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Introducing a new international standard ISO/TS 20660: Specification of characteristics and measurement methods for antibacterial silver nanoparticles

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Abstract

This paper introduces a new international standard [(International Organization for Standardization/Technical Specification (ISO/TS) 20660)]: Specification of characteristics and measurement methods for silver nanoparticles. The new standard provides a guideline of essential and additional characteristics for silver nanoparticles used as antibacterial agents in consumer products, along with the relevant measurement methods. The main rationale behind this standard is to establish relevant and comparable characterization of antibacterial silver nanoparticle products, while boosting consumer trust and confidence.

Introduction

Silver nanoparticles (AgNPs) are receiving growing attention due to their antibacterial, chemical, electrical and catalytic properties that have important industrial applications. In particular, AgNPs are increasingly used in consumer products to control the growth of microorganisms on external and internal surfaces. Several consumer product databases now list products containing nanosilver or AgNPs. For example, Nanodata shows 68 AgNP products among 3060 nanoproducts [1] while the Woodrow Wilson consumer product inventory shows 443 AgNP products (highest subgroup) among 1833 nanoproduct [2]. Although antibacterial nanoproducts containing AgNPs are now widely commercially available, most AgNP-containing products are sold without providing any information on their physicochemical properties and health & safety data. In most countries, consumer products are not covered by current SDS (Safety Data Sheet) regulations that require disclosure of physicochemical properties and health & safety data. Most AgNP manufacturers only provide product specifications based on

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their own practices. Therefore, the new TS attempts to provide standard guidelines for the characterization and measurement of AgNPs in powder or colloidal form that are used as antibacterial agents in consumer products. The new working item proposal for antibacterial AgNPs was already accepted by the ISO Technical Committee (TC) 229 (Nanotechnologies) and technical specification (TS) 20660 was developed by working group 4 (Material specifications) [3]. The new technical specification is intended to help manufacturers provide the appropriate physicochemical characteristics of AgNPs used as antibacterial agents in consumer products, while also ultimately boosting consumer confidence.

Initial market survey of antibacterial AgNP products

Since this survey is for market survey, we did not use existing organizations created databases such as Woodrow Wilson New nanotechnology consumer products inventory [2], Danish Nanoproduct Inventory [4], or Korean nanofusion product database Nanoin [5]. Additionally, we searched published papers that used silver nanoparticles [6]. Based on internet search using keywords such as antibacterial silver, nanosilver silver nanoparticles, silver nanomaterials, etc, among 834 products, 394 antibacterial products that contained AgNPs smaller than 100 nm were analyzed as regards the provided specifications. The results are summarized in Table 1. Among the 394 antibacterial AgNP products, 165 included primary particle size information with an average size of 39.8 nm. The average particle size for the 394 AgNP products was 60 nm. 305 AgNP products included surface charge information, where the average was -38.8 mV, and 66 products included surface area information, where the average was 14.2 m^2/g. 76 products included particle aggregation information, where 67 products claimed no aggregation and 9 products reported aggregation. Consequently, based on this information, the working group formulated essential and additional specification requirements for antibacterial AgNP products.

Scope of technical specification

The new TS provides guidance for specifying the characteristics and relevant measurement methods for silver nanoparticles in powder or colloidal form that are intended for antibacterial application in consumer products. Particularly, the new TS is intended to help the manufacturer provide the physicochemical characteristics of silver nanoparticles used as antibacterial agents, and does not cover considerations specific to health and safety issues either during manufacturing or use.

Characterization and measurement methods required and recommended in TS

The new characteristic specification for antibacterial silver nanoparticles consists of two categories: essential and additional characteristics, as described in Tables 2 and 3, respectively. As such, to comply with TS 20660, manufacturers of antibacterial AgNPs will need to provide all the essential characteristics listed in Table 2, and will have the option to provide the additional characteristics listed in Table 3. The essential characteristics are all intrinsic to the material, including the average size and distribution of primary particles, zeta potential, surface area, and total silver content. The TS for AgNPs is applicable to both powder and colloidal forms of AgNPs, yet not aerosol forms. All the characteristics need to be measured using the methods and units prescribed in the TS to allow direct comparison among AgNP products. The additional characteristics cover the hydrodynamic size and silver nanoparticle number concentration.

Table 1: Market survey of antibacterial AgNP products

	Primary particle size (nm)	Particle size (nm)	Surface charge (mV)	Surface area (m^2/g)	Aggregation
No. of Samples	165	394	305	66	76
Average	39.8	60.0	-35.8	14.3	Not Aggregated 67; Aggregated 9
S.D.	23.6	22.3	13.7	11.6	
Max.	93.5	99.9	5.0	90.0	
Min.	1.0	9.0	-57.7	6.4	
Median	36.0	59.2	-38.8	11.5	

Table 2: Essential characteristics (Adapted from ISO 20660 Table 1 and Annex Table A.1)

Characteristics	Units	Reason	Measurement method	Application form	Guidance	Reference
1) Average size & distribution of primary particles	M	Critical parameter in assessment of EHS aspects of nano-objects AgNP size is closely related with antimicrobial activity [7]	SEM	Powder or colloidal	TEM is a microscopy technique in which a beam of electrons is transmitted through a specimen to form an image. The specimen is most often an ultrathin section less than 100 nm thick or a suspension on a grid. An image is formed from the interaction of the electrons with the sample as the beam is transmitted through the specimen. The image is then magnified and focused onto an imaging device, such as a fluorescent screen, layer of photographic film, or sensor such as a charge-coupled device. Coupling with EDS is then widely used for elemental and chemical analyses.	ISO 16700 [8]

			TEM	Powder or colloidal	SEM is a type of electron microscope that produces images of a sample by scanning the surface with a focused beam of electrons. The electrons interact with atoms in the sample, producing various signals that contain information about the sample's surface topography and composition. The electron beam is scanned in a raster scan pattern, and the beam's position is combined with the detected signal to produce an image. SEM can achieve a resolution better than 1 nanometre. For conventional SEM, the specimens are observed in a high vacuum, while for environmental SEM, the specimens can be observed in a low vacuum or under wet conditions with variable pressure and at a wide range of cryogenic or elevated temperatures. Guidelines on the application of this method and the sample preparation process can be found in ISO 16700 and 10798.[Source: ISO 16700, modified]	ISO 10797 [9]
2) Zeta potential	V	Key factor determining stability in suspension with capping agents [10]	DLS	Colloidal	Zeta potential is the electrostatic potential at the slipping plane (which marks the region where the liquid molecules surrounding the particles first begin to move with respect to the surface) relative to the potential in the bulk solution. ISO 13099-2 provides methods for measuring the electrophoretic mobility using optical means and for calculating the zeta potential.	ISO 13099-2 [11]
3) Specific surface area	m^2/kg	Critical parameter in chemical and antibacterial reaction [12-13]		Powder	A technique based on the model developed by Brunauer, Emmet and Teller that allows the surface area of powders to be estimated by the amount of gas that is adsorbed. Typically, nitrogen or carbon dioxide is used, but gases such as krypton or argon may be used for low surface area materials because of their sensitivity (mass gain per unit area). The specific surface area is the ratio of surface area to mass.	ISO 9277 [14], ISO 18757 [15]
4) Total silver content	kg/kg or mol/mol	Critical determinant in assessment of antibacterial activity and purity [16]	ICP-MS	Powder or colloidal	ICP-MS uses an inductively coupled plasma source to ionize sample materials for analysis by a mass spectrometer. ICP-MS provides accurate and quantitative determinations of elemental impurities using ICP-MS.	ISO 17294-1 [17], ISO 17294-2 [18]
			ICP-OES	Powder or colloidal	ICP-OES is an analytical technique used for the detection of trace metals. It is a type of emission spectroscopy that uses inductively coupled plasma to produce excited atoms and ions that emit electromagnetic radiation at wave lengths characteristic of a particular element. It is a flame technique with a flame temperature in a range from 6 000 to 10 000 K. The intensity of this emission is indicative of the concentration of the element within the sample.	ISO 11885 [19]
			AAS	Powder or colloidal	Any metals in a solution can be readily determined by flame (direct aspiration) atomic absorption spectrophotometry.	ISO 26845 [20]

SEM: scanning electron microscopy; TEM: transmission electron microscopy; DLS: dynamic light scattering; ICP-MS: inductive coupled plasma-mass spectrometry; ICP-OES: inductive coupled plasma-optical emission spectrometry; AAS: atomic absorption spectrometry.

Table 3: Additional characteristics (Adapted from ISO 20660 Table 2 and Annex Table A.2)

Characteristics	Units	Reason	Measurement method	Application form	Guidance	Reference
1) Hydrodynamic size	M	Determines particle size for NPs in aqueous solution	DLS	Colloidal	This method measures the hydrodynamic diameter from Brownian motion. It is applicable to the measurement of particle diameters greater than 3 nm, depending on the test material.	ISO 22412 [21]

			PTA	Colloidal	PTA is based on measuring the diffusion movement of particles in a suspension by means of laser illumination, imaging of scattered light, particle identification and localization, and individual particle tracking. The hydrodynamic diameter of the individual particles, droplets or bubbles is related to Brownian motion parameters via the Stokes–Einstein equation.]	ISO 19430 [22]
2) Silver nanoparticle number concentration	#/kg	Determines number-based particle size distribution of nanoparticles and quantifies dissolved fraction of AgNP suspension	spICP-MS	Powder or colloidal	spICP-MS is able to detect single nanoparticles at very low concentrations, and can determine the size of AgNPs in aqueous suspensions. The particle number concentrations that can be determined in aqueous suspensions range from 106 particles/L to 109 particles/L, corresponding to mass concentrations in the range of approximately 1 ng/l to 1 000 ng/l. The actual numbers depend on the type of mass spectrometer used and type of nanoparticle analyzed. spICP-MS can also determine the ionic concentrations in the suspension.	ISO/TS 19590 [23]
			SAXS	Powder or colloidal	SAXS can determine the NP size distribution, the size and shape of monodispersed NPs, and the silver nanoparticle number concentration.	[24]

DLS: dynamic light scattering; PTA: particle tracking analysis; spICP-MS: single particle inductive coupled plasma-mass spectrometry; SAXS: Small angle X-ray scattering.

Sampling and test report

The new TS requires representative sampling of the parent population of nanoparticles in a suspended powder form in accordance with ISO 14488 [25] and ISO 14887 [26]. Since many nano-objects are reactive and their physicochemical properties can be affected by the sampling point and storage, the manufacturer and end-producer need to agree on the sampling point and sample storage for result comparability. The test report should contain 1) all details generally necessary to identify the test product (product name, chemical name); 2) reference to the new TS; 3) a sample description; 4) the relationship between the sample used for the measurements and the test product to which the characteristics are assigned; 5) the test date, name of the testing laboratory, and a statement on the quality system of the testing laboratory; 6) measurement results for the characteristics, including the measurement methods, as in Table 2 and if applicable Table 3; 7) any special information supporting the reliability of the measurement results. If available, the results of any antibacterial performance testing should be provided, along with the documented test procedures.

Antibacterial performance test

After a great deal of discussion on whether to include antibacterial performance tests in the new TS, the technical committee decided against this antibacterial performance test due to the lack of any current standardization of the antibacterial performance of silver nanoparticles and because antibacterial performance tests are beyond the scope of the new TS. Relevant antibacterial performance tests include ISO/TS 16550 [27] and the performance standards for the antimicrobial disk & dilution susceptibility test: M2-A9 from the Clinical and Laboratory Standards Institute [28]. The requirements outlined by national pharmacopeia or regulatory bodies can also be consulted and followed if appropriate. Plus, the jurisdictions where the material may ultimately be sold should be considered.

Discussion

ISO TC 229 (Nanotechnologies) aims to support the sustainable and responsible development and global dissemination of emerging nanotechnologies; to facilitate global trade in nanotechnologies, nanotechnology products, and nanotechnology-enabled systems and products; to support improvement in quality, safety, security, consumer and environmental protection, together with the rational use of natural resources in the context of nanotechnologies; to promote good practice in the production, use, and disposal of nanomaterials, nanotechnology products, and nanotechnology-enabled systems and products. Initially, the TC focused on the terminology and nomenclature, metrology and test methods, and health, safety, and the environment. The working group for material specification (WG 4) was created in 2008 and published several standards, including Materials specifications - Guidance on specifying nano-objects (ISO 12805) [26], Clay nanomaterials - Part 1: Specification of characteristics and measurement methods for layered clay nanomaterials (ISO/TS 21236-1) [27], and Magnetic nanomaterials - Part 1: Specification of characteristics and measurements for magnetic nanosuspensions (ISO/TS 19807-1) [28]. Although antibacterial AgNP products are already produced and used worldwide, a standardized product specification is not yet available. This lack of consensus on how manufacturers of antibacterial products prepare product specifications for the market also affects consumer confidence in antibacterial AgNP products. Therefore, the new TS for antibacterial AgNP products guides manufacturers on which essential and additional characteristics to include in their product specifications. Furthermore, the new TS prescribes particular measurement methods to provide comparable specification data among products, thereby ultimately helping to boost consumer confidence in AgNP-applied nanoproducts. In addition to providing essential and additional specification requirements for antibacterial AgNP, this TS also provide characterization methods for the specification requirements to have consistency on specification data among the products. The published standard will influence on the future market for AgNP applied nanoproducts and will build consumer trust as well as the facilitation of communication between seller and buyer in more details by utilizing this standard to fill the gap of reliable measurement protocol or methods.

Although the working group initially considered the inclusion of antibacterial performance tests in the new TS, this was dropped due to the current lack of any standardization of antibacterial AgNP performance and because this issue was determined beyond the scope of the working group. Finally, it is hoped that the new technical specification will encourage the commercialization of nanotechnologies by promoting good practice in production and building consumer confidence.

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