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# <1153> DRUG PRODUCTS CONTAINING NANOMATERIALS

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## 1. INTRODUCTION

The current interest in nanotechnology and its application to the medical field has historical precedent. Initial products employed general physical chemistry of colloids to produce stable drug suspensions and improve bioavailability. The later introduction of liposomes began the evolution to today's more sophisticated and potentially revolutionary new technologies, which have accompanied the rapid growth in biotechnology product opportunities, notably including targeted drug delivery products.

The term "nanomaterials" by recent convention describes materials that have features or structures that exist on the 1–100 nm scale in any of the three spatial dimensions. However, the existence of a large number of formulations containing nanomaterials that are currently under development or review, or that have already received approval from the FDA, emphasizes the need to identify important properties of these formulations, as well as methods of measuring these properties to ensure quality and performance. Accordingly, the FDA has authored guidance on nanomaterials <sup>▲(1-2)</sup> that recognizes material of end products engineered to:

- Have at least one external dimension, or an internal or surface structure, in the nanoscale range (approximately 1–100 nm).
- Exhibit properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to 1 μm (1000 nm). <sup>▲(USP 1-May-2024)</sup>

These materials often require measurements with specialized instruments (see [Table 1](#)).

**Table 1. Names and Definitions**

Name of the Nanomaterial	Subcategory	Definition, Structure, and Description
Dendrimers <sup>(3)</sup>	—	Dendrimers are highly branched star-shaped macromolecules consisting of polymers [e.g., polyamidoamine (PAMAM)]. These structures can be linked to drug substances or used by physical/steric association to encapsulate drug substances.
Drug nanoparticles/nanocrystals <sup>(4)</sup>	—	Nanoparticles consist of crystalline or amorphous forms of pure drug substance and are used as a formulation strategy to enhance bioavailability by increasing drug solubility as described by the <sup>(5)</sup> Kelvin equation and dissolution rate as described by the Noyes-Whitney equation. Examples of nanocrystal products include those used for cancer (megestrol acetate), organ rejection (sirolimus), emesis (aprepitant), and dyslipidemia (fenofibrate). Nanocrystal drug products may be solid dosage forms or prepared as aqueous or nonaqueous suspensions. The latter often require stabilization with surfactants or polymeric stabilizers. A common route of administration is the oral route. Nanocrystals are made using milling, homogenization, and precipitation

Name of the Nanomaterial	Subcategory	Definition, Structure, and Description
Liposomes (6)	—	<p>methods, as well as a combination of these methods.</p> <p>▲Liposomes are lipid vesicles with at least one lipid bilayer that entraps at least one aqueous compartment.▲ (USP 1-May-2024)</p> <p>Liposomes have been employed to formulate both water-soluble and water-insoluble drug substances. Due to their hydrophilic nature, the former can be incorporated into the internal aqueous compartment(s) of liposomes and the latter into the hydrophobic core of the lipid bilayer. Examples of drug substances used in liposome drug products include anticancer agents (i.e., doxorubicin, daunorubicin, vincristine, irinotecan, cytarabine), antifungals (i.e., amphotericin B, itraconazole), analgesics (i.e., morphine, bupivacaine), and vaccines (i.e., influenza, hepatitis A). Liposomes can be manufactured by extrusion (filtration), homogenization, and micromixing processes. The drug substance can be incorporated during liposome formation or by loading into empty preformed liposomes. Routes of administration include topical, parenteral (with intravenous administration as the most common route), and inhalation.</p>
Micelles	—	<p>Nano-scaled colloidal structures are formed by self-assembly of amphiphilic molecules. The constituents of the micelles can be either surfactants or block copolymers (7). For block copolymers, there are constructs in which the polymers employ different hydrophobic blocks [e.g., poly(propylene oxide), poly(L-amino acids), or poly(esters)]. An example of such block copolymers is poly(ethylene glycol)-block-poly(lactide) (PEG-PLA) polymers]. Polymeric micelles are used to target biological sites and minimize toxicity. As an example, a PEG-PLA polymeric micelle product improves the solubility of paclitaxel. Its route of administration is typically intravenous.</p> <p>Classical micelles (8) are thermodynamically stable self-associating surfactant structures used to increase the solubility of sparingly soluble drug substances. Micelles are frequently used for parenteral delivery of anticancer agents, e.g., docetaxel.</p>
Nanobubbles (9)	—	<p>Nanobubbles are created using oscillating vibration sources to disperse air in water,</p>

Name of the Nanomaterial	Subcategory	Definition, Structure, and Description
		usually in the presence of surfactant. Nanobubbles can be employed as contrast agents and also to deliver drug substance by virtue of their incorporation into the stabilizing agent at the surface of the bubble.
Nanoemulsions	—	Submicron oil-in-water (o/w) or water-in-oil (w/o) emulsions are stabilized with surfactants and cosurfactants. By definition, they have droplet sizes below 100 nm, but typically ranging less than 1 µm. Nanoemulsions (o/w) are used primarily to administer water-insoluble drug substances. They are made by high-shear emulsification methods or low-energy emulsification methods (phase inversion). Nanoemulsions are used in ophthalmic and oral products, for example, to deliver cyclosporin for dry eyes and for prophylaxis of organ rejection and immune regulation (10).
Nanofibers (11)	—	Nanofibers are rarely seen in pharmaceutical preparations. Nanofibers are nanoscale in one dimension and are used frequently in electrospun polymer-containing drugs (12) or alone, for example, as a wound-healing matrix (13).
Nanotubes	Carbon (14)	Nanotubes are rarely seen in pharmaceutical preparations. They may be manufactured from a variety of substances. Usually an allotrope of carbon that forms into cylindrical carbon structures. These nanotubes have novel properties that make them potentially useful for a variety of pharmaceutical applications (e.g., controlled drug release) and tissue-engineering applications (e.g., as a scaffold for cell growth).
Nanotubes	Self-assembled	Another nanotube example is the peptide drug lanreotide, which self-assembles at high concentrations to form nanotubes (liquid crystals). The lanreotide nanotube structure extends the bioavailability of the peptide for 1 month following a single intramuscular injection (15).
Nanoparticles	Inorganic (16)	Inorganic nanoparticles are discrete nanomaterials consisting of inorganic materials (e.g., gold, silver, silica). These inorganic nanoparticles are used as a core substrate to which active moieties, e.g., small molecules or biomolecules, can be attached, particularly for antimicrobial agents, immune therapeutics and vaccines.

Name of the Nanomaterial	Subcategory	Definition, Structure, and Description
		<p>Iron oxide nanoparticles (colloids) are used for diagnostic imaging and iron replacement therapies.</p> <p>Titanium dioxide and zinc oxide nanoparticles are used in sunscreens for the prevention of erythema.</p>
▲Nanoparticles	Lipid	Lipid nanoparticles may contain ionizable lipid, phospholipid, cholesterol, lipid-anchored poly(ethylene glycol), and a drug substance, such as mRNA or siRNA. ▲ (USP 1-May-2024)
Nanoparticles	Polymeric (natural and synthetic) (17)	Solid particles prepared by one of several methods involving either dispersion of preformed polymer or in situ polymerization. Polymers used in preformed particles include various naturally occurring proteins, polysaccharides, and synthetic polymers, e.g., polylactide▲ (USP 1-May-2024), poly(lactide-co-glycolide)▲▲ (USP 1-May-2024), poly(ethylene glycol)-block-poly(lactide)▲▲ (USP 1-May-2024), and other polyesters. In situ polymerization of monomers requires cross-linking. The drug is often incorporated into polymeric nanoparticles by an emulsion evaporation technique (18).
Nanoparticles	Solid lipid (19)	▲Solid lipid▲ (USP 1-May-2024) nanoparticles are drug substances embedded in a solid lipid core, which is usually stabilized by a monolayer of phospholipids. Lipid nanoparticles are proposed for use in the delivery of hydrophobic drug substances. This also includes drug complexes with other components such as protein, lipid, polymer, or metal.
▲Viral vectors	Viral capsid	Viral vectors are used to deliver genetic materials into cells. Examples of viral vectors include adenovirus vaccines and adeno-associated virus gene therapies.

**Excipients**

Some excipients may comprise nanoparticles, for example, fumed silica (Colloidal Silicon Dioxide) is manufactured to obtain nanoparticles. Other excipients such as, Titanium Dioxide, Talc, Magnesium Stearate, and Sodium Stearyl Fumarate, may include nanoparticles. The presence of nanoparticles will depend on the manufacturing process and the particular grade (if there is more than one grade). In particular, excipients in which the ( $D_{50}$ ) is up to 20  $\mu\text{m}$  may be anticipated to contain some particles with diameters up to 1000 nm, i.e., in the nanoparticle size range. Micellar or liposomal delivery systems can be made up of lipidic or polymeric excipients, e.g., pluronics and poly(lactide-co-glycolide) (LG polymer) for encapsulation and controlled release. Beside the quality test methods for excipients, testing of the final drug product is critical to ensure that performance, quality, and stability of the formulations are consistent.

If the grade or source of a nanomaterial excipient changes, the impact of this change on the safety or efficacy of the product should be addressed. When an excipient is deliberately modified into a nanomaterial, an adequate safety evaluation should be provided when the

nanomaterial's safety is not fully demonstrated by existing safety data with respect to level of exposure, duration of exposure, and route of administration. ▲ (USP 1-May-2024)

## General Quality Tests of Drug Products Containing Nanomaterials

The following list is not comprehensive but represents the most common properties characterized for nanomaterials used in drug products.

### AERODYNAMIC PARTICLE SIZE DISTRIBUTION (APSD)

Products for inhalation are subject to aerodynamic particle size assessment by multistage cascade impactor in accordance with [Inhalation and Nasal Drug Products: Aerosols, Sprays, and Powders—Performance Quality Tests \(601\)](#), if intended for administration by inhalation aerosol or powder or in accordance with [Products for Nebulization—Characterization Tests \(1601\)](#), if intended for administration by a nebulizing system. The proportion of therapeutic aerosol found in the cascade impactor size fraction is determined by differences in particle inertia. Furthermore, quantification of drug substance mass is possible through chemical assay of the collected subfractions. These differences are related directly to the aerodynamic size, which is indicative of the likely deposition location(s) in the human respiratory tract. Although the size range within which these apparatuses operate is larger than the size range associated with single nanoparticles, their delivery in the formulated drug product to the respiratory tract will likely occur as microaggregated powder particles or as a suspension in liquid droplets. A small proportion of the aerosol may be generated as ▲nanoparticles▲ (USP 1-May-2024), for which alternative methods, in particular, low-pressure cascade impactors, might be considered in conjunction with conventional cascade impactors to extend the range within which sizing is undertaken (20).

### COMPOSITION AND STRUCTURE

Methods of determining composition depend on the nature of the material under investigation. For example, for inorganic molecules, elemental analysis by atomic absorption spectroscopy and atomic emission spectroscopy with flame ionization or inductively coupled plasma mass spectrometry can be employed. For organic polymeric systems, gel permeation chromatography/size exclusion chromatography with refractive index detection may be supplemented with viscosity determinations and application of the Mark-Houwink equation to estimate the molecular weight (21). If a multi-angle light scattering (MALS) detector is added, the weight average molecular weight can be determined. Photon correlation spectroscopy (dynamic light scattering) also may be used for molecular weight determination. ▲Additionally, complementary multidetector separation techniques like Asymmetrical Flow Field-Flow Fractionation (AF4) together with a suitable detection method can be used for analysis of molecular weight and size distribution of both organic polymeric systems and inorganic systems (22–25).▲ (USP 1-May-2024) At a fundamental level, surfactants and polymer-based systems can be subjected to elemental analysis or spectroscopy methods. Electron microscopy techniques such as cryogenic transmission electron microscopy may be used for liposome/lipid-based nanoparticle formulations to determine their size and morphology (e.g., lamellarity). Other scattering methods, e.g., small-angle X-ray scattering (SAXS) and small-angle neutron scattering (SANS), may also be used to generate information on nanomaterial size. These scattering techniques are not routine due to their technical complexity and instrument availability but can also provide detailed information on form (shape), surface, and material interactions.

### PURITY

In some cases, the purity of the materials used to generate nanostructures is characterized to assure homogeneity among different batches. For example, the chemical composition of the bilayer of liposomes or micelles or the chemical purity of inorganic particles can be characterized to demonstrate batch-to-batch consistency.

### DISSOLUTION/IN VITRO RELEASE

Multiple methods exist for dissolution testing. Importantly, care should be taken to ensure that the nanomaterial does not interfere with or interact with the testing materials or otherwise confound results. For example, an undissolved nanomaterial may pass through filters, resulting in a false elevation of solubility. To address this problem, the use of membrane diffusion and microdialysis has been proposed to separate particles from dissolved material (26). Fiber optic probes may also be employed. Some caution may be required when using the fiber optic probe technique with ultraviolet-visible (UV-Vis) detection to accurately estimate the quantity of dissolved material (27). However, the use of a fiber optic probe with different detection systems, such as infrared (IR) (28) or Raman (29) spectroscopy, may be a viable approach. Nanomaterials may also influence the accuracy of results by reacting with the surfaces of the dissolution apparatus. Therefore, novel dissolution methods may need to be developed.

### ENCAPSULATION EFFICIENCY

For nanomaterials in which the drug substance is encapsulated in an excipient, e.g., lipid or polymer, the loading and encapsulation efficiency is usually determined. Encapsulation efficiency can be achieved by separating the drug substance in the nanomaterial from the free drug substance, typically using centrifugal filter devices. Size-exclusion spin columns or solid phase extraction (SPE) columns are used to separate free from encapsulated or carrier-associated drugs, performing an appropriate quantitative assay of free drug versus encapsulated drug as a proportion of the total drug present.

PARTICLE SIZE ▲AND PARTICLE SIZE DISTRIBUTION▲ (USP 1-May-2024)

Dynamic light scattering (DLS), also known as photon correlation spectroscopy (PCS), can be used to measure the particle size and particle size distribution of nanomaterials. This method measures fluctuations in scattered light intensity from particles in Brownian motion to calculate the sample particle size and distribution.

▲Low-angle▲ (USP 1-May-2024) laser light scattering ▲(laser diffraction)▲ (USP 1-May-2024) can also be used to measure the particle size and distribution of nanoparticles, although this technique may be somewhat limited depending on the size of the nanomaterials to be measured. ▲Further information on this technique, including methodology, measurement, and analysis is provided in [Light Diffraction Measurement of Particle Size \(429\)](#).

Scanning electron microscopy (SEM), transmission electron microscopy (TEM), and atomic force microscopy (AFM) can be used to measure the particle size and particle size distribution of individual nanoparticles.▲ (USP 1-May-2024)

SHAPE ▲AND MORPHOLOGY

Microscopy techniques such as SEM, TEM, and AFM are useful tools▲ (USP 1-May-2024) for three-dimensional analysis of nanoparticles. ▲These techniques▲ (USP 1-May-2024) will allow measurement of particle size, shape, and surface texture.▲▲ (USP 1-May-2024) SAXS and SANS may also be used to generate information on nanomaterial shape. MALS may be used for determining shape, as it can also give information on the conformation (e.g., sphere, coil, and rod) of the molecules when coupled with separation techniques.

SOLUBILITY

Typical methods for assessing solubility (e.g., the shake-flask method) may not be suitable for use with nanomaterials because the undissolved particles cannot be readily separated from the solution. Methods to assess the solubility of nanomaterials (i.e., nanoparticles or nanocrystals) sometimes use characterization of the particle size distribution and changes in the particle size distribution as a function of time as a surrogate or complementary data to dissolution data. More generally, solubility assessments for nanomaterials often use highly selective separation techniques (e.g., size exclusion chromatography or ultracentrifugation) capable of differentiating the dissolved and undissolved nanomaterials. To address this problem, the use of membrane diffusion and microdialysis has been proposed to separate particles from dissolved material (26). Fiber optic probes may also be employed, although some caution may be required when using the fiber optic probe technique with UV-Vis detection to accurately estimate the quantity of dissolved material (27). However, the use of a fiber optic probe with different detection systems, such as IR (28) or Raman (29) spectroscopy, may be a viable approach.

SURFACE AREA

Gas adsorption techniques (generally using nitrogen or krypton) allow measurement of the nanoparticle surface area. Samples are exposed to varying pressures at which the incrementally dosed analysis gas will adsorb onto the surface of the nanoparticles. The surface area is then calculated. This technique may also be utilized to measure the average particle size.

SURFACE PROPERTIES

Chemical composition (for example, as detected by X-ray photoelectron spectroscopy/secondary-ion mass spectrometry), charge, and reactivity influence surface properties. Measurement of the ζ (zeta) potential and isoelectric point via electrophoretic or electroacoustic methods are often used to help predict whether nanomaterials will tend to aggregate or agglomerate or whether they will remain as discrete particles in the liquid vehicle. A high (positive or negative) ζ potential is one indication of a system in which nanoparticles will repel each other and remain as discrete particles, whereas a system with a low ζ potential (near zero, the isoelectric point) may be more likely to aggregate or agglomerate. Freeze-fracture scanning electron microscopy may also be useful in studying the aggregate or agglomerate morphology.

PHYSICAL STABILITY

Physical stability, in terms of propensity of nanomaterial to aggregate or agglomerate can be assessed using methods such as controlled centrifugation techniques, which apply a force to the system and assess the level of segregation/separation/sedimentation, combined with DLS to assess the apparent particle size (hydrodynamic diameter) distribution. These techniques may be used as a part of standard stability testing. The integrity of the nanosystem with regard to the retention of drug substance should also be evaluated.

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**2. GENERAL QUALITY TESTS**

The methods shown in [Table 2](#) relate to the properties of a drug product that may alter due to the presence of nanomaterials.

**Table 2**

Name	Recommended Methods
Dendrimers	All general quality tests identified in <a href="#">General Quality Tests of Drug Products Containing Nanomaterials<sup>a</sup></a>

Name	Recommended Methods
<p>▲Drug nanoparticles in the amorphous state and nanocrystals▲                      (USP 1-May-2024)</p>	<p>All general quality tests identified in <a href="#">General Quality Tests of Drug Products Containing Nanomaterials<sup>a</sup></a></p>
<p>Liposomes</p>	<p><b>Dissolution/In vitro release<sup>a</sup></b>—<a href="#">Dissolution (711)</a> and <a href="#">Oral Dosage Forms—Performance Tests (1711)</a>.  <b>High resolution microscopy</b>—<a href="#">Scanning Electron Microscopy (1181)</a>. Transmission and atomic force microscopy are described elsewhere (<a href="#">30</a>).  <b>Dynamic light scattering</b>—<a href="#">Analytical Methodologies Based on Scattering Phenomena—Light Diffraction Measurements of Particle Size (1430.2)</a>.  <b>Solubility</b>—<a href="#">Solubility Measurements (1236)</a>.  <b>Zeta potential</b>—<a href="#">Determination of Zeta Potential by Electrophoretic Light Scattering (432)</a> and <a href="#">Analytical Methodologies Based on Scattering Phenomena—Electrophoretic Light Scattering (Determination of Zeta Potential) (1430.4)</a>.</p>
<p>Micelles</p>	<p><b>Dissolution/In vitro release</b>—<a href="#">(711)</a> and <a href="#">(1711)</a>.  <b>High resolution microscopy</b>—<a href="#">(1181)</a>. Transmission and atomic force microscopy are described elsewhere (<a href="#">30</a>).  <b>Dynamic light scattering</b>—<a href="#">(1430.2)</a>.  <b>Solubility</b>—<a href="#">(1236)</a>.  <b>Zeta potential</b>—<a href="#">(432)</a> and <a href="#">(1430.4)</a>.</p>
<p>Nanobubbles</p>	<p><b>Dissolution/In vitro release</b>—<a href="#">(711)</a> and <a href="#">(1711)</a>.  <b>High resolution microscopy</b>—<a href="#">(1181)</a>. Transmission and atomic force microscopy are described elsewhere (<a href="#">30</a>).  <b>Dynamic light scattering</b>—<a href="#">(1430.2)</a>.  <b>Zeta potential</b>—<a href="#">(432)</a> and <a href="#">(1430.4)</a>.</p>
<p>Nanoemulsions</p>	<p><b>Dissolution/In vitro release</b>—<a href="#">(711)</a> and <a href="#">(1711)</a>.  <b>High resolution microscopy</b>—<a href="#">(1181)</a>. Transmission and atomic force microscopy are described elsewhere (<a href="#">30</a>).  <b>Dynamic light scattering</b>—<a href="#">(1430.2)</a>.  <b>Solubility</b>—<a href="#">(1236)</a>.  <b>Zeta potential</b>—<a href="#">(432)</a> and <a href="#">(1430.4)</a>.</p>
<p>Nanofibers</p>	<p>All general quality tests identified in <a href="#">General Quality Tests of Drug Products Containing Nanomaterials<sup>a</sup></a></p>
<p>Nanoparticles (drug)</p>	<p>All general quality tests identified in <a href="#">General Quality Tests of Drug Products Containing Nanomaterials<sup>a</sup></a></p>
<p>Nanoparticles (inorganic)</p>	<p>All general quality tests identified in <a href="#">General Quality Tests of Drug Products Containing Nanomaterials<sup>a</sup></a></p>
<p>Nanoparticles (polymeric, natural, and synthetic)</p>	<p>All general quality tests identified in <a href="#">General Quality Tests of Drug Products Containing Nanomaterials<sup>a</sup></a></p>
<p>Nanoparticles (solid lipid)</p>	<p>All general quality tests identified in <a href="#">General Quality Tests of Drug Products Containing Nanomaterials<sup>a</sup></a></p>
<p>Nanotubes (carbon)</p>	<p><b>Dissolution/In vitro release</b>—New or existing general chapter  <b>Scanning, transmission, and atomic force microscopy</b>—<a href="#">(1181)</a>. Transmission and atomic force microscopy are described elsewhere (<a href="#">30</a>).  <b>Dynamic light scattering</b>—<a href="#">(1430.2)</a>.  <b>Solubility</b>—<a href="#">(1236)</a>.</p>

Name	Recommended Methods
	<p><b>Gas adsorption surface area measurement</b>—<a href="#">Specific Surface Area (846)</a>.</p> <p><b>X-Ray photoelectron spectroscopy and secondary ion mass spectrometry</b>—Techniques are described elsewhere <a href="#">(31)</a>.</p> <p><b>Zeta potential</b>—<a href="#">(432)</a> and <a href="#">(1430.4)</a>.</p> <p><b>Sedimentation methods/Centrifugation</b>—Techniques are described elsewhere <a href="#">(32)</a>.</p>

<sup>a</sup> Where included in an aerosol dosage form, [\(601\)](#) should be consulted.

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### 3. DESCRIPTION OF PRODUCT QUALITY TESTS

- **Dissolution:** [\(711\)](#) and [\(1711\)](#).
- **Dynamic light scattering:** [\(1430.2\)](#).
- **Crystallinity:** [Crystallinity \(696\)](#).
- **Gas adsorption surface area measurement:** [\(846\)](#).
- **High resolution microscopy (scanning, transmission, and atomic force microscopy):** [\(1181\)](#). Transmission and atomic force microscopy are described elsewhere [\(30\)](#).
- **Inertial impaction:** [\(601\)](#).
- **Solubility:** [\(1236\)](#).
- **Ultracentrifugation (sedimentation):** Techniques are described elsewhere [\(32\)](#).
- **X-ray photoelectron spectroscopy and secondary ion mass spectrometry:** Techniques are described elsewhere [\(31\)](#).
- **Zeta potential:** [\(432\)](#), and [\(1430.4\)](#).

▲In addition, depending on route of administration, further tests may be considered. ▲ (USP 1-May-2024)

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### REFERENCES

- ▲US Department of Health and Human Services, Food and Drug Administration, Office of the Commissioner. Guidance for industry: Drug Products, Including Biological Products, that Contain Nanomaterials. ▲ (USP 1-May-2024)
- US Department of Health and Human Services, Food and Drug Administration, Office of the Commissioner. Guidance for industry: Considering whether an FDA-regulated product involves the application of nanotechnology. Rockville, MD: Food and Drug Administration; June 2014.
- Nanjwade BK, Bechra HM, Derkar GK, Manvi FV, Nanjwade VK. Dendrimers: emerging polymers for drug-delivery systems. *Eur J Pharm Sci.* 2009;38(3):185–196.
- Chang T-L, Zhen H, Liang D, Liang J. Polymeric micelles for drug delivery. *Front Chem Sci Eng.* 2015;9:1–14.
- Narang AS, RK Chang, MA Hussain. Pharmaceutical Development and Regulatory Considerations for Nanoparticles and Nanoparticulate Drug Delivery Systems. *J Pharm Sci.* 2013;DOI:10.1002/jps.23691.
- Pattni BS, Chupin VV, Torchilin VP. New Developments in Liposomal Drug Delivery. *Chem Rev.* 2015;115(19):10938–10966.
- Croy SR, Kwon GS. Polymeric micelles for drug delivery. *Curr Pharm Des.* 2006;12(36):4669–4684.
- Porter CJ, Trevaskis NL, Charman WN. Lipids and lipid-based formulations: Optimizing the oral delivery of lipophilic drugs. *Nat Rev Drug Discov.* 2007;6(3):231–248.
- Ma J, Xu CS, Gao F, Chen M, Li F, Du LF. Diagnostic and therapeutic research on ultrasound microbubble/nanobubble contrast agents (review). *Mol Med Rep.* 2015;12(3):4022–4028.
- Jaiswal M, Dudhe R, Sharma PK. Nanoemulsion: An advanced mode of drug delivery system. *3 Biotech.* 2015;5(2):123–127.
- Reneker D, Yarin A, Fong H, Koombhongse S. Bending instability of electrically charged liquid jets of polymer solution in electrospinning. *J Applied Phys.* 2000;87(9):4531–4536.
- Thakkar S, Misra M. Electrospun polymeric nanofibers: New horizons in drug delivery. *Eur J Pharm Sci.* 2017;107:148–167.
- Vannuruswamy G, Rathna G, Gadgil B, Gadad A. Polymer blends of shellac as nanofiber formulations for wound healing. *J Bioact Compat Pol.* 2015;30:472–489.
- Bianco A, Kostarelos K, Prato M. Applications of carbon nanotubes in drug delivery. *Curr Opin Chem Biol.* 2005;9(6):674–679.
- Wolin EM, Manon A, Chassaing C, Lewis A, Bertocchi L, Richard J, et al. Lanreotide depot: An antineoplastic treatment of carcinoid or neuroendocrine tumors. *J Gastrointest Cancer.* 2016;47(4):366–374.
- Kim T, Hyeon T. Applications of inorganic nanoparticles as therapeutic agents. *Nanotechnology.* 2014;25(1):012001.
- Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids Surf B Biointerfaces.* 2010;75(1):1–18.
- Dinarvand R, Sepehri N, Manoochehri S, Rouhani H, Atyabi F. Polylactide-co-glycolide nanoparticles for controlled delivery of anticancer agents. *Int J Nanomedicine.* 2011;6:877–895.

19. Muller RH, Mader K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery - a review of the state of the art. *Eur J Pharm Biopharm.* 2000;50(1):161–177.
20. Marjamäki M, Keskinen J, Chen D-R, Pui D. Performance evaluation of the low-pressure impactor (ELPI). *J Aerosol Sci.* 2000;31:249–261.
21. Martin A. *Physical Pharmacy: Physical Chemical Principles in the Pharmaceutical Sciences.* 4th ed. Philadelphia, PA: Lea and Febiger; 1993:562.
22. ▲International Organization for Standardization. *Nanotechnologies—Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation.* ISO/TS 21362:2018.
23. Clogston JD, Hu Y. *NCL Method PCC-19: Asymmetric-flow field-flow fractionation.* NCI Hub. 2020. doi:10.17917/8S1D-BN17.
24. Parot et al. Understanding the performance of magnetic nanoparticles in nanomedicine. *Journal of Controlled Release.* 2020;320:495–510. doi:10.1016/j.jconrel.2020.01.049.
25. Caputo F, Mamusa M, Caboi F, et al. Characterization of industrial bioplastics by *Asymmetrical Flow Field-Flow Fractionation (AF4)* coupled with multiple detectors. *Journal of Chromatography A.* 2021;1637:461737. doi:10.1016/j.chroma.2020.461737. ▲ (USP 1-May-2024)
26. Shen J, Burgess DJ. In vitro dissolution testing strategies for nanoparticulate drug delivery systems: Recent developments and challenges. *Drug Deliv Transl Res.* 2013;3(5):409–415.
27. Van Eerdenbrugh B, Alonzo DE, Taylor LS. Influence of particle size on the ultraviolet spectrum of particulate-containing solutions: implications for in-situ concentration monitoring using UV/Vis fiber-optic probes. *Pharm Res.* 2011;28(7):1643–1652.
28. McFearin CL, Sankaranarayanan J, Almutairi A. Application of fiber-optic attenuated total reflection-FT-IR methods for in situ characterization of protein delivery systems in real time. *Anal Chem.* 2011;83(10):3943–3949.
29. McCreery R, Fleischmann M, Hendra P. Fiber optic probe for remote Raman spectrometry. *Anal Chem.* 1983;55(1):146–148.
30. Baumann F, Heucke SF, Pippig DA, Gaub HE. Tip localization of an atomic force microscope in transmission microscopy with nanoscale precision. *Rev. Sci. Instrum.* 2015;86:035–109.
31. Marcus HL. Surface techniques for the study of materials: AES, ESCA, SIMS. *JOM* 2014;29:20–24.
32. Robertson JD, Rizzello L, Battaglia G. Purification of nanoparticles by size and shape. *Sci Rep.* 2016;6:27494.

**Auxiliary Information** - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
<1153> DRUG PRODUCTS CONTAINING NANOMATERIALS	<a href="#">Kahkashan Zaidi</a> Principal Scientific Liaison	GCDF2020 General Chapters - Dosage Forms 2020

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