Innovating Process Analytics for Nanomedicine:

towards Continuous manufacturing and Real-time Release

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PAT4nano
Real-time Nanoparticle Characterization

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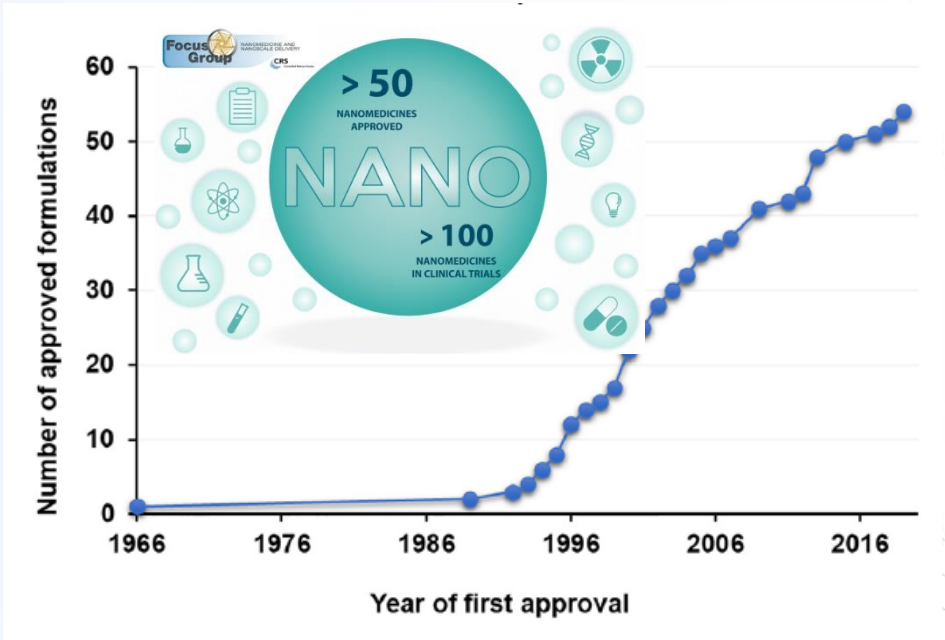
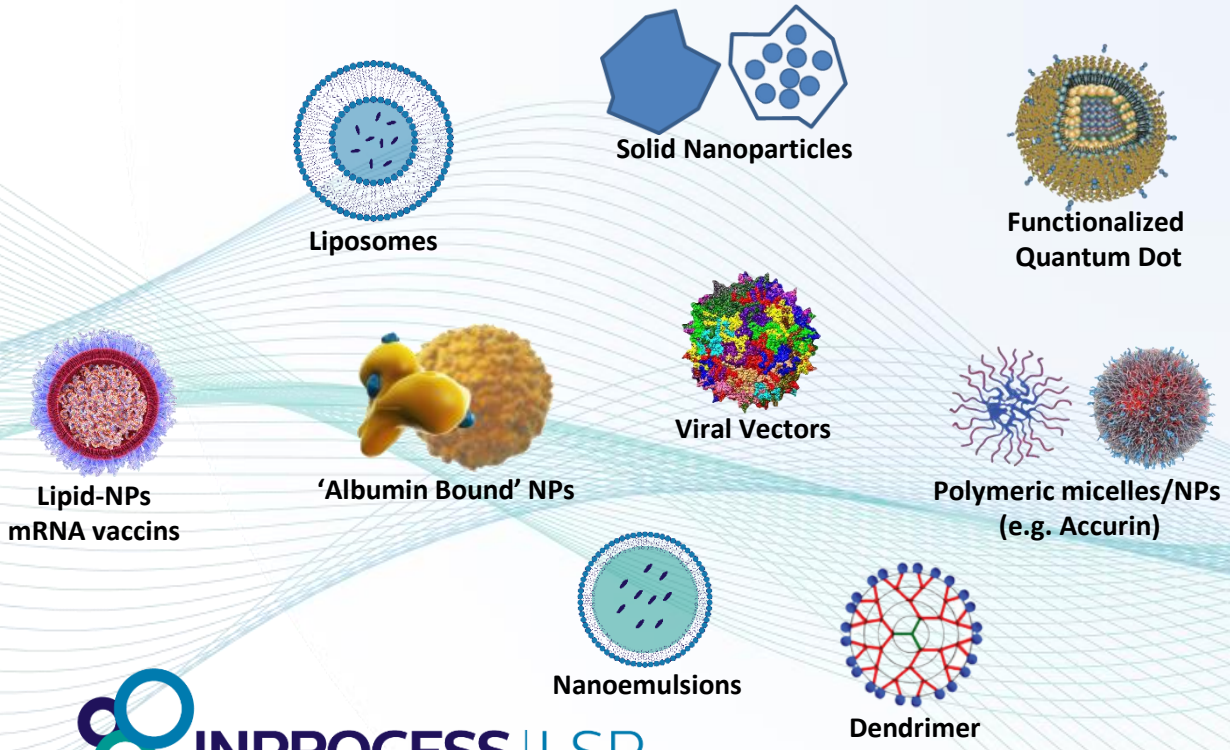
Nanomedicine – a hype ?

- Oncology treatments
- Controlled Release indications
- Vaccines
- .....

Germain, 2020, J. Controlled Release





Maturing Field

- Some promises (yet) unmet (targeting/therapeutic challenges)
- Yet, 'solid' contributions to viral therapeutics, cancer therapeutics/diagnostics, and other areas

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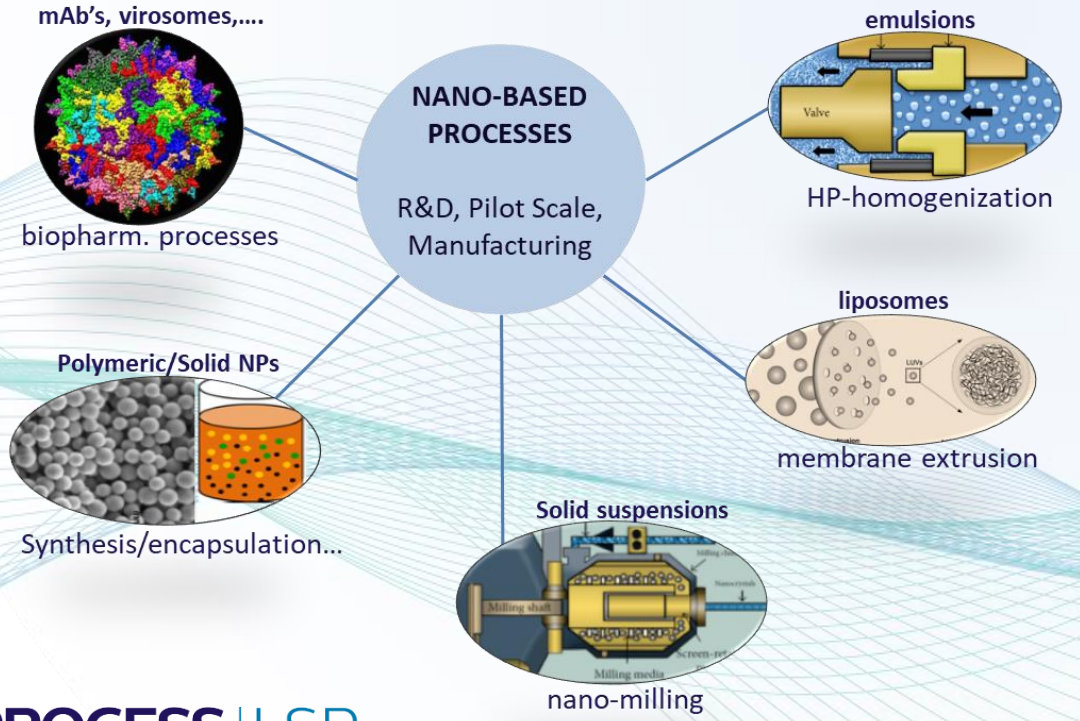
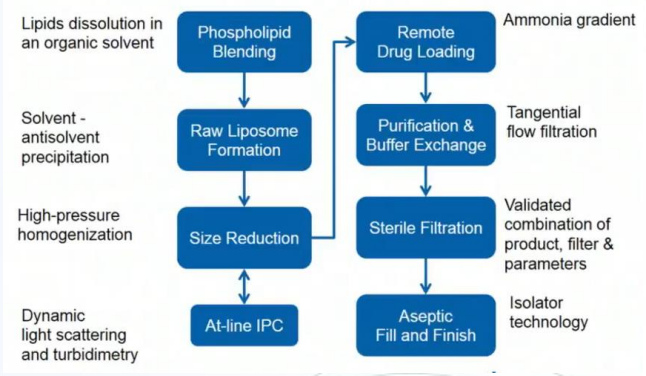
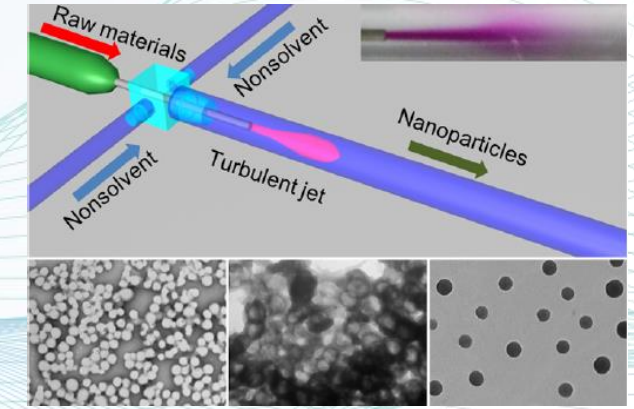
Nanomed: Pharmaceutical Development Challenges

- **'..bottlenecks to Nanoparticle (NP) medicine commercialization.'** (Tinkle, Ann.N.Y.Ac.Sci. 2014)
  - lack of precise control over NP manufacturing parameters and control assays
  - reproducibility issues: control of **Particle Size Distribution**
  - lack of QC / scalability issues / enhancing production rate

- **Process complexity**







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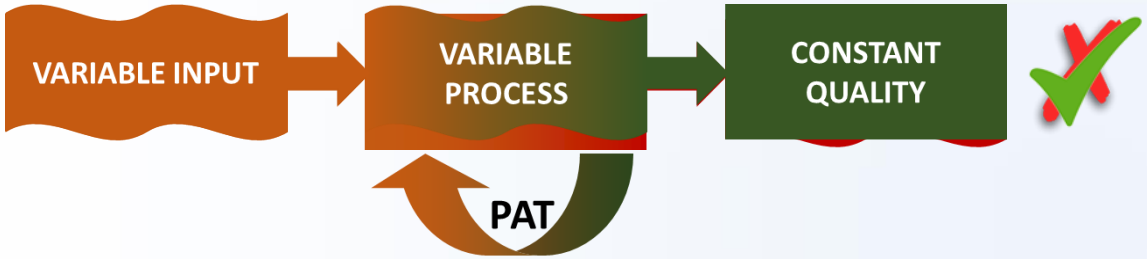
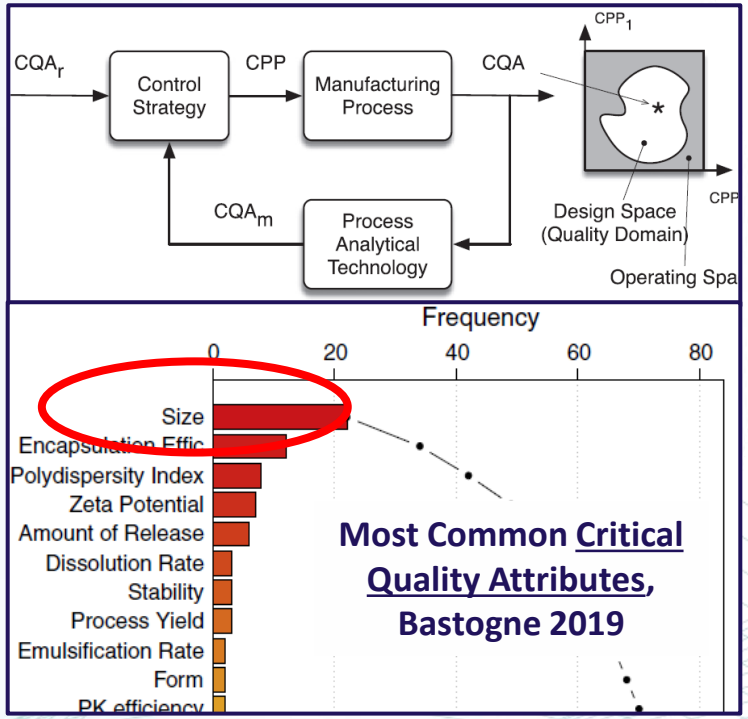
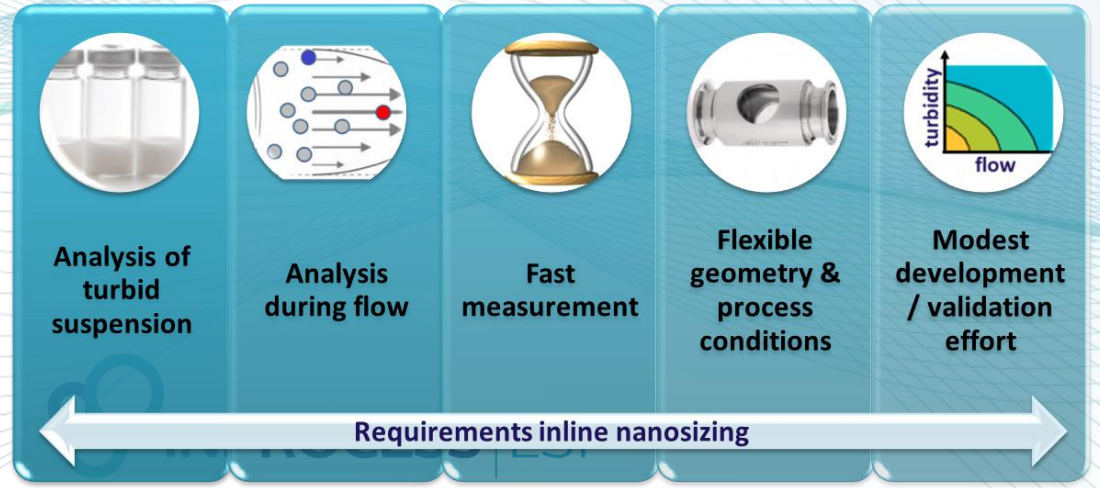
Process Analytical Technology

PAT: improve process understanding in **development** and **manufacturing**, and ensure constant final product quality, by **in/online product characterization**, ideally to provide **feedback for process control**



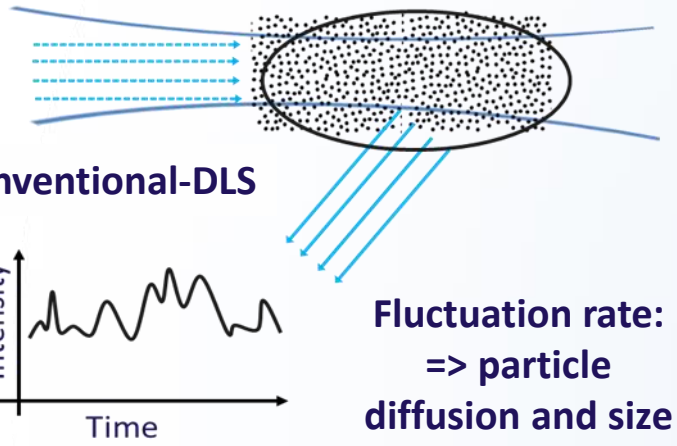


Most Common Critical Quality Attributes, Bastogne 2019



NanoMed: PAT measurement needs beyond standard instrument capabilities

The innovation: Spatially Resolved Dynamic Light Scattering



Fluctuation rate:
=> particle
diffusion and size

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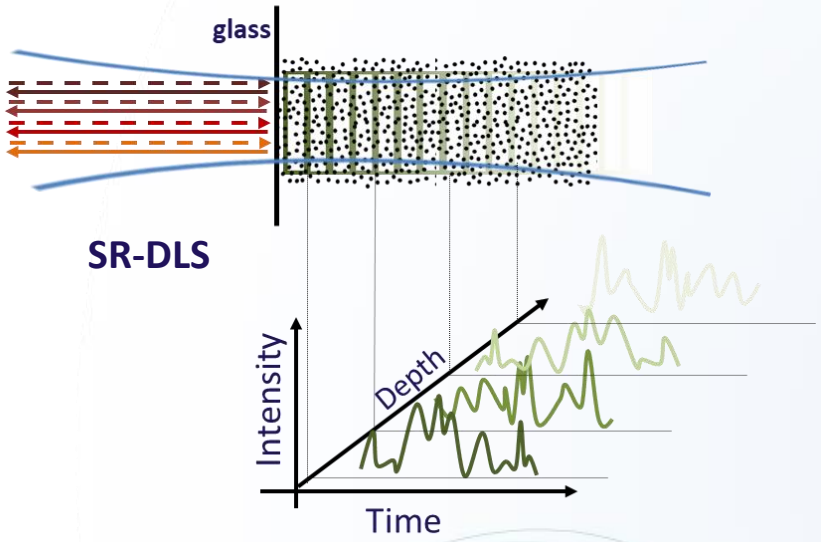
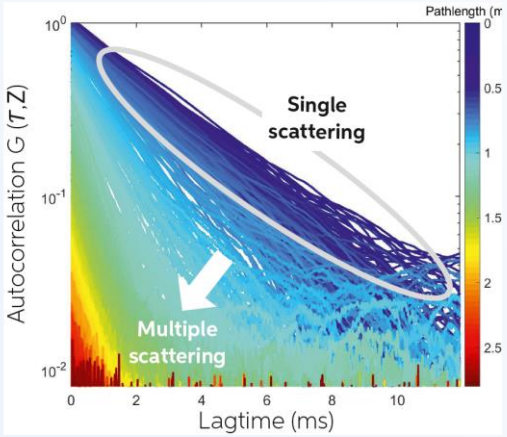
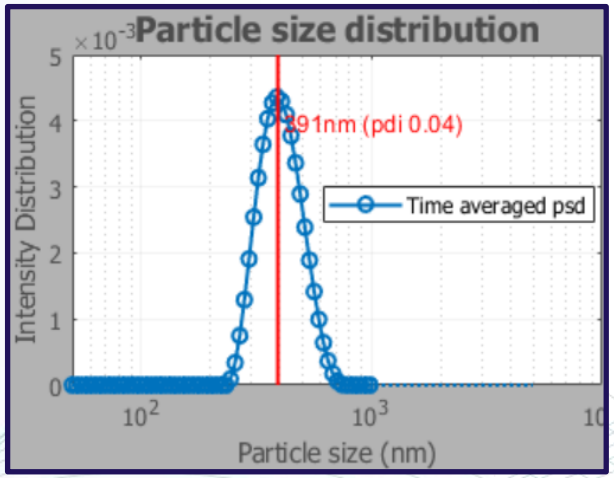
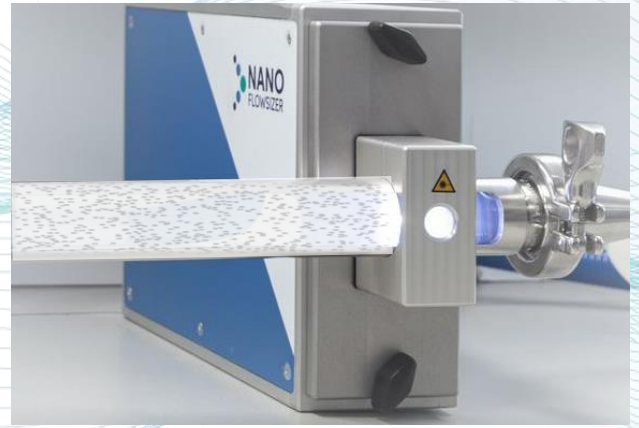
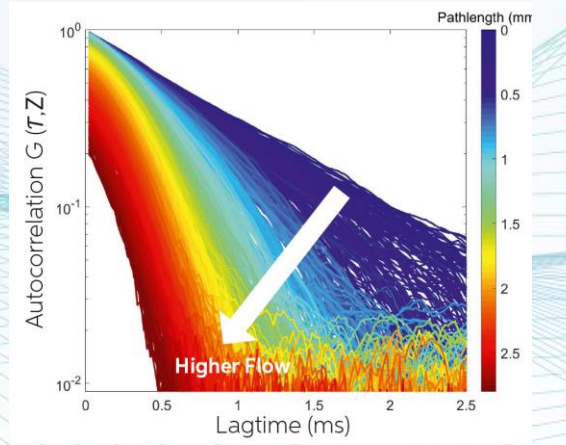
The innovation: Spatially Resolved Dynamic Light Scattering

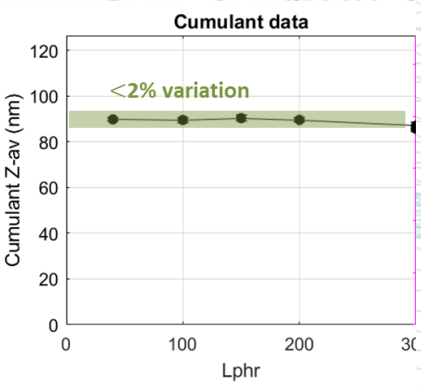










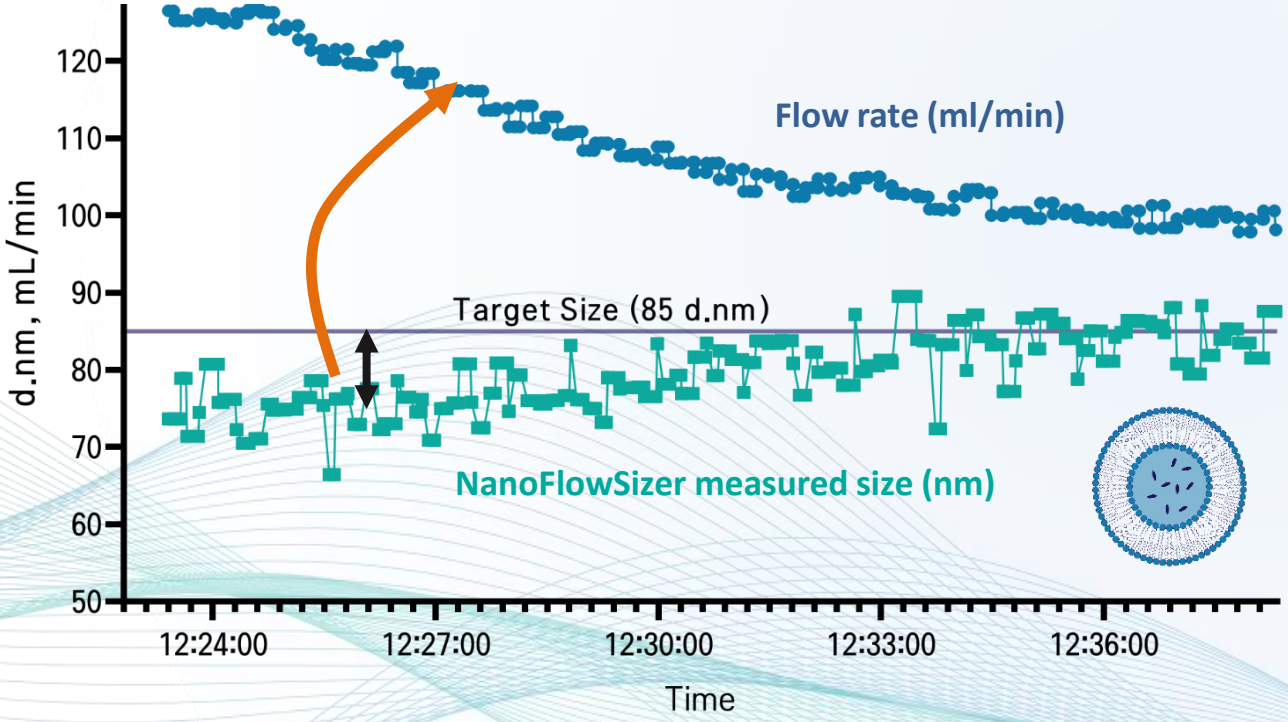


⇒ **Adds a dimension to standard DLS !**

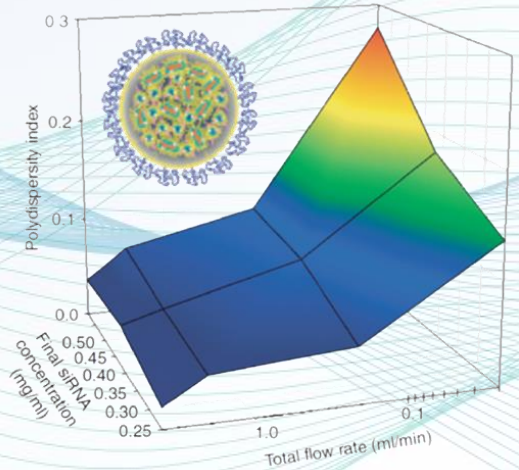
⇒ **Enables nanosizing to high turbidity and in flow**

Process control in Liposome manufacturing

- NanoFlowSizer integrated with Liposome Manufacturing Platform
  - => PAT enables Process control & Precision manufacturing
  - => **Continuous manufacturing method !**



- Rapid process development – assessment of 'Design Space':



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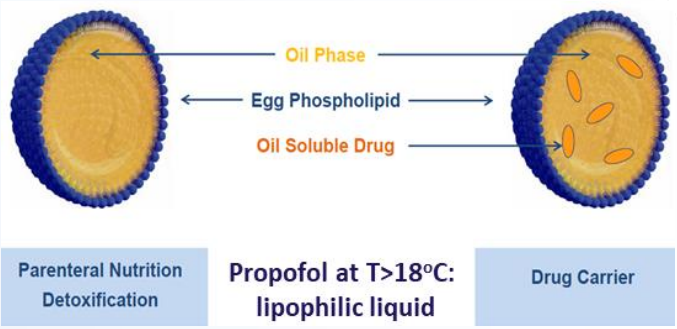
Multi-PAT for Anaesthetic Preparation

- Dissolving Propofol in LipidEmulsion for <u>extemporaneous prep</u>
  (anaesthetic shortage for COVID patients, May 2020)

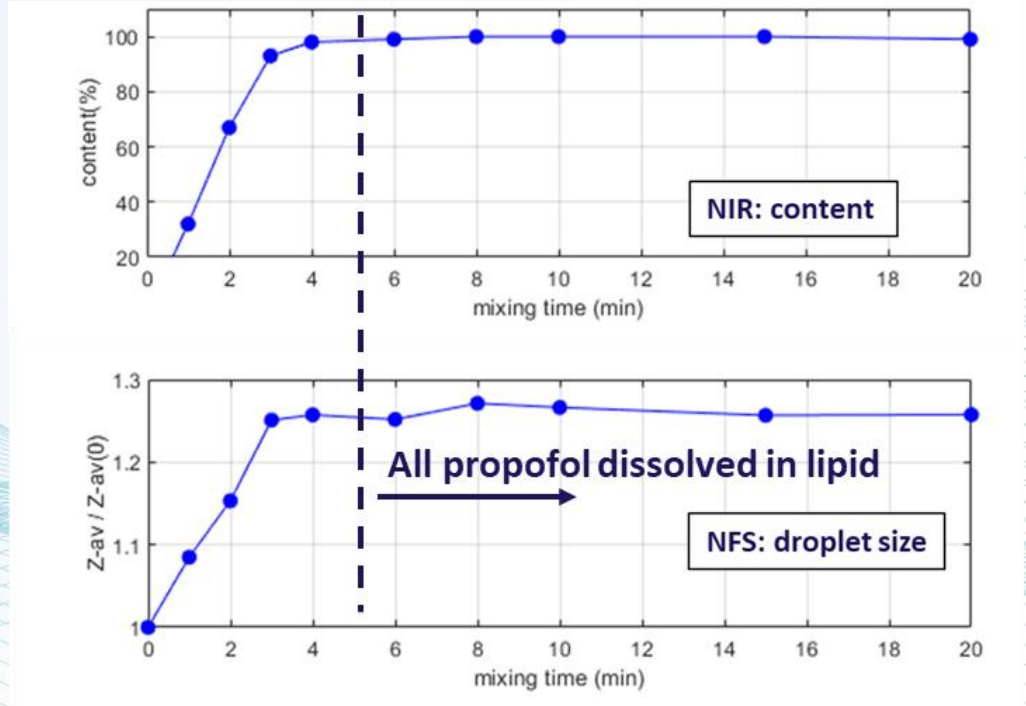
- <u>Sterile, noninvase monitoring</u> of clinical prep method: unique for NFS



Shaking time

NIR: **content info**

NFS: **size info**



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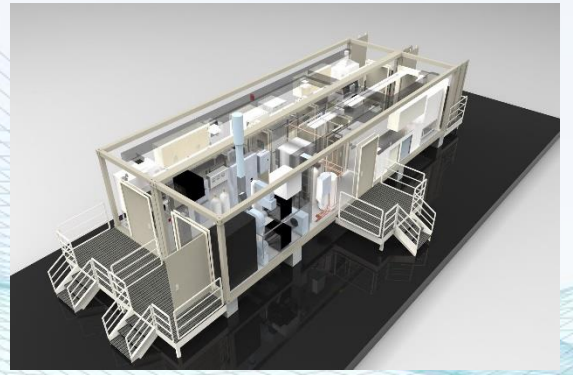
Future Perspectives Pharma Dev. & Mfg.

- Nanotechnology: an important ingredient for our future arsenal of medicines
- Faster product development/manufacturing requires new methodologies → PAT
- Growing demand for small-scale, mobile mfg. facilities (personalized/local need)
- Challenge: continuous and cost-effective quality monitoring for ‘Realtime Release’

Typical Pharmaceutical production



Mobile, continuous manufacturing

‘Personalised’ clinical production

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