NANO FLOWSIZER

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Frequently Asked Questions

Application

1. **What is the applicable size measurement range of the NanoFLowSizer?**
   Nanoparticles between 10 and 1000nm are within operating range. Larger particles up to some micrometers can be measured as well provided sedimentation of particles does not occur.
2. **Do you need flow to perform good measurements?**
   No, measurements can be applied under flow conditions as well as under static conditions.
3. **In which markets can the NanoFlowSizer be used for size measurement of nanoparticles ?**
   In addition to Pharmaceutical markets, other industries such as Food & Dairy, inks, cosmetics, minerals and specialty chemicals have applications which perfectly suits the capabilities of the NanoFlowSizer.
4. **What are typical differences between the NanoFlowSizer and conventional DLS technologies?**
   The NanoFLowSizer makes use of Spatially Resolved Dynamic Light Scattering (SR-DLS), developed by InProcess-LSP, which allows direct measurement of highly turbid samples in static conditions or in flow. Conventional DLS equipment requires in most cases dilution of the sample and measurement in a static condition. Conventional DLS technologies may work for nanoparticle sizes down to 1nm, while the NanoFlowSizer can measures down to 10nm (depending on optical properties down to 5nm may be feasible). Measurements with conventional DLS technologies will take longer and are invasive. Conventional DLS technologies are not suitable for process monitoring and PAT.
5. **Is it possible to measure volume based distributions?**
   Yes, similar as for conventional DLS technologies the intensity based PSD can be re-processed into a volume based PSD when refractive index data of the nanoparticles are known.
6. **Is it possible to measure shape of particles?**
   No, the shape of particles is not measured. All reported sizes are translated as if particles were spherical.
7. **Is it possible to measure highly turbid samples?**
   Yes, in contrast to conventional DLS technologies, SR-DLS is capable to measure samples with significantly higher turbidity without the need to dilute the sample.

8. **What is the highest possible concentration which can be measured well?**
   The highest possible concentration to be measured is, besides concentration, dependent on optical properties of the particles. For highly scattering particles concentration limits are lower compared to lower scattering particles. In practice samples like silica can be measure up to 40% without dilution.
9. **Is it possible to measure nanoparticles in a matrix with much larger particles?**
   If the bulk of the sample contains larger than a few micron particles the backscatter signal will be overwhelmed due to the larger particles which will prevent the system to analyze nanoparticle size adequately. In case a lower fraction of large particles is present, nanoparticle size measurements will in most cases be possible.
10. **Is the maximum flow rate also related to the particle size to be measured?**
    Yes, the larger the particle size of interest, the lower the maximum applicable flow rate. Since larger particles show slower diffusion rates, it takes more time to measure diffusion rates accurately. Applicable flow rates in our documentation is commonly based on 100nm particle size.
11. **Does the NanoFlowSizer needs extensive method development for new products?**
    No, the NanoFlowSizer can be applied directly to your sample without extensive method development. Based on turbidity and complexity of the sample fine tuning of data acquisition settings is recommended to obtain to optimal result. In case diffusion of particles is hindered due to corresponding high concentrations or strong interactions, an additional calibration factor may be needed to extract the accurate particle size.

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Equipment

12. **What are applicable flow rates?**
    Flow rates close to zero are applicable up to about 300L per hour. Depending on flow rates differently sized flow cells are applied. Above 300L/hour a bypass option is a feasible option.
13. **Does the NanoFlowSizer need to be calibrated?**
    No, the system translates diffusion rates into particle size which is a directly obtained property without calibration. Calibrated standards can be applied for confirmation of adequate performance.
14. **Is the measurement invasive?**
    No, the measurement is performed through a glass interface, either a flow cell, sight glass or vial, without direct contact with the sample. Since dilution or other sample preparation is not required, measurements are non-invasive.
15. **How much time takes one measurement?**
    A single measurement takes 5 to 10 seconds.
16. **What particle size properties are measured?**
    The hydrodynamic size of a nanoparticle is measured, similar as for conventional Dynamic Light Scattering technologies. Besides Z-average and main peak size, the particle size distribution (PSD) together with d10, d50 and d90 values are reported together with polydispersity index.
17. **How does NanoFlowSizer data compare with conventional DLS?**
    Both techniques are based on dynamic light scattering of particles, therefore data should be similar in most cases. The NanoFlowSizer, based on Spatially Resolved-DLS (SR-DLS), is capable to measure significantly higher turbidity ranges without dilution and can measure under flow conditions. Due to variance in light source the sensitivity for larger particle detection is prevalent in SR-DLS, meaning variations in PSD and PDI might occur for typical polydisperse samples. Lower particle size limit for the NanoFlowSizer is about 5-10nm while conventional DLS can measure particles down to ~ 1nm.
18. **If it possible to create a dedicated sample module for my vial or syringe samples?**
    Yes, in case there is a specific need for non-invasive measurements through vials or syringes with specific dimensions, a dedicated sampling module can be provided by InProcess-LSP.
19. **Is the NanoFlowSizer system in compliance with GMP and 21CFR part11 regulations.**
    In Q4 of 2021 a fully GMP compliant system is available with full compliance to 21CFR part 11 regulations. Current NanoFlowSizer systems are formally non-GMP.

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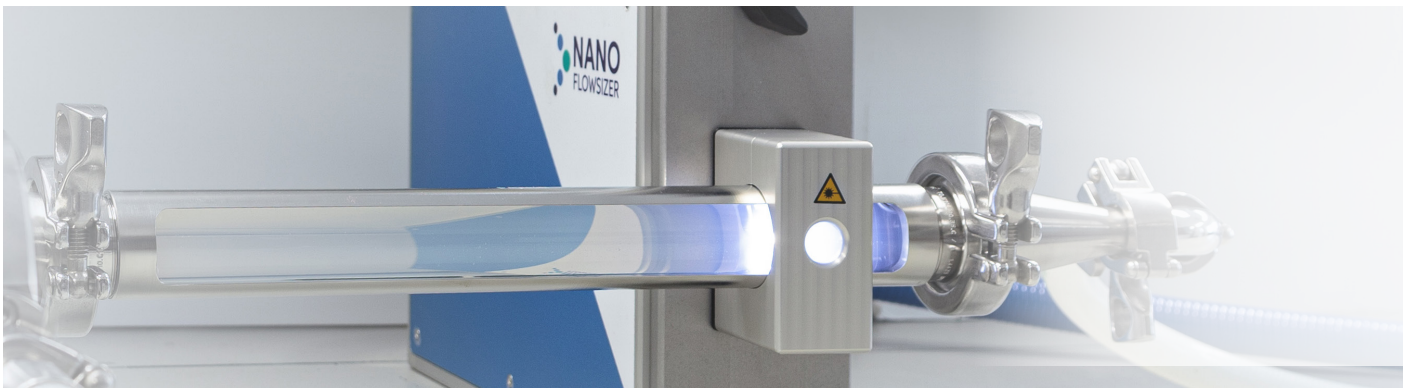
20. **Can the system be applied for samples and processes at different scales?**
    Yes, a variety of interchangeable sampling modules is available which allows connections to mL and configurations up to Liters.
21. **Is it a problem if the sample contains air bubbles?**
    Air bubbles produce large backscatter signals and may destroy the signal, therefore as much as possible avoidance of air bubbles is recommended. In case some air bubbles are present, the system can detect a-typical reflectance from air bubbles and filter these data from the valid data.
22. **Can the NanoFlowSizer operate at low and high temperatures?**
    The system can operate between 0 and 100°C, for higher temperatures the level of heat transfer to the probe unit must be evaluated.
23. **Is it possible to connect the NanoFlowSizer data to data management / SCADA systems like SIPAT?**
    Yes, the NanoFlowSizer system can 'talk' to other systems by dedicated OPC drivers. In case specific connection to other systems is desired, please contact us to discuss possibilities.
24. **Is it possible to post-process the data?**
    Yes, with each instrument an additional license for offline reprocessing is included. Recorded data is stored in such a way that smoothing or other statistical functions may be altered during re-processing of the data.
25. **Can the system operate in ATEX environment?**
    The NanoFlowSizer is not certified for ATEX environment. However, possibilities exist to install a NanoFlowSizer in ATEX environment. In case ATEX is a hard requirement, please contact us to discuss possibilities.
26. **How can the NanoFlowSizer be connected to the process?**
    The NanoFlowSizer is connected to the process by a sampling module. Sampling modules exist in different sizes for varying scales and situations. A number of (pharma grade) flow cells are available which can be integrated in the process inline or online (via a bypass). In case of static or gently stirred solutions, the system can measure directly through the glass wall in (closed) vials or flasks.
27. **Can the NanoFlowSizer measure zeta potential?**
    No, this is not a standard feature but could be developed depending customer needs.

28. Why is a laminar flow required for measurements under flow?

The NanoFlowSizer uses highly advanced flow correction algorithms to extract Brownian motion of particles from flow rate dependent movement of particles. The algorithms work optimal for laminar flow profiles. When flow patterns become turbulent, flow correction algorithms will perform not optimally.



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Support

29. Can InProcess-LSP test my formulations?

Yes, InProcess-LSP has fully equipped application labs with several NanoFlowSizers in active operation. Also homogenization, nanomilling and synthesis of nanoparticles are possible in most cases for inline testing.

30. Does InProcess-LSP operate and support globally?

Yes, the NanoFlowSizer is available globally. In various countries InProcess-LSP works with partners to support regional business.

31. How to assess feasibility for my application?

InProcess-LSP will support customers with feasibility studies varying from paper feasibility (based on known properties of the materials and objectives of the application) up to extensive testing in our laboratory or on-site at the customer.

32. Does InProcess-LSP guarantee the performance of the NanoFlowSizer equipment?

The NanoFlowSizer comes with a standard one year guarantee package. There are also various post guarantee service packages available which include preventive maintenance. For more information please contact us.

33. Can I lease or rent the NanoFlowSizer equipment?

Yes, InProcess-LSP has rental and lease possibilities including lease-buy options for the NanoFlowSizer. Contact us if you require a proposal.

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General

34. What is Brownian motion?

Brownian motion is the, by nature, existing movement of nanoparticles. The Brownian motion (or diffusion) of nanoparticles is directly related to the size of the particles. Small particles show higher diffusion rates compared to larger particles.

35. What is the difference between Spatially Resolved DLS and conventional DLS?

The NanoFlowSizer Spatially Resolved DLS technology is based on low coherence interferometry providing light scattering information as function of optical pathlength. The depth resolved light scattering holds information on particle movement caused by both Brownian motion as well as flow rate. The contribution due to Brownian motion is used for calculation of the particle size characteristics, while the flow rate information is obtained instantaneously for every measurement as well. Standard DLS measurements need to be performed under static conditions ensuring that particle movement is solely caused by Brownian motion and not influenced by other factors like liquid flow.

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