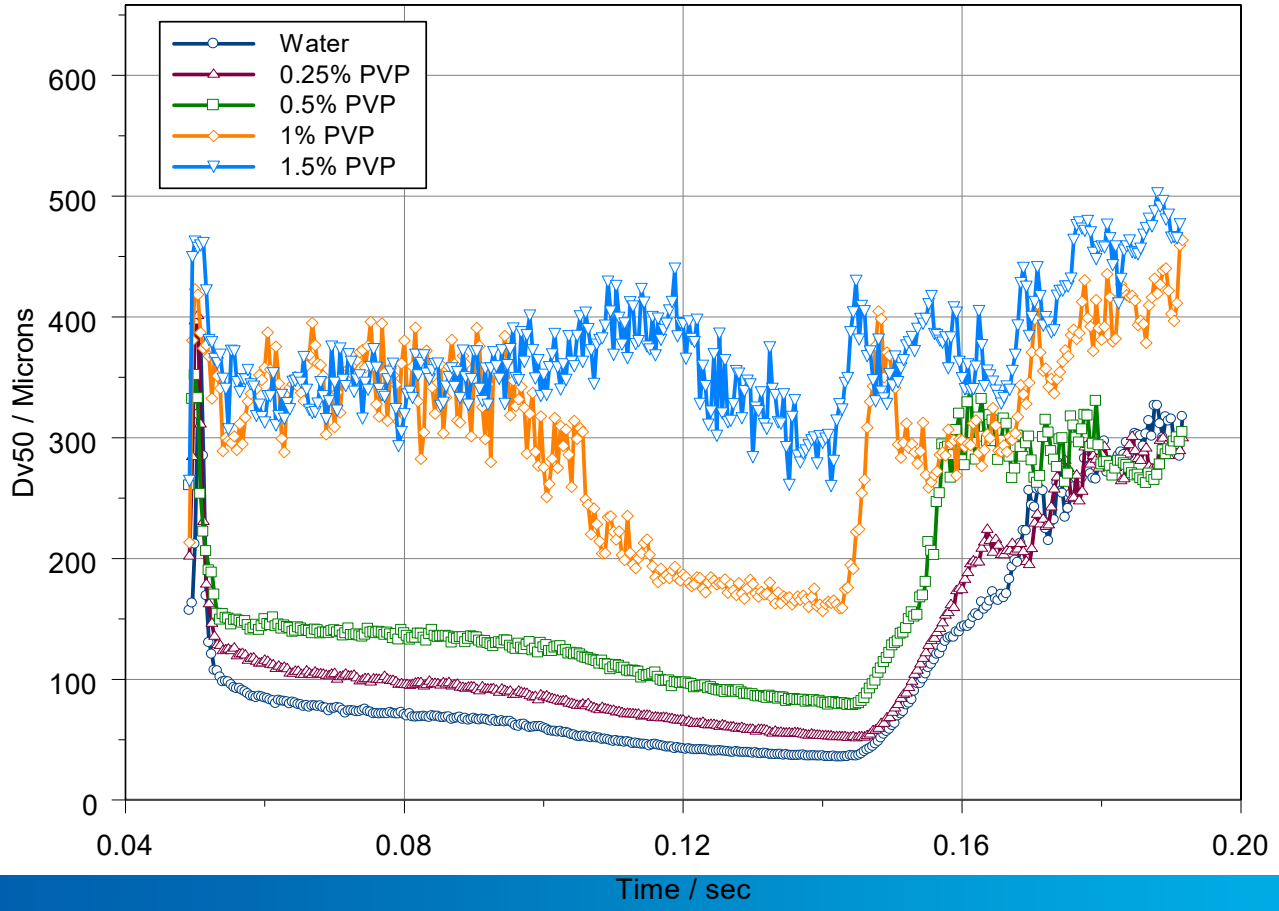
# Measurements specified by the FDA



- Assessment of the spray dynamics
  - Provide “size history” of the spray event
  - Allows Formation, Stable (Fully Developed) and Dissipation phases to be observed
- Provide following parameters for the Fully Developed Phase:
  - Dv10
  - Dv50 (Median)
  - Dv90
  - Span ((Dv90-Dv10)/Dv50)
  - *(%<10 microns)*
- Measurements required for the B and E life stages
- Distance dependence need to be studied
  - Distance of between 2cm and 7cm
  - Separation of at least 3cm required.
- 3 repeats required for each measurement to assess reproducibility
- Use of automated actuation stations is recommended

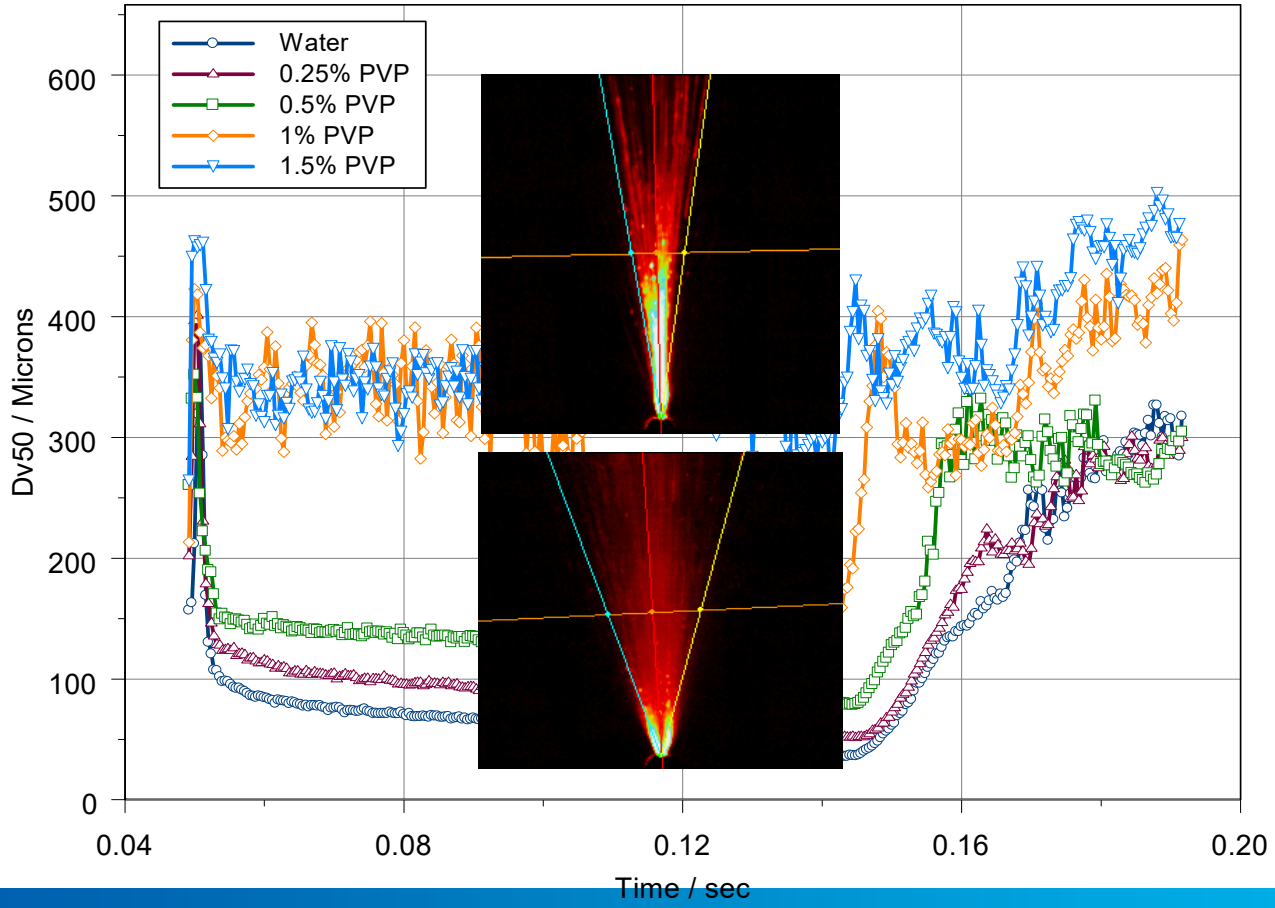
# Nasal sprays

## Formulation viscosity



# Nasal sprays

## Formulation viscosity



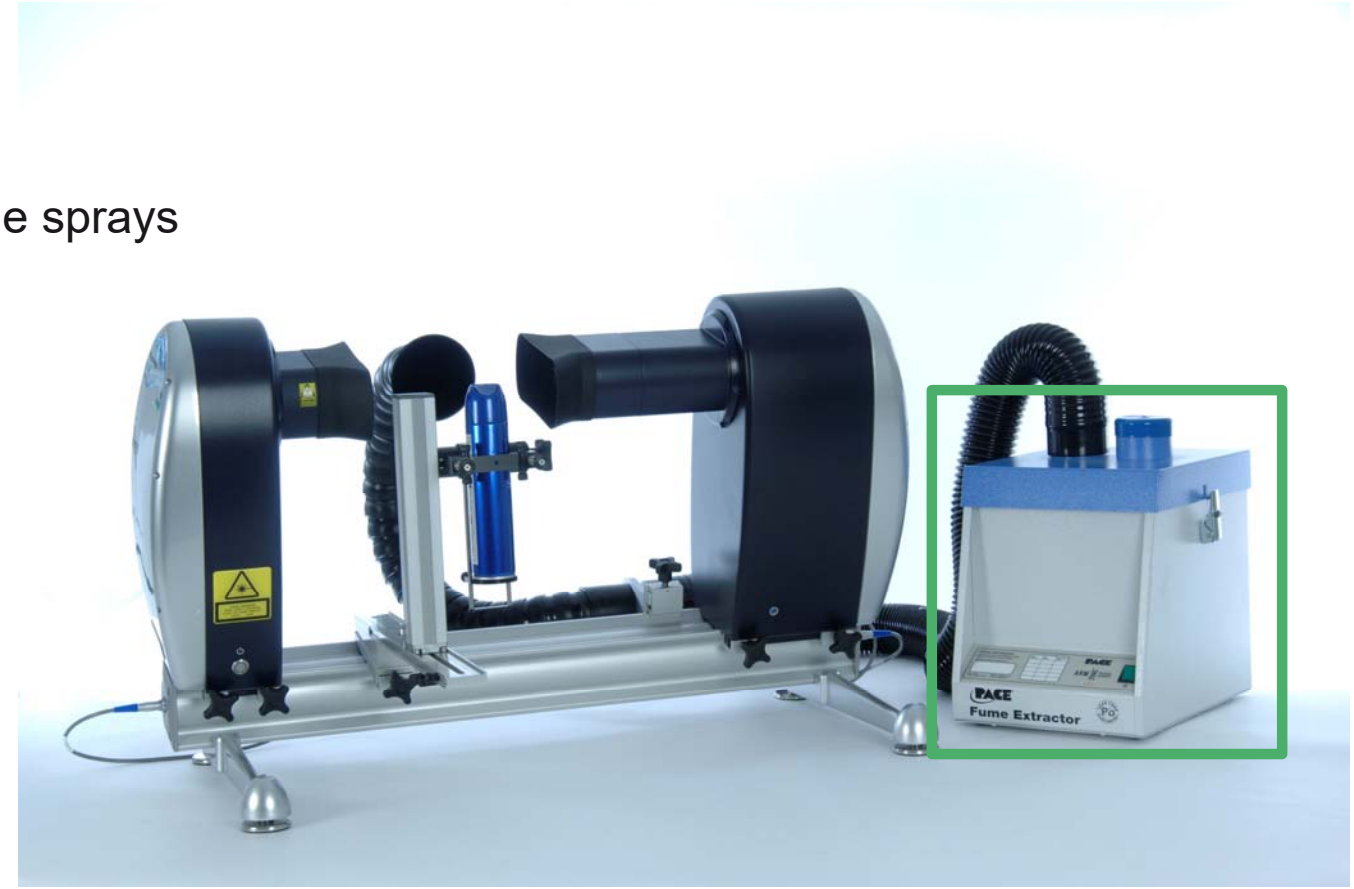
# Nasal spray set-up

- Spraytec, short bench, 300mm lens (STP5311)
- Nasal spray support, NSs (STP2213 or 2214)
- Actuator
  - Proveris Solo (supplied by Malvern, STP2325)
  - Proveris Vereo
  - Innova systems
- Extractor (if none available in the lab)
  - STP2499 (110v) & STP2500(220v)

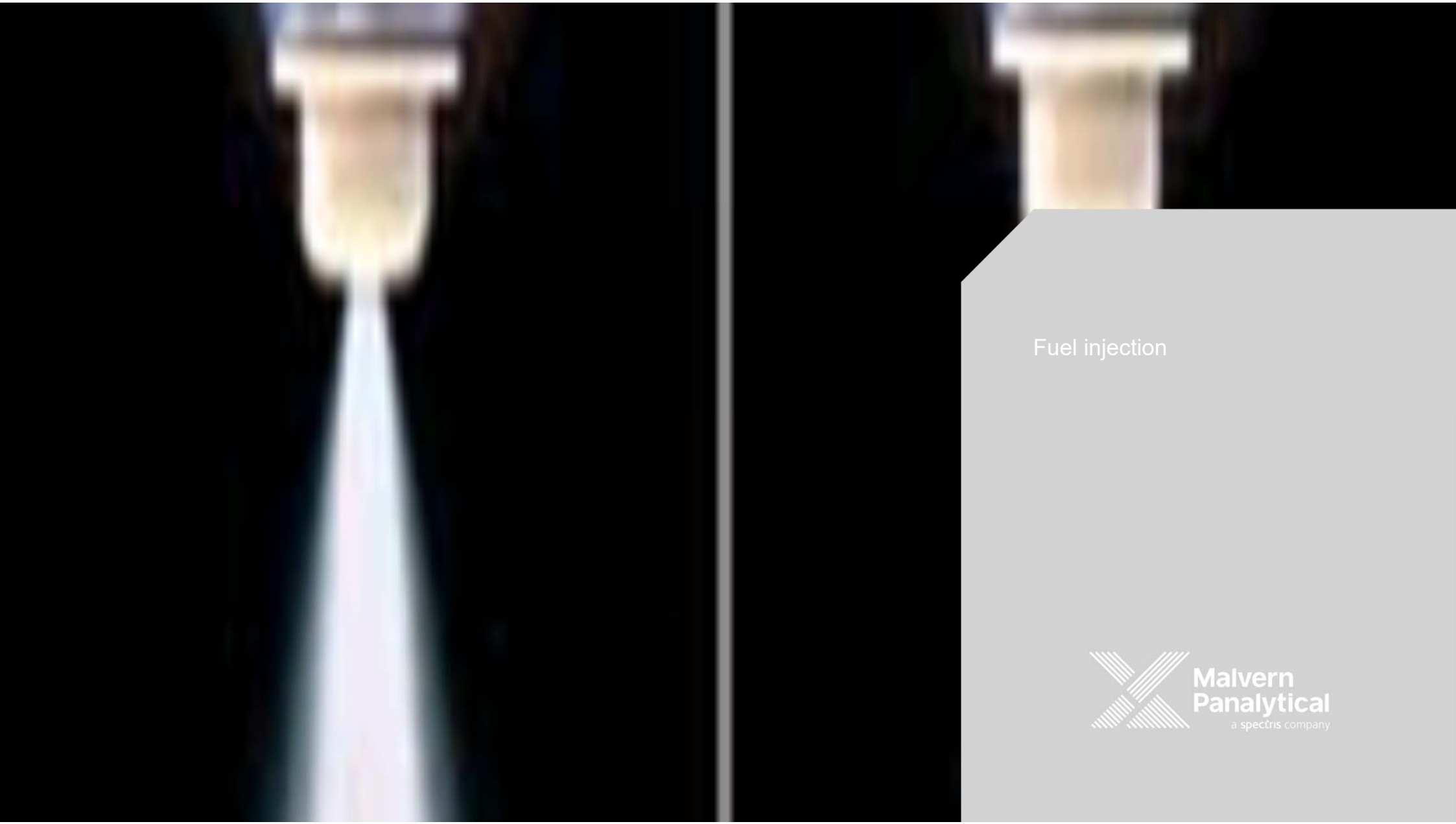
# Spraytec extraction system

# STP2499 (110v) & STP2500(220v) Extraction system

- For the extraction of low volume sprays
  - » Domestic aerosols,
  - » nasal sprays
  - » and personal products.
- Includes
  - » spray collector assembly,
  - » tubing,
  - » HEPA filter unit
  - » switching box to synchronise with the Spraytec



# Spraytec fuel injection application



Fuel injection

Malvern Panalytical
a spectris company

# Pulsed sprays: Fuel injection systems

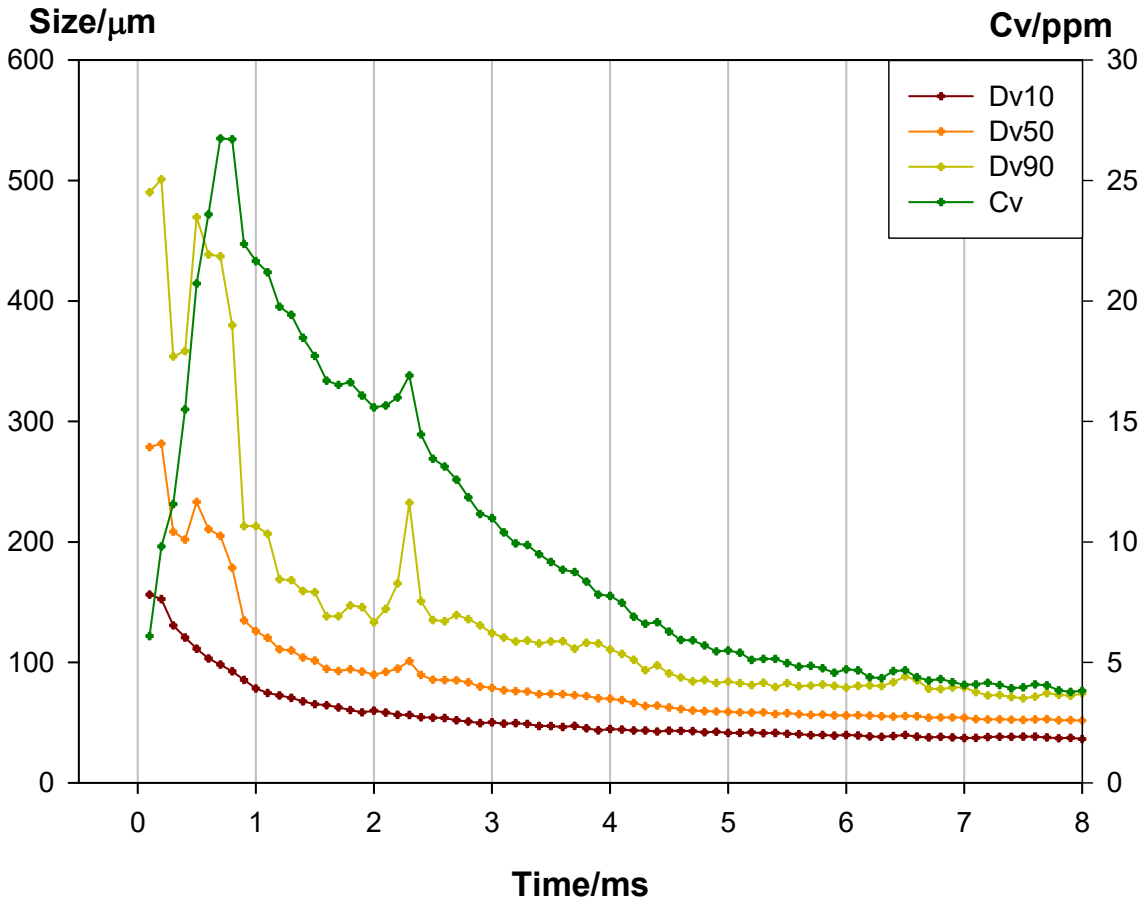
- Particle size is related to:
  - Combustion efficiency
  - Production of harmful emissions
- Small droplet size:
  - Increases available surface area
    - Faster evaporation
  - Decreases spray penetration
    - Affects mixing process
- Important parameters include:
  - Injection pressure
  - Injector type / geometry
  - Valve timing / operating speed

# Fuel injection experiment

- Rapid
  - 10kHz (needs software key)
  - Minimum scattering alarm: 5
- Short events
  - 10ms
- Multiple events
  - 5-20
- Water or fuel
- Possible beam steering from evaporation

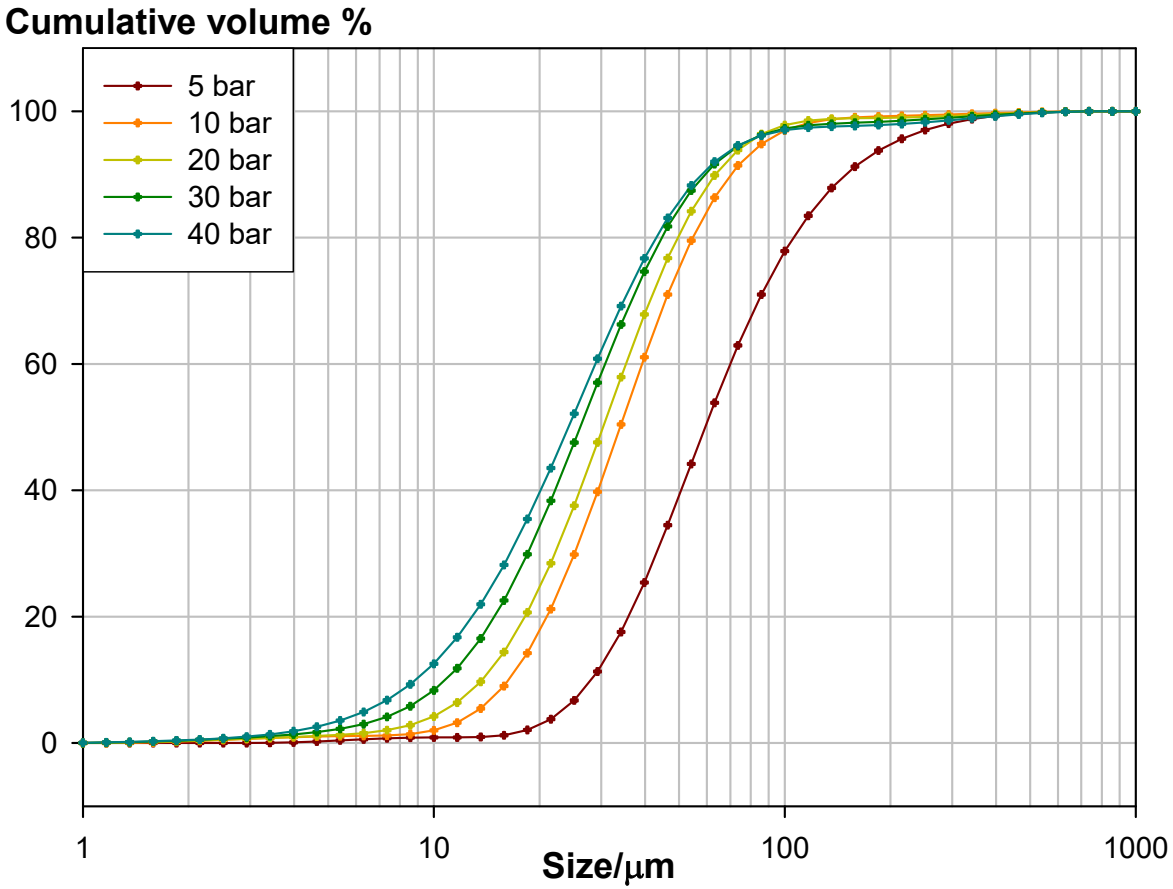
# Fuel injection

## Single injection event



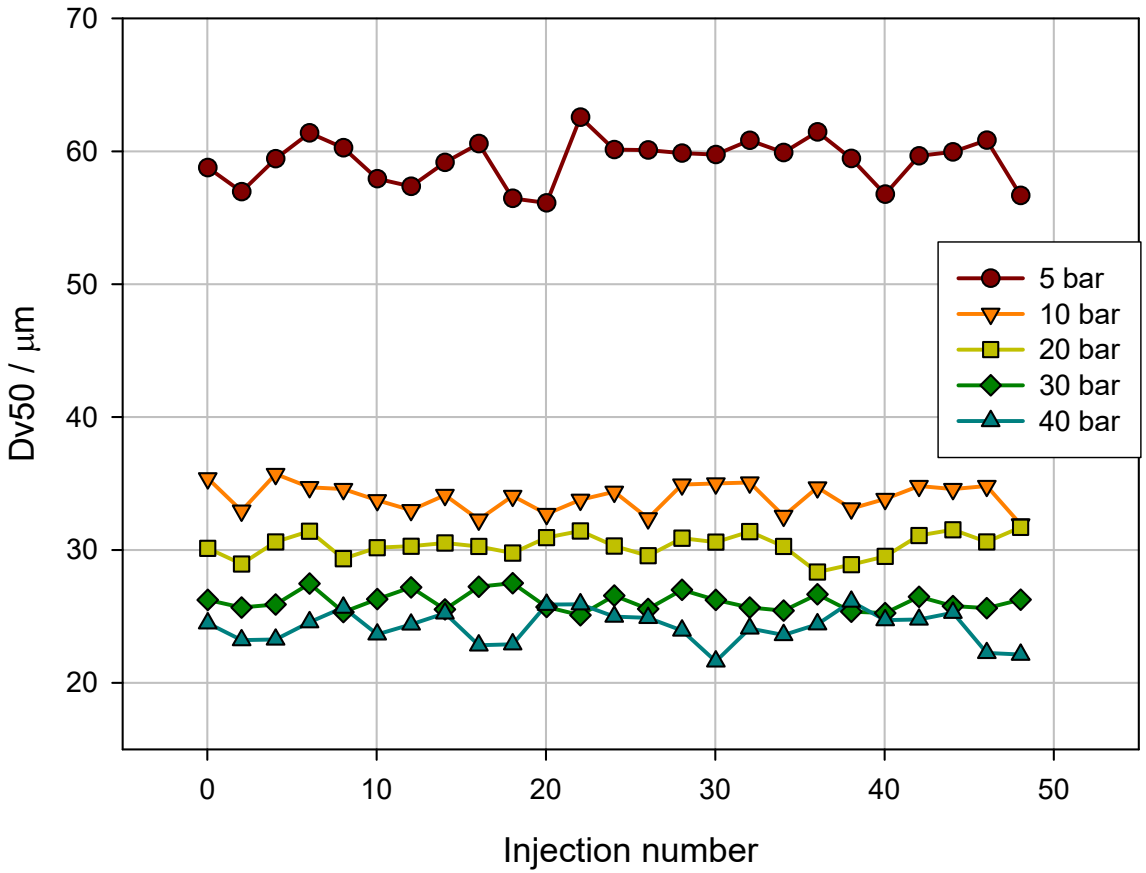
# Fuel injection

## Affect of fuel pressure



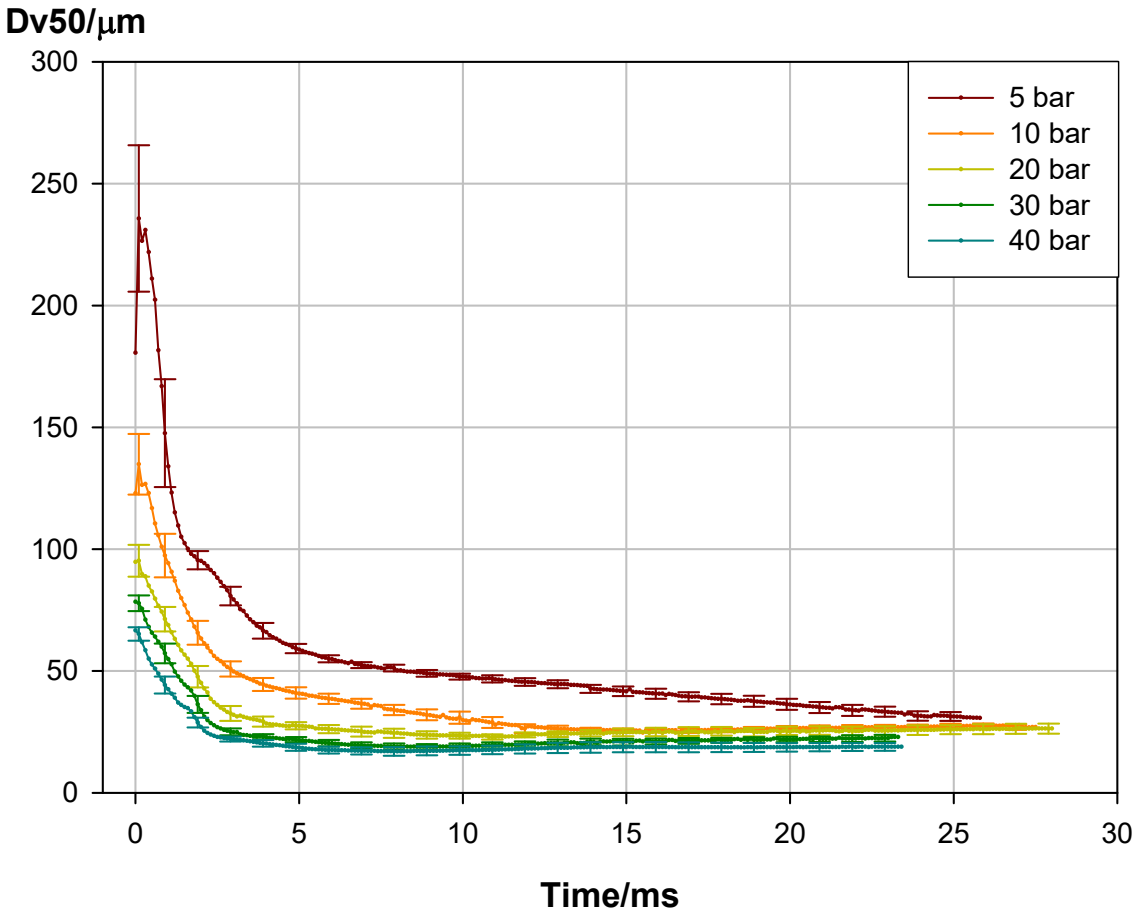
# Fuel injection

## Assessing pulse variation



# Fuel injection

## Effect of pressure on variability



# Spraytec aggrochemical sprays application

# Continuous sprays

## Agricultural sprays

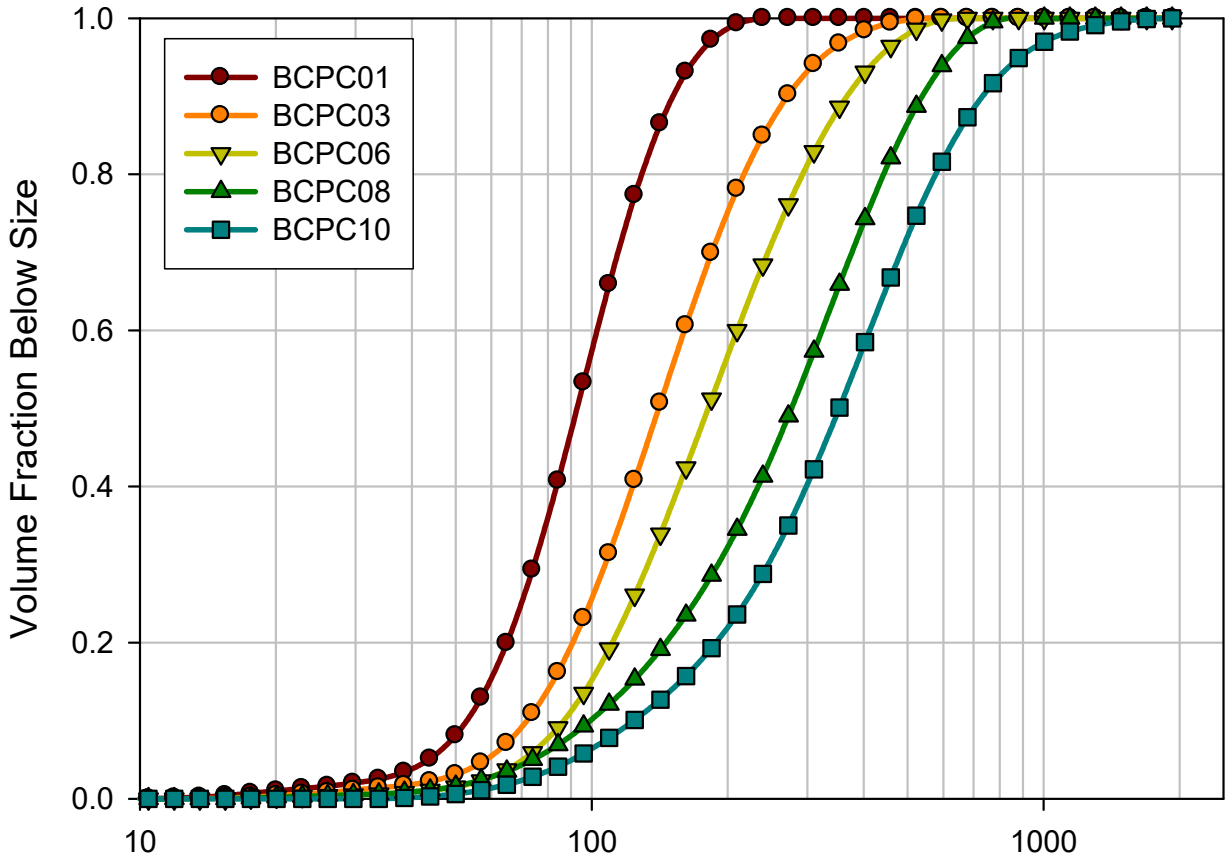
- Sprays enable efficient coverage of large areas.
- Why is droplet size important
  - » Targeted absorption
    - Finer droplets deposit on leave
    - Larger droplets penetrate the canopy
  - » Reduce risk of run off
    - Associated with large particles
  - » Reduce the risk of spray drift
    - Associated with small particle
- Nozzles are characterised to match target and environ

# Agrochemical spray experiment

- 750mm lens + long bench
  - » Can use 300mm lens for demo if necessary
- Continuous
  - » Max 1 hour at 1 Hz
- Water or formulation
- Possible beam steering from air currents with long benches
- Protect alignment by using shrouds to prevent liquid settling on the X95

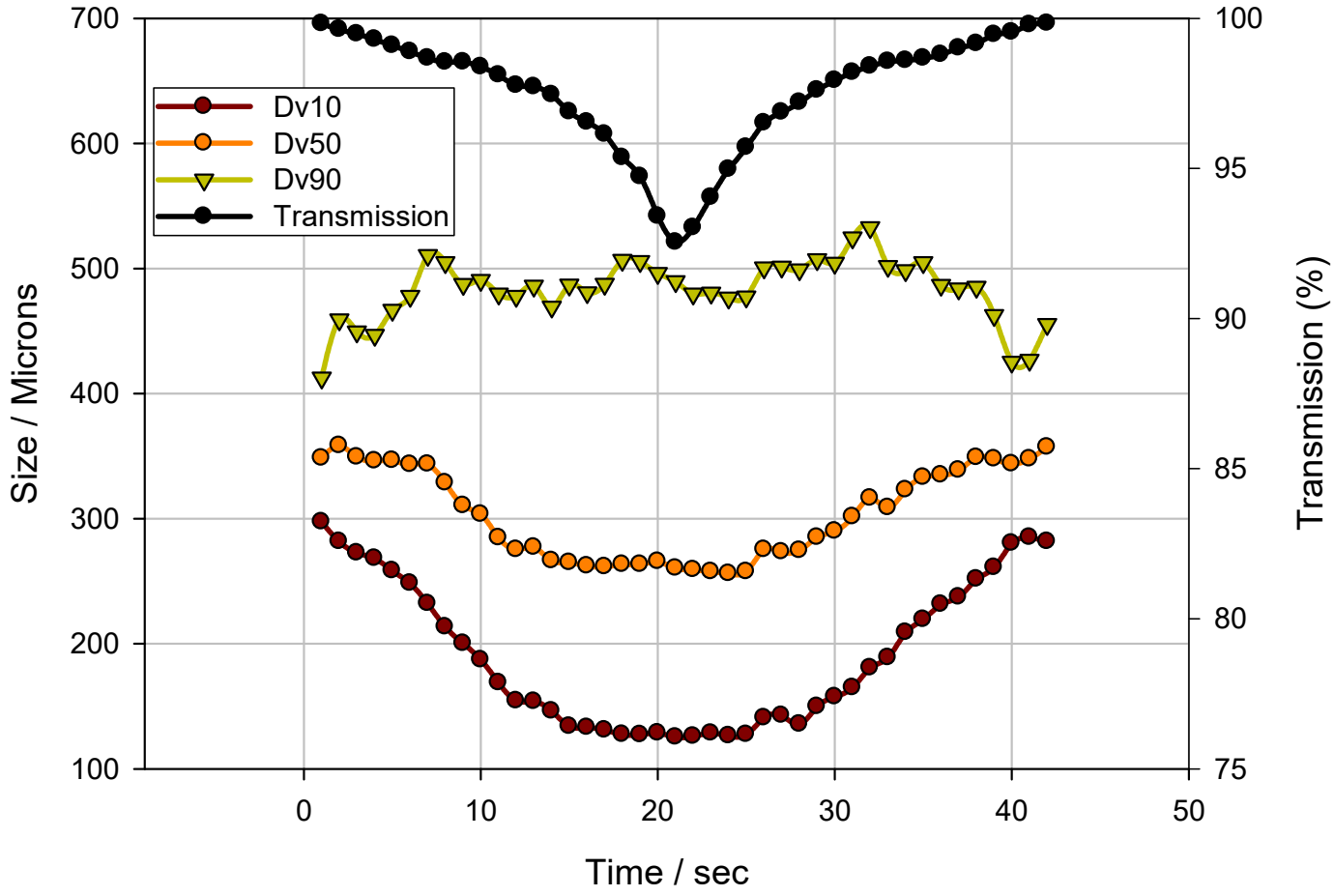
# Agrochemical sprays

## BCPC boundary nozzles



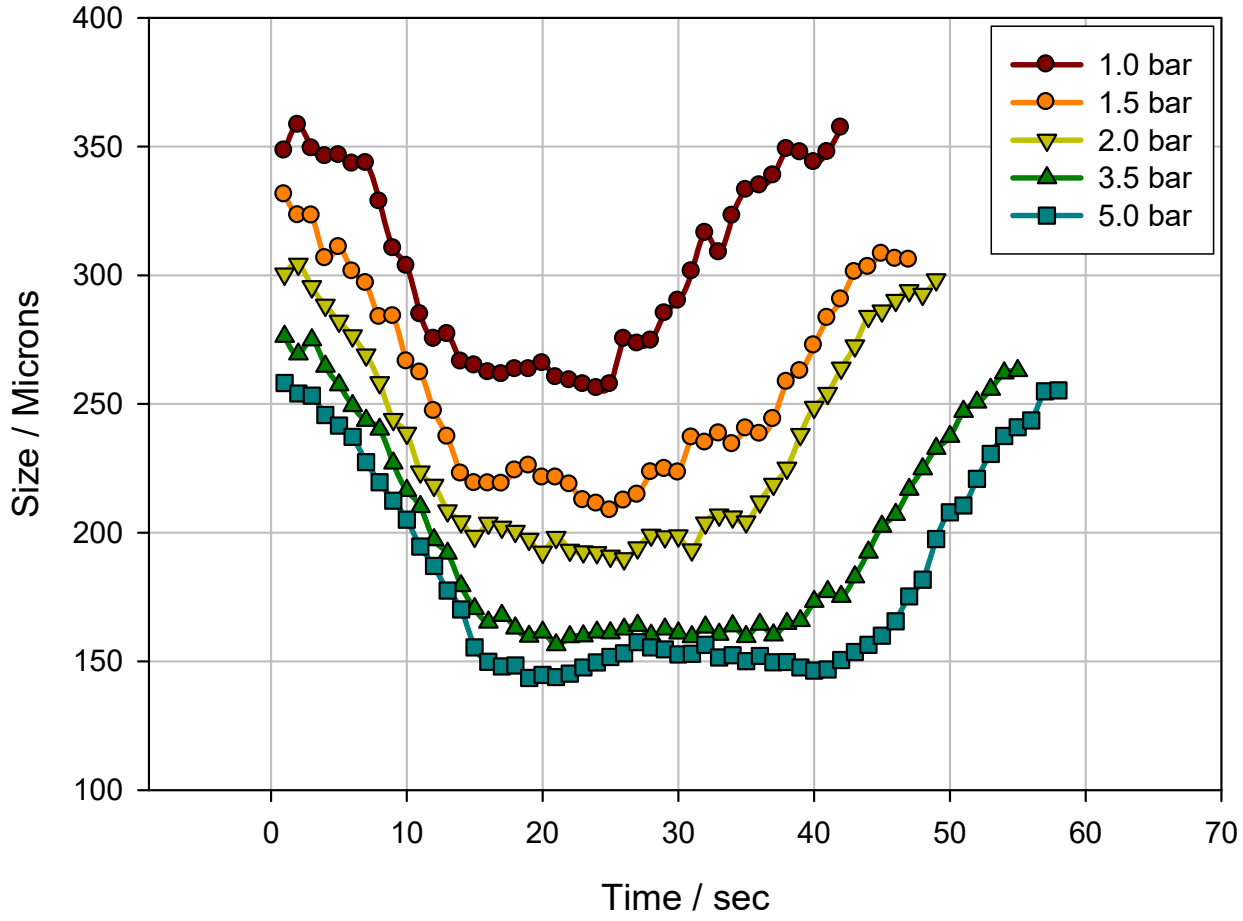
# Agrochemical sprays

## Nozzle traverse



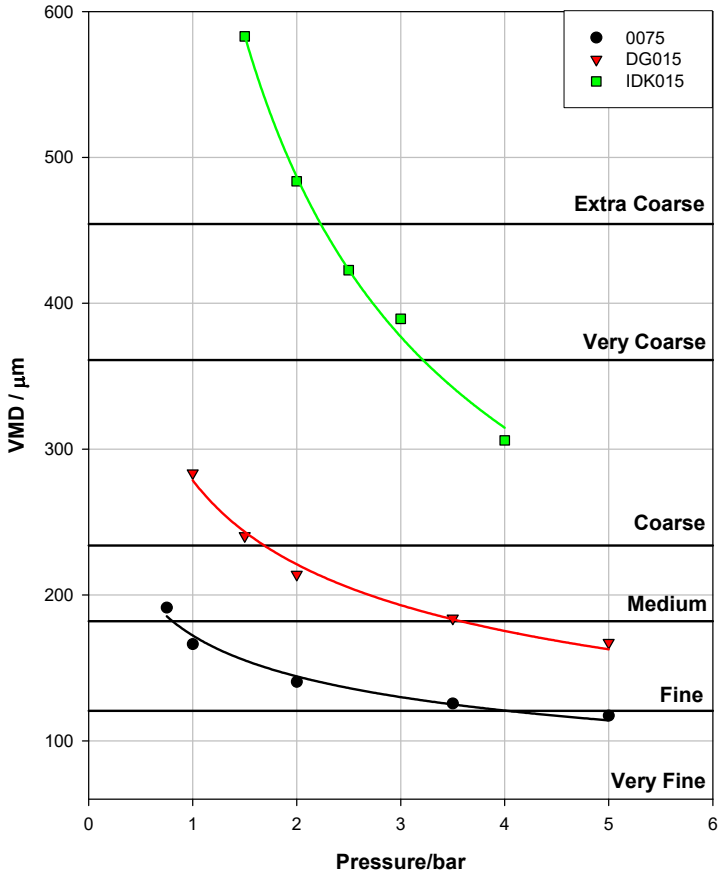
# Agrochemical sprays

## Affect of pressure



# Classification of agrochemical nozzles

- Size boundaries defined by BCPC nozzles
- Each nozzle has been measured over a range of pressures
- Nozzles can then be classified according to their size over standard pressure ranges



# Spraytec household and domestic sprays application

# Personal and domestic products

- Very large market for spray systems
- Products include:
  - Perfumes
  - Deodorants
  - Hair Sprays
  - Furniture Polish
  - Air Fresheners
  - Cleaning products
  - Pest control
- Particle size important in order to:
  - Ensure even surface converge
  - Provide rapid evaporation / drying
  - Reduce “wetness”
  - Prevent lung deposition (no particles < 10µm in size)

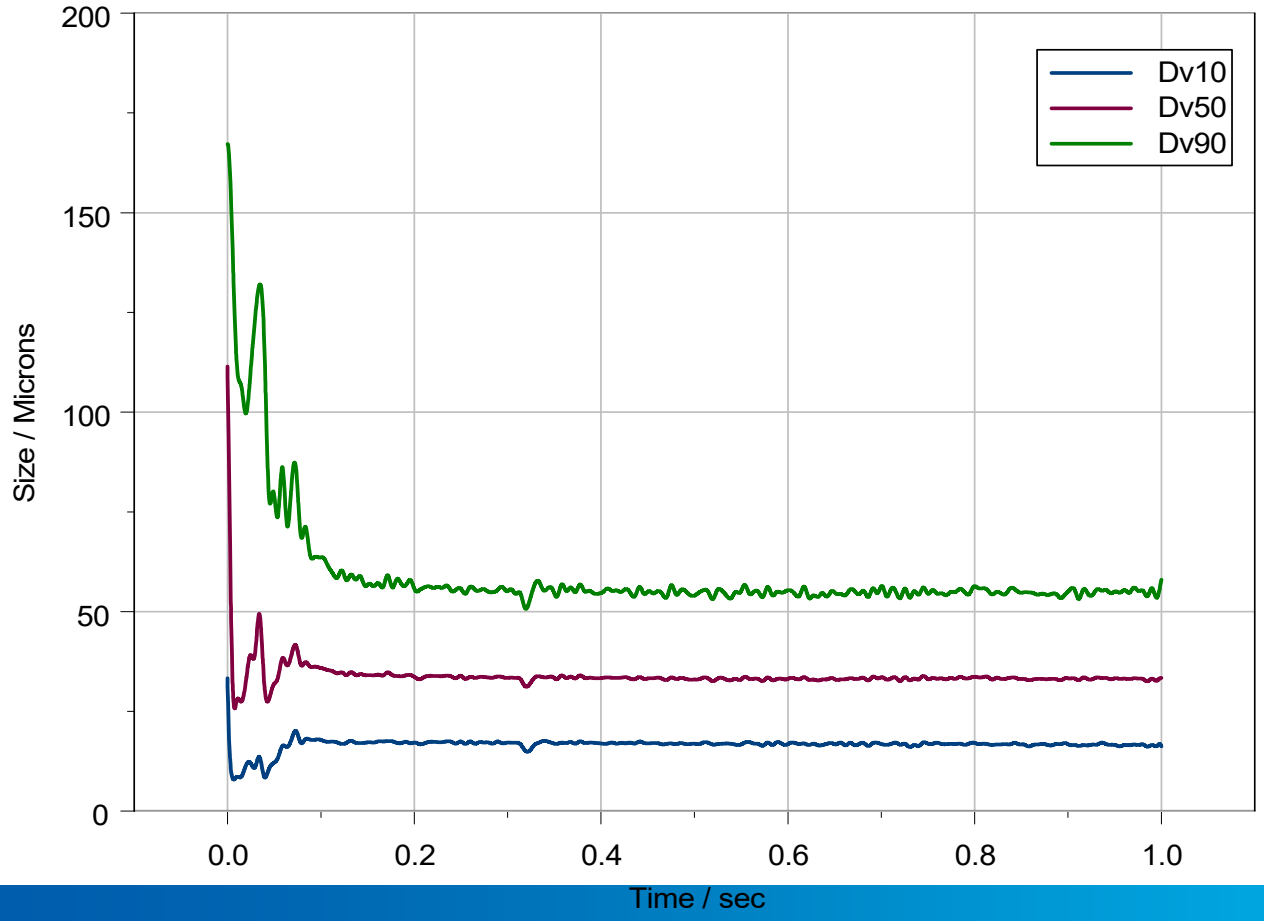
# Aerosol experiments

- Continuous
  - » Acetone or standard opaque particle
  - » Beam steering from propellant

- Rapid
  - 100Hz – 2.5kHz
  - » Medium-long events
    - 500ms – 5000ms
  - » Multiple events
    - 3 – 5
  - » Water
  - » Possible beam steering from evaporation

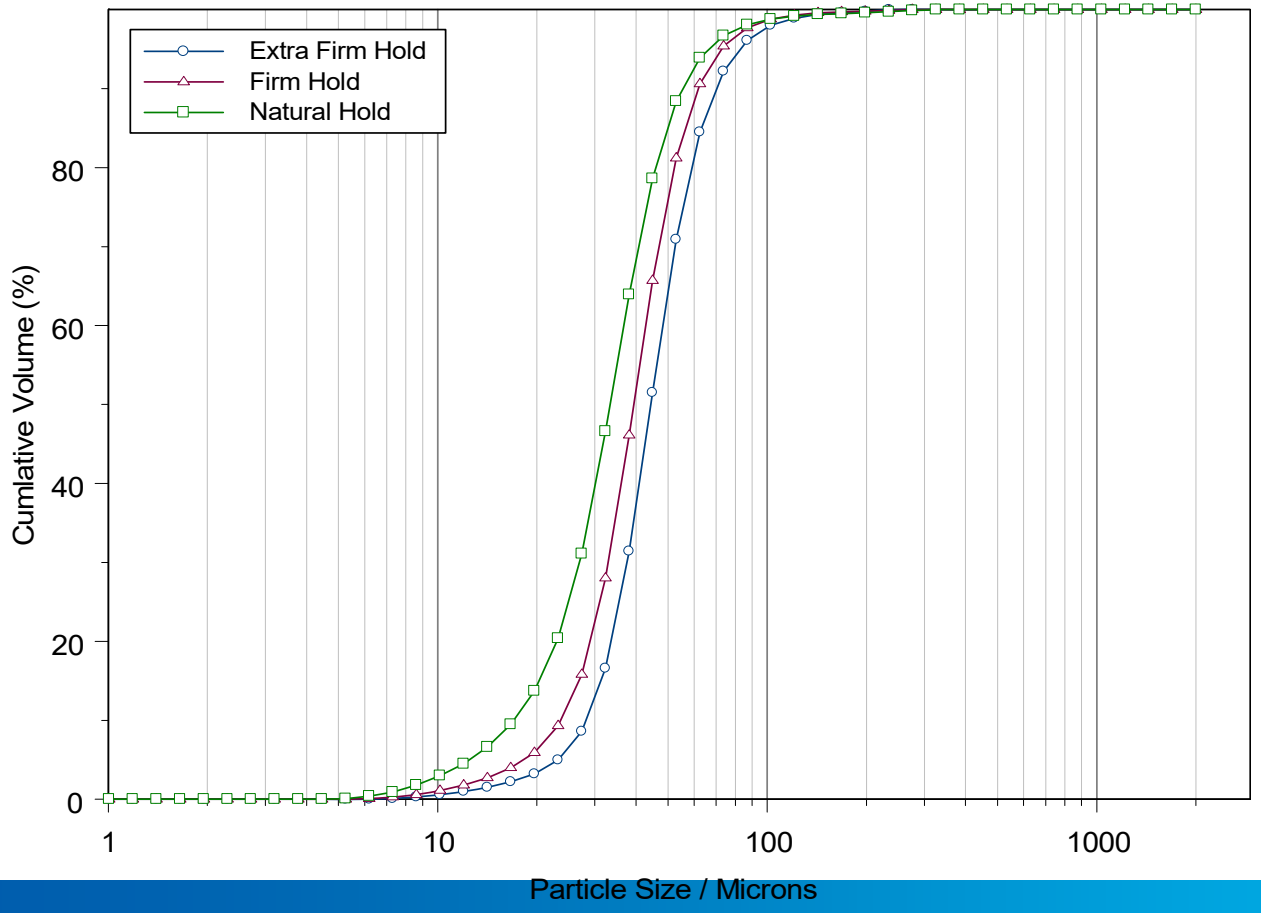
# Personal products

## Hairspray formulations



# Personal products

## Hairspray formulations



# Spraytec wet dispersion

**Wet dispersions**


sysmex