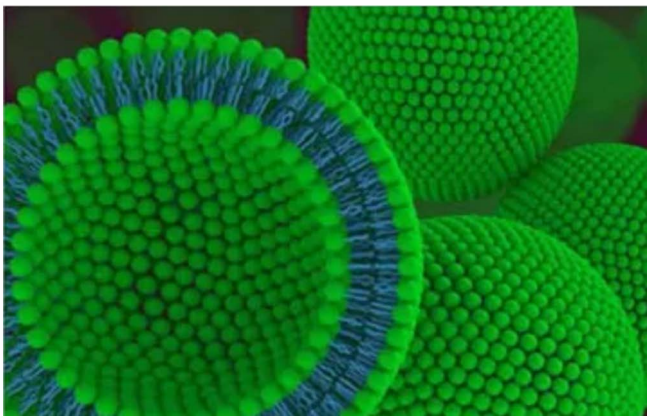
Precision in Every Drop: Controlling Particle Size Distribution with High-Pressure Homogenisation

In biopharmaceutical manufacturing, particle size distribution (PSD) is a key determinant of product performance, fundamental for product quality, efficacy, and regulatory compliance. From liposomal vaccines to protein formulations and nano emulsions, PSD influences bioavailability, stability, and reproducibility. Achieving stringent control is therefore central to formulation design and process robustness.

Why Particle Size Distribution Matters

A narrow and reproducible PSD offers several benefits due to particle dimensions significantly influencing the pharmacological profile and stability of a biologic product. Poor control over this parameter can introduce unacceptable batch-to-batch variability, compromise therapeutic effectiveness, or even raise safety concerns.

Impact	Description
Biovailability & Drug Delivery	Smaller, uniform particles facilitate improved uptake, distribution, and enhanced membrane permeability offering predictable pharmacokinetics.
Product Stability	Reducing polydispersity through accurate PSD control mitigates physical instability mechanisms such as aggregation and sedimentation, while extending shelf life.
Immunogenicity & Efficacy	Particle size can dictate the release profile, target engagement, and the subsequent therapeutic window or immune response.
Regulatory Compliance	Regulatory bodies such as the EMA and FDA identify PSD as a critical quality attribute for nano and micro structured therapeutics [1, 2]. It is therefore imperative to demonstrate rigorous evidence of consistent and reproducible PSD across all manufacturing batches to ensure product equivalence and quality.



The Role of High-Pressure Homogenisation

High-pressure homogenisation **(HPH)** achieves size reduction by forcing a fluid through a narrow orifice at pressures typically between 10,000-30,000 psi. The rapid acceleration, shear, and cavitation forces fragment particles or droplets into smaller, more uniform sizes [4].

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Process Variables Influencing Particle Size Distribution (PSD) in High-Pressure Homogenisation (HPH)

Process Variable	Description	Influence on PSD / Key Considerations
Pressure and Pass Number	The applied homogenisation pressure and number of passes determine the intensity and frequency of shear and impact forces.	Increasing pressure and multiple passes generally narrow the PSD by promoting finer dispersion, up to the point where thermal or mechanical limits are reached.
Temperature Control	HPH inherently generates heat due to energy dissipation during pressure release.	For every ~1,000 psi (~70 bar) increase in pressure, the product temperature can rise by approximately 1°c, requiring effective cooling systems to prevent degradation of heat-sensitive materials [5].
Valve Geometry	The design and adjustability of the homogenisation valve affect flow dynamics and energy dissipation,	Adjustable valve systems allow operators to fine-tune flow patterns and optimise PSD, balancing efficiency and product integrity.
Feed Characteristic	The physical and chemical properties of the feed material (e.g., viscosity, solids content, pre-processing).	High viscosity or solid concentration can reduce homogenisation efficiency; appropriate pre-processing enhances performance and reproducibility.

In Summary...

High pressure homogenisation, HPH, provides a reproducible and scalable approach to achieving controlled particle-size reduction, enabling consistent performance from laboratory to industrial scale. It can offer an important solution across a range of bioprocessing applications. For instance, it can transforms multilamellar liposomes and lipid nanoparticles into uniform unilamellar structures, enhancing encapsulation efficiency and stability [6].

The technique also generates nano emulsions and nano suspensions with droplet sizes below 200 nm, improving dissolution and optical clarity for poorly soluble APIs [7]. Additionally, HPH enables efficient mechanical lysis of microbial and mammalian cells without chemical reagents, preserving product integrity [8]. Reproducible PSD underpins both consistent processing and reliable product performance.

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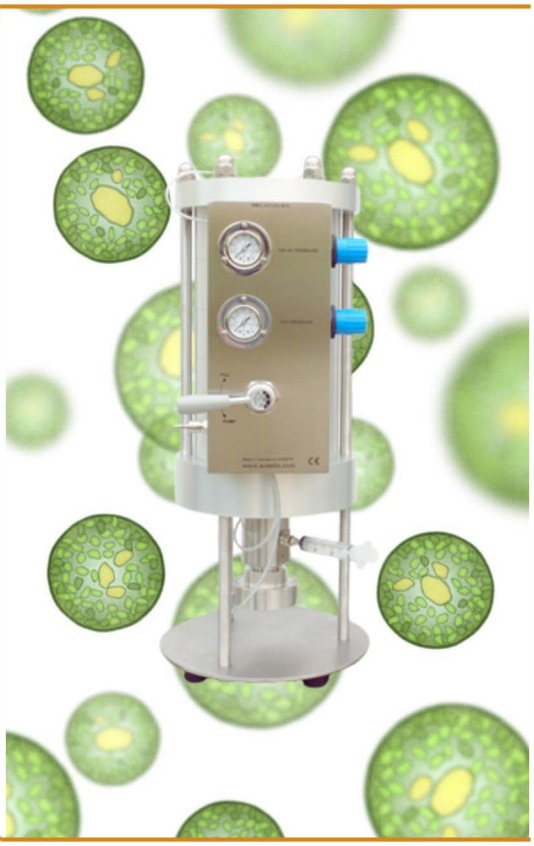
Consistency Across Scale

Scaling laboratory results to pilot and manufacturing environments requires consistent energy input and flow dynamics. Systems with geometrically matched flow paths and homogenising valves ensure PSD reproducibility across scales. Avestin's EmulsiFlex range demonstrates this principle, employing identical valve designs in R&D and GMP-scale equipment to maintain consistent energy dissipation and particle-size outcomes [9].



Conclusions

Controlled particle size distribution is essential for robust, reproducible biopharmaceutical formulations. **HPH** provides a scalable, reliable approach, and with precise pressure regulation, thermal management, and adaptable valve geometry, it enables consistent PSD, ensuring product quality, performance, and process predictability at every scale.

References

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