Entegris

# Nanoparticles Drive the Nanotechnology Revolution

*White paper*

## INTRODUCTION

Nanotechnology has been referred to as potentially being the next technical revolution that could change the modern world. Perhaps the developments seen to date do not yet match this build up, but the combined investment by governments, universities, and industry is significant with global government investment exceeding $9 billion annually and growing.[1] The United States government alone has invested over $27 billion since from 2001 – 2019.[2] The global nanotechnology market has been estimated to be between $10 – 50 billion annually depending on definitions and sources.[3,4]

A large portion of the diverse realm of nanotechnology is the manipulation of matter on the atomic scale. The United States National Nanotechnology Initiative[2] defines nanotechnology as the manipulation of matter with at least one dimension sized from 1 to 100 nanometers (nm). The scope of technologies considered nanotechnology has expanded considerably to now include fields such as Micro-Electro-Mechanical Systems, or MEMS, and microelectronics. But nanoparticles remain a major focus of both research and industrial products. This paper intends to help define nanoparticles, their various uses, and the analytical techniques used for their physical characterization.

## WHAT ARE NANOPARTICLES?

Several standards organizations and governmental bodies have provided agreed upon definitions of what a nanoparticle is[5,6,7,8,9,10] including:

"A term referring to a wide range of technologies that measure, manipulate, or incorporate materials and/or features with at least one dimension between approximately 1 and 100 nanometers (nm). Such applications exploit the properties, distinct from bulk/macroscopic systems, of nanoscale components."[5]

In the European Union the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) developed a more complex definition[11] when addressing potential toxicology issues associated with some nanomaterials. Figure 1 shows the decision tree that establishes three categories of materials and risk assessment based on size scale.

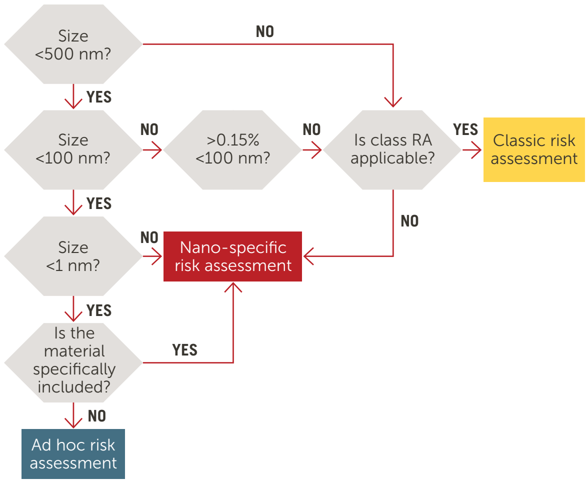


*Figure 1. Risk Assessment on nanomaterials, tiered approach.[11]*

In addition, several countries (Australia, Canada, France, Switzerland, Taiwan, China, others) have issued specific definitions that slightly differ from other accepted documents.

In the United States the FDA has issued a Guidance for Industry document[12] addressing nanomaterials. The FDA did not establish regulatory definitions of nanotechnology, nanomaterial, nanoscale, or other related terms. It rather describes current thinking at the FDA on deciding if FDA regulated products involve the application of nanotechnology.

## OTHER TERMS

If the longest to shortest lengths differ significantly, then the terms nanotube, nanofiber, nanorod, or nanoplate are sometimes used.

The term "nanostructured materials" is used when nanoscale regions or surfaces exist within a material with larger external dimensions.

## METHODS OF ANALYSIS

Important nanoparticle physical parameters include size, shape, surface properties including charge, dispersion state, and crystallinity. A wide range of analytical techniques are used to quantify these properties.

**Microscopic techniques:** The most direct size and shape analysis technique is microscopy and a range of microscopic techniques are utilized for nanoparticles including:

- Scanning Electron Microscopy (SEM), Figure 2
- Transmission Electron Microscopy (TEM)
- Scanning Tunneling Microcopy (STM)
- Atomic Force Microscopy (AFM)

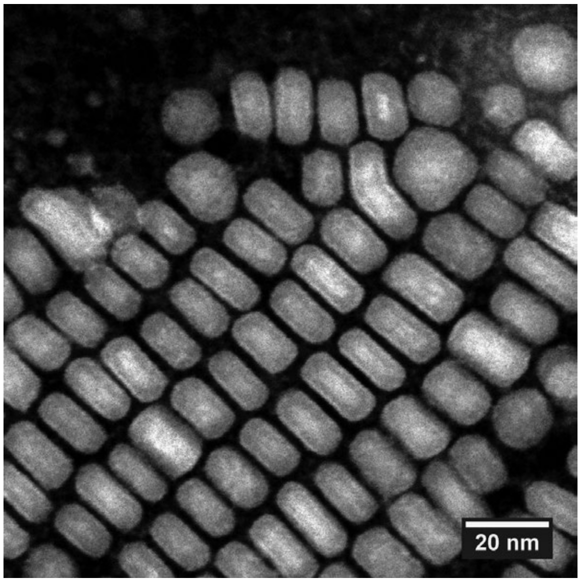


*Figure 2. SEM image of nanoparticles with scale.*

**Spectroscopic techniques:** The interaction between particles and electromagnetic radiation as a function of wavelength is used for some classes of nanoparticles to determine size and other properties. Some of these spectroscopic techniques include:

- Nuclear Magnetic Resonance (NMR)
- UV – Visible
- Infrared (IR)
- Fluorescence, Figure 3

*Figure 3. Fluorescent nanoparticles (quantum dots).*

**Light scattering techniques:** Several light scattering methods can be used to measure particle size including:

- Small Angle Neutron Scattering (SANS)
- Small angle X-ray
- Laser diffraction
- Dynamic Light Scattering (DLS)

The most common light scattering technique utilized is dynamic light scattering (DLS). The basic principle of DLS is based on the time signature of the scattering caused by the Brownian motion of the particles. Smaller particles diffuse more quickly while larger particles diffuse more slowly. Figure 4 shows a simplified optical diagram of a DLS system.

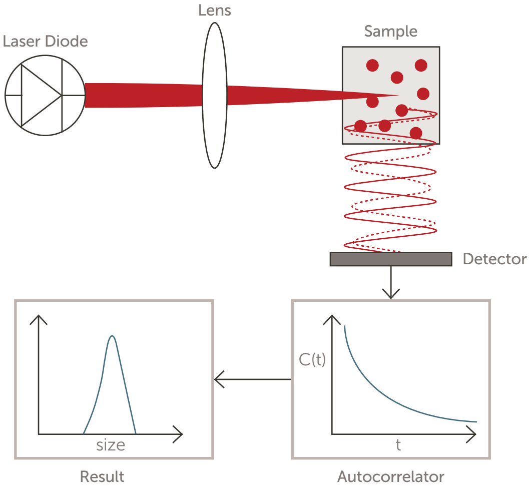


*Figure 4. Optical diagram of a DLS system. Source: Entegris*

The detector counts photons and feeds this raw data into the correlator. The measured correlation function is used to determine the diffusion coefficient, D, which is then used to calculate the particle size using the Stokes-Einstein equation:

$$D = kT/6\pi \eta R$$

*Where:*
*D = Diffusion coefficient*
*R = Particle radius*
*k = Boltzmann's constant*
*T = Temperature Kelvin*
*η= Shear viscosity of the solvent*

**Other techniques:** Other commonly used particle characterization techniques for nanoparticles include:

- BET specific surface area (SSA), that can then be used to calculate a mean particle size
- Mass Spectrometry (MS) for particle mass
- X-ray diffraction for crystal structure
- Electrophoretic Light Scattering (ELS) for particle charge

Particle charge (zeta potential) influences the stability of nanoparticles and is a function of the specific surface chemistry of a dispersion. The zeta potential is measured using Electrophoretic Light Scattering (ELS) by applying an electric field to the sample and then measuring the direction and speed of the particle motion, Figure 5.

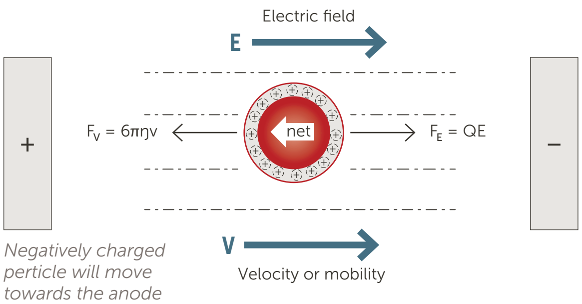


*Figure 5. Electrophoretic Light Scattering (ELS) technique. Source: Entegris*

The direction indicates if the particles are positively or negatively charged. The speed of the particles indicates the magnitude of the charge. Particle velocity can be measured using either phase analysis light scattering (PALS) or using frequency analysis. PALS is the newer, more sensitive approach and is now the preferred method for most samples.

## EXAMPLES AND INDUSTRIES OF NANOPARTICLES

Nanoparticles are used in many products for their unique properties over traditional materials. Below are several examples of incorporating nanoparticles. In many cases this creates a new product that has improved and more desirable properties.

| | |
|---|---|
| Automobile tires | To improve mechanical properties and wear |
| Polymers | Nanoclays added to polymers improve strength and impact resistance |
| Food packaging | Nanoflakes of clay moderate moisture and gas through the film |
| Paint and coatings | Antibacterial properties for hospitals and medical facilities |
| Flame retardants | Used in plastics, replace flammable organic halogens for lower emissions |
| Batteries | High surface area of the nanoparticles increases storage capability |
| Ceramics | The nanoparticles with polymers create more resiliency and can add electrical properties |
| Diode white light | Coating the bulb to modify the wavelengths can create a white light LED |
| Sunscreen | Optisol replaces traditional sunscreen ingredients, eliminating the health risk |
| Medicine | Small sizes can circulate throughout the body delivering payloads of drugs to specific areas, cells, tumors, and other diseased tissue. Can be used to enhance images on MRI and PET. Drug delivery to the brain via inhalation has considerable promise for Parkinson's, Alzheimer's, and Multiple Sclerosis. |

## NANOPARTICLES FOR DRUG DELIVERY

One of the more active and exciting fields where nanoparticles are being employed is drug delivery. Many of these drug products are developed to enhance targeting. A passive targeting approach increases the circulation time by reducing the size and cloaking the nanoparticle with a coating such as polyethylene glycol (PEG). An active targeting approach modifies the surface of the nanoparticle to seek and adhere to specific parts of the body such as cancer tumors while avoiding healthy tissue. Cell specific ligands on the surface of the nanoparticle can be added to bind specifically to complementary receptors, Figure 6.

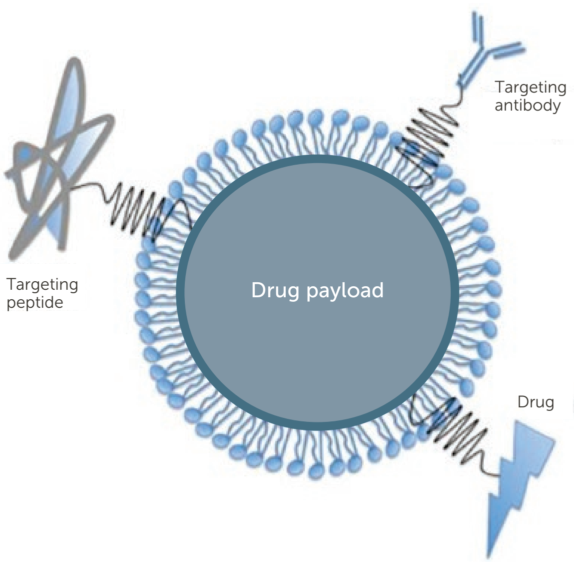


*Figure 6. Surfaced modified nanoparticle for drug targeting and delivery.*[13]

Controlling the size of nanoparticles used for drug delivery is critical, therefore proper analytical methods must be used to assure the size is within desired specifications. DLS remains the most commonly used particle sizing technique for these applications. Figure 7 shows both DLS and SEM results[14] for lipid based liquid crystalline nanoparticles (LCNPs). These are self-assembled structures prepared by high shear energy dispersing of a nonlamellar liquid crystalline matrix into the water phase.

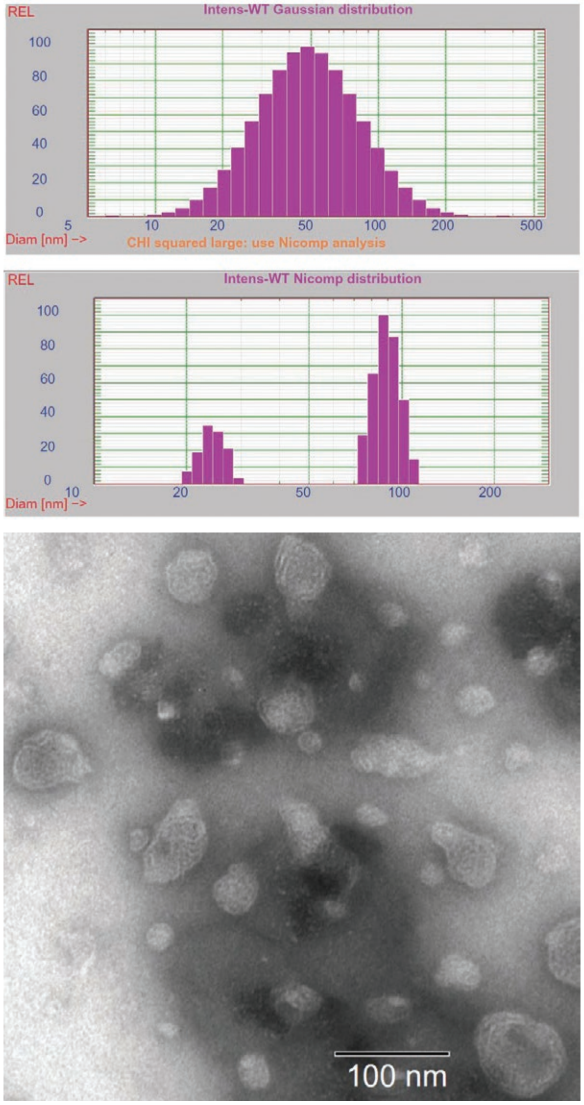


*Figure 7. DLS and SEM results for liquid crystalline nanoparticles.*[14]

Both the SEM and the multimodal DLS (lower left graph) confirm the existence of both smaller (25 nm) and larger (90 nm) size populations.

## CONCLUSIONS

The creation, control, and use of nanoparticles is a critical segment within the larger field on nanotechnology. Significant research and development into nanoparticles for many uses is accelerating in both academic and industrial laboratories. Nanoparticle-based products are now on the market in a range of industries and nanoparticles for drug delivery hold promise for significant improvements in health benefits.

## ABOUT ENTEGRIS

Entegris is a leader in specialty chemicals and advanced materials solutions for the microelectronics industry and other high-tech industries. Entegris is ISO 9001 certified and has manufacturing, customer service, and/or research facilities in the United States, China, France, Germany, Israel, Japan, Malaysia, Singapore, South Korea, and Taiwan. Additional information can be found at www.entegris.com

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[13] Graphic source: https://en.wikipedia.org/wiki/Nanoparticles_for_drug_delivery_to_the_brain Graphic by Andrea Trementozzi – Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=30082797

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