

BIONTER

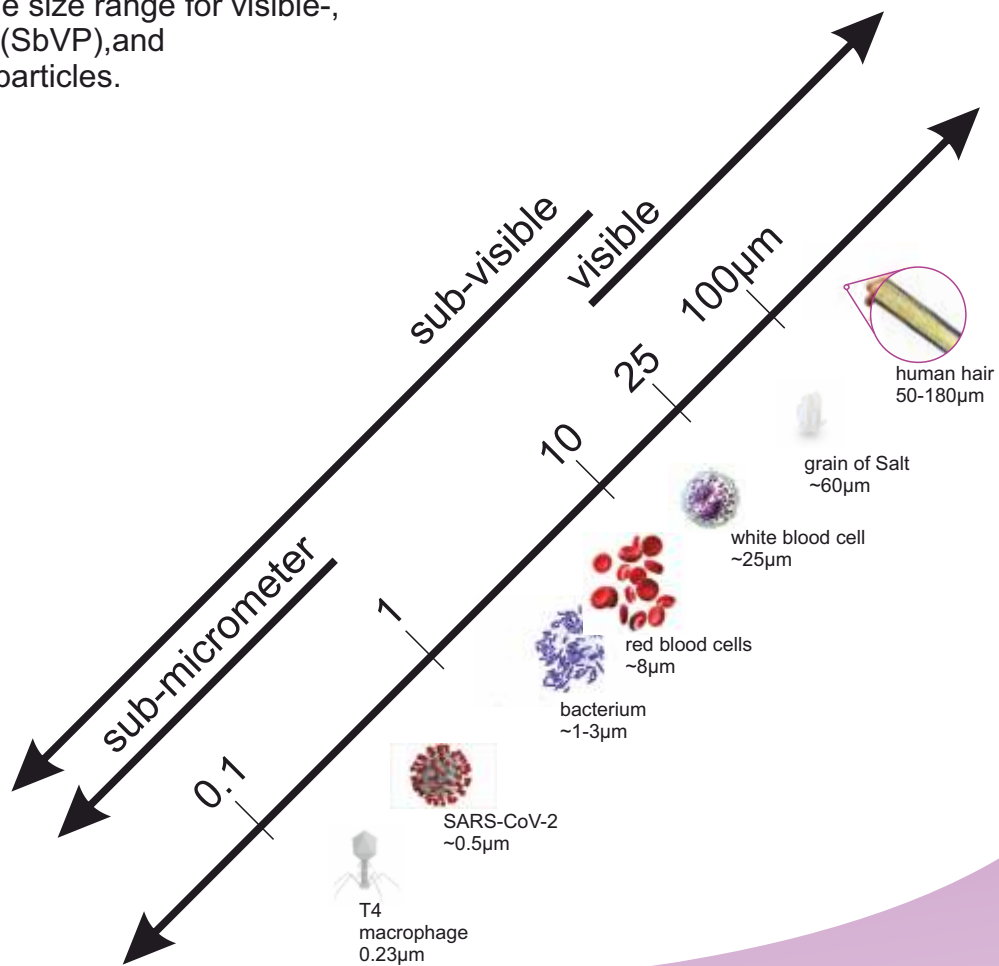


A fully automated particle counter solution with optimized light-obscuration technology for increased efficiency



Particle counting is necessary in any parenteral drug

In the pharmaceutical industry, particulate matter is an obligatory critical quality attribute (CQA) for parenterally administered drugs. Particulate contamination in drug products can range in size from visible ($> 100 \mu\text{m}$) to sub-visible ($1 \mu\text{m}$ to $100 \mu\text{m}$). The United States Pharmacopeia (USP <1788>) describes the size range for visible-, sub-visible- (SbVP), and below $1 \mu\text{m}$ particles.



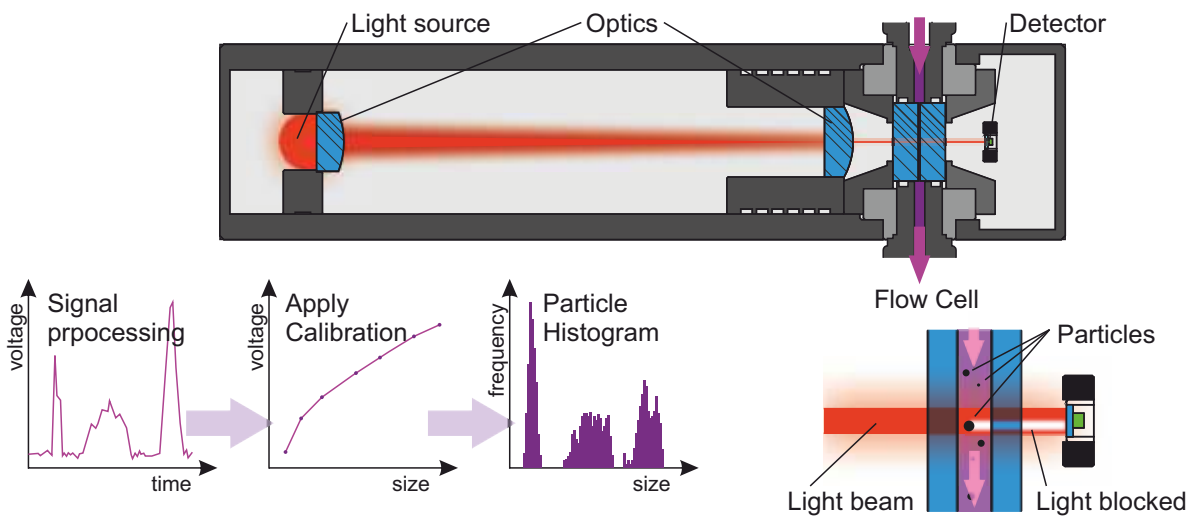
The regulatory authorities have introduced stringent requirements over the past few years regarding visible and sub-visible particles.

The recommended methods to detect sub-visible particles are light obscuration and secondly membrane microscopy, which are outlined in the USP <788> or the equivalent Ph Eur 2.9.19 and the Japanese Pharmacopeia General Chapter 20. These methods were designed to protect patients against the risk of -for example- capillary occlusion through the infusion of “foreign” particulate matter.

	Small Volume Parenterals	Large Volume Parenterals
USP, EP, JP	<6000/container @ $\geq 10 \mu\text{m}$ <600/container @ $\geq 25 \mu\text{m}$	<25/ml @ $\geq 10 \mu\text{m}$ <3/ml @ $\geq 25 \mu\text{m}$

Light Obscuration: A robust and recommended method for patient safety

Light obscuration is based upon the amount of light a particle blocks, when passing through the detection window of the particle counter. The light source is a laser diode, which creates a light beam. When a particle goes through the beam, a “shadow” or obscuration is generated. This “shadow” is detected by a calibrated optical sensor. Light obscuration detects sub-visible particles between 1 and 150 µm of size.



Current shortcomings of Light Obscuration and Bionter’s subsequent Solution

Biggest Challenges of LO	Current Issues	Bionter's Solution EVE	Impact
Destructive method	Samples are lost during testing	non-destructive testing	minimize sample consumption; Monitor particle evolution on a single vial; in case of particle findings use orthogonal methods on identical sample
Manual handling steps	time consumption of highly trained professionals; Risk of sample contamination	smart automated workflow	Leave system unattended; no sample contamination due to pooling, transfer or dilution
Sample viscosity	undercounting particles; false positive particle results	compensates for viscosity and adjusts to the calibrated flow rates	ability to accurately measure in a viscosity range >60cp
Large sample volume required	requires pooling of units with smaller volume; risk of contamination and false positive results; higher costs	minimal sample volume, no pre-run required	Lower costs; no volume loss

Meet 

A particle counter that goes beyond Light Obscuration

EVE - a major step toward a fully automated workflow

The system utilizes LO technology as industry standards with smartly optimized features to facilitate a leaner and more efficient particle counting workflow. A solution created by scientists for scientists.

Reduce manual work in your lab

EVE is fully automated. The solely human interaction is that users simply need to load samples onto the conveyor belt, refill the cleaning solution, if necessary, empty the waste or refill the stack of single-use consumables.

Racks for samples: all standard formats are readily available. Special formats are available upon request.

Conveyor belt that transports the samples to an analysis area

Bottles for cleaning media and waste

Fluidic system including the particle sensor

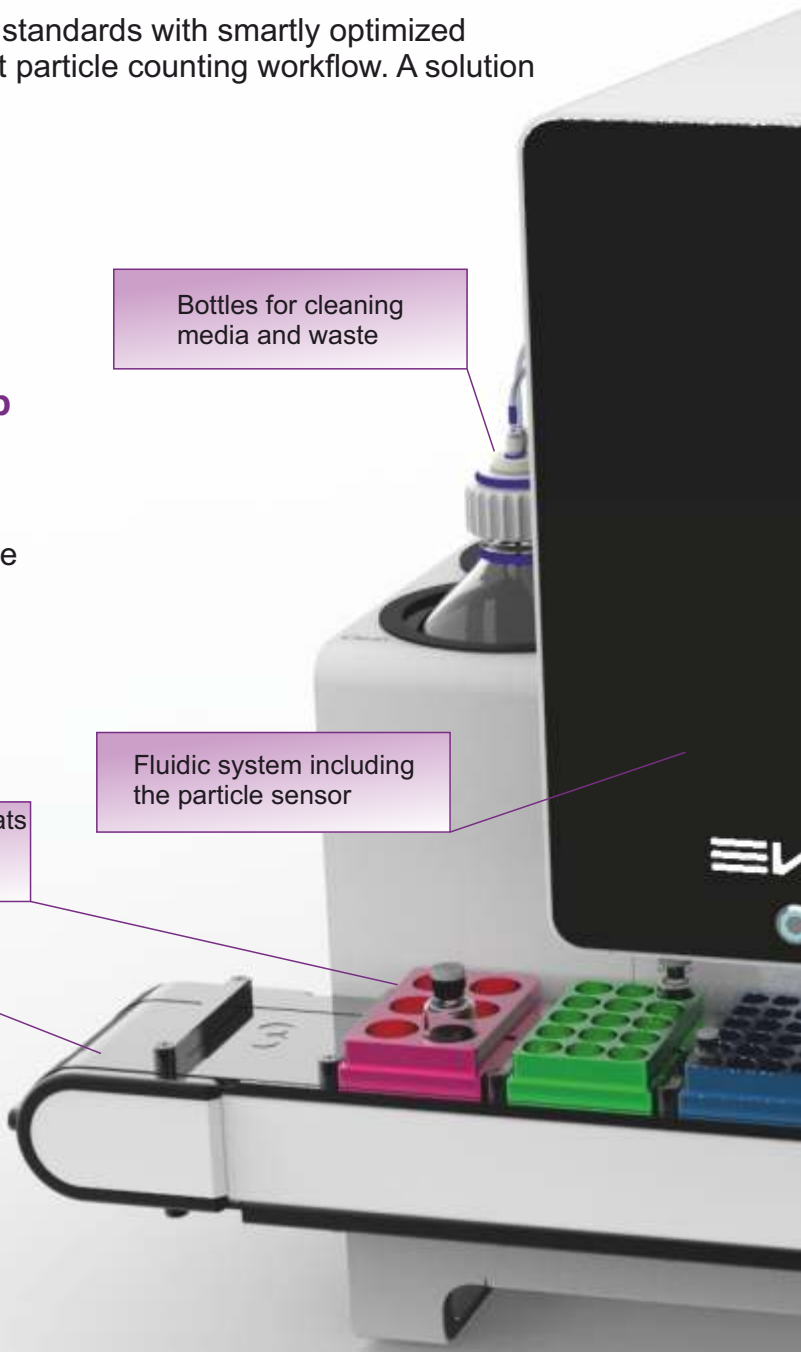
Use higher viscose solutions

EVE Provides accurate measurements for viscosities even greater than 60cp. An integrated time-pressure system adjusts the necessary flow rate according to the sample viscosity.



Choose a bench or laminar flow

EVE does fit in a laminar air flow, however as it is a self-contained system with limited human interaction, you can also place it on your regular lab bench.





Work non-destructively with your sample

Due to the unique integration of the single-use container, the sample is reusable after measurement. EVE facilitates an optimized workflow for light-obscuration (see next page).



Single-use consumable Rack (up to 72)



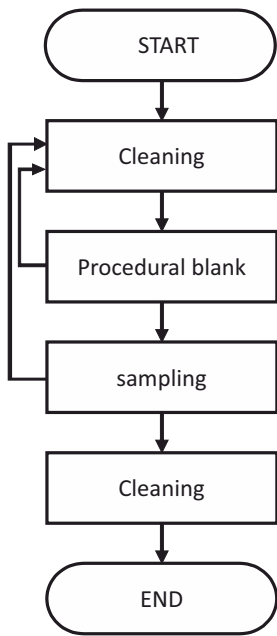
Rely on compliance with current regulations

EVE is based on light-obscuration and hence is ready to be used in any regulated environment. The software is USP/EP/JP and 21CFR part 11 compliant.

Special designed piercing needle to omit drop formation and stopper fragmentation

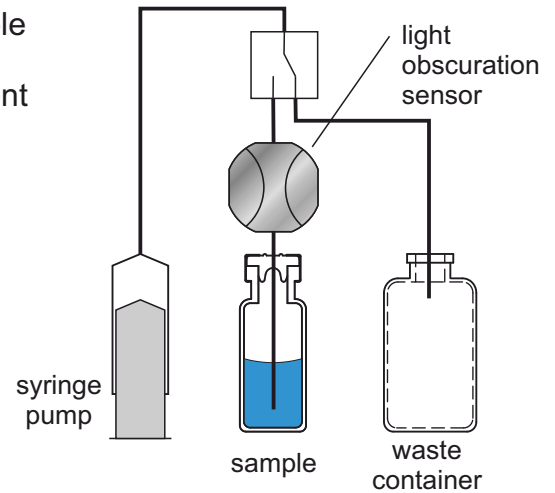
The magic behind a non-destructive workflow

Current Light Obscuration
(destructive process)



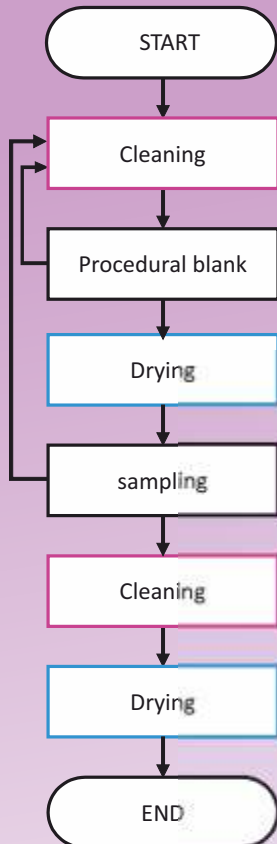
Current Solutions

In a destructive workflow, the sample solution is “contaminated” with the solution used for blank measurement and cleaning.



To prevent this, EVE contains an integrated drying step. Unlike others, EVE uses pressurized filtered air to move liquids and not a syringe.

Bionter's EVE
(non-destructive)



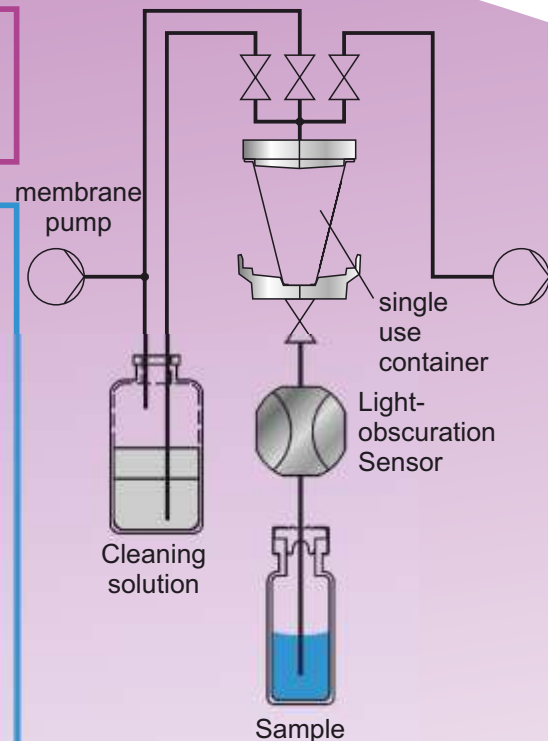
EVE's innovation

Cleaning innovation: system knows when it is clean independent of the sample properties as it measures the conductivity

Drying innovation: the “last” drop inside the fluid system is hard to remove. In EVE’s workflow 97% of the volume in the liquid path is taken out between each sample by the support of a removable single-use container.



single use container,
recyclable
free of particles
max volume 25ml



Significant cost and material saving potential with EVE: Comparison of different setups of a typical stability study:

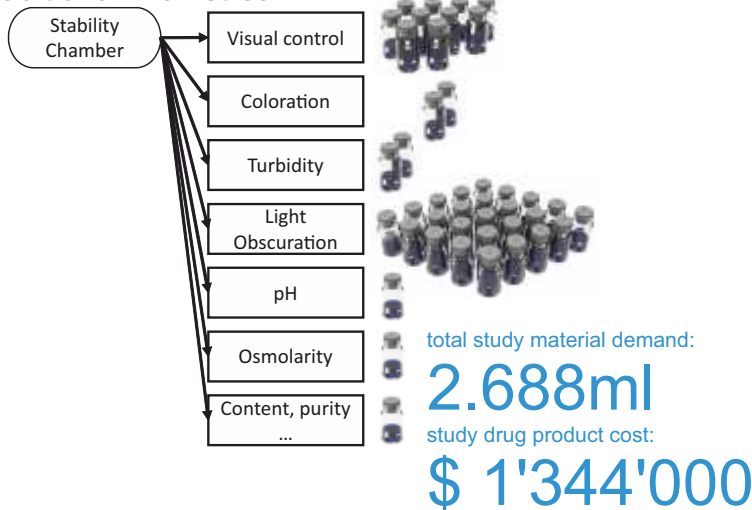
Early development platform formulation screen:

- 4 mAB formulations 50mg/ml
- 1ml fill volume in 2ml Vial
- Drug Product cost per vial: \$500

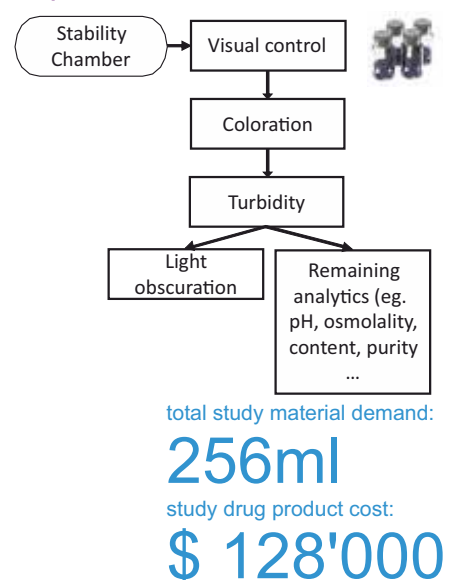


Climate condition	timepoint						
	t=0	1m	3m	6m	12m	18m	24m
5°C		x	x	x	x	x	x
25°C/60%	x	x	x	x	x	x	x
40°C/75%		x	x	x			

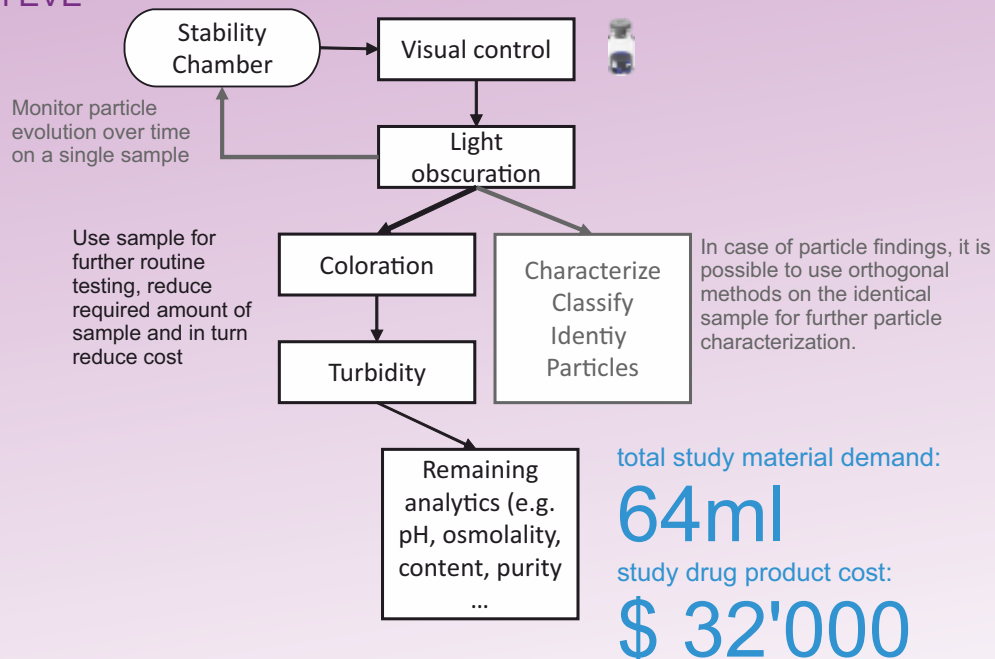
Traditional Workstream



Optimized Workstream



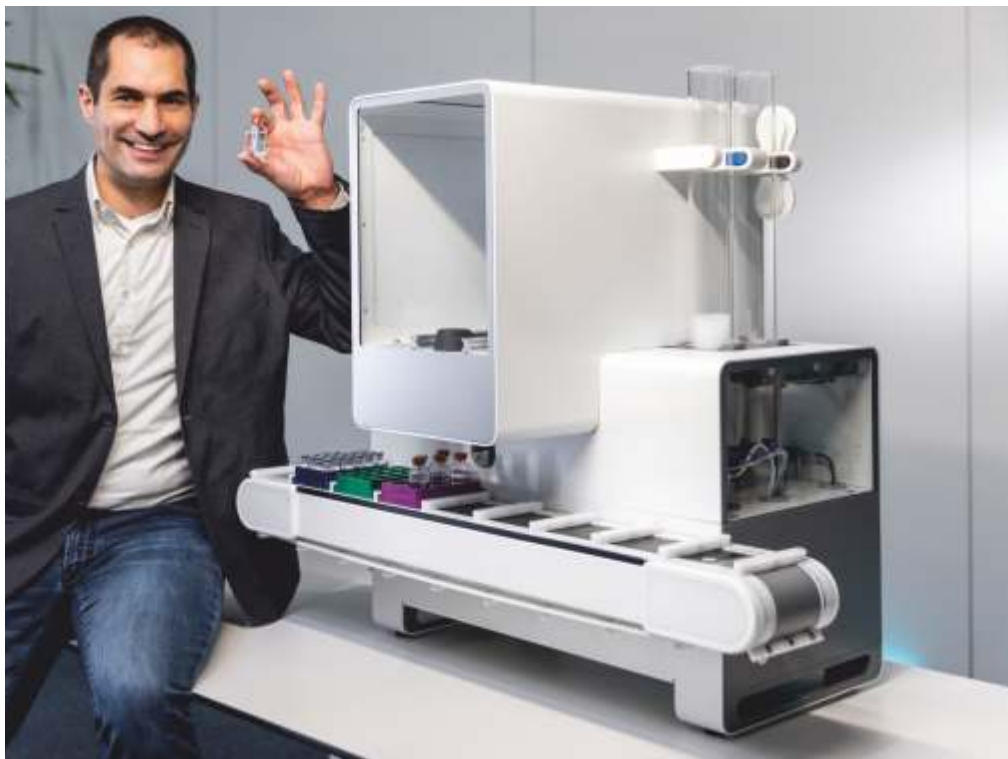
With EVE



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Our Partners

