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## THE USE OF NANOPARTICLE CERTIFIED REFERENCE MATERIALS IN BIOMEDICAL RESEARCH WITHIN THE CONTEXT OF NANOSAFETY

**Abstract.** The authors conducted an analytical review of open online resources and databases aimed at searching for accessible and user-friendly nanoparticle certified reference materials. Resources from the International Organization for Standardization, ASTM International, the International Electrotechnical Commission, as well as databases of scientific articles in the field of nanotechnology for biomedical applications, were analyzed. Due to increased interest in standardization and safety in biomedical research, the authors conclude the necessity of actively searching for new nanoparticle certified reference materials that meet the requirements of the evolving dynamics of nanomaterial research.

**Keywords:** nanomaterial standardization, nanoparticle certified reference materials, nanosafety, biomedical research.

### Significance of the Research

The expansion of nanotechnologies applied across various industries, medicine, and science has led to an understanding of the necessity for standardization of research and the implementation of innovations considering nanosafety. Since the late 1990s, integrating nanomaterials into various products and processes has been parallel to resolving issues related to the development of standards for their assessment, testing, safety, and regulation. Since the mid-2000s, numerous scientific and industrial organizations, as well as governmental and non-governmental entities, have actively worked in this direction.

Standardized approaches to research in nanotechnologies help avoid a range of problems related to the potential adverse effects of nanoinnovations. This is primarily associated with the emergent properties of nanoparticles, which can determine the direction of the toxic effects of nanomaterials on the environment and human health. Standards and guidelines for the safe production, handling, use, and disposal of nanomaterials significantly reduce risks at all stages of the nanomaterial lifecycle. Additionally, standardized approaches ensure the reliability and repeatability of research and testing results of nanomaterials.

A comparative assessment of various nanomaterials, their properties, and their characteristics is crucial in selecting the most suitable materials for specific applications and evaluating their effectiveness and safety. For these purposes, nanomaterials that have been meticulously characterized and certified based on their physicochemical and biological properties are utilized - these are known as nanoparticle certified reference materials (CRMs) [1]. They serve as precise and reproducible benchmarks for comparing and calibrating other nanomaterials. The certification process involves carefully measuring and evaluating characteristics such as particle size and shape, surface properties, chemical composition, structure, and toxicity using various analytical methods, such as scanning electron microscopy, X-ray absorption spectroscopy, and so on.

Knowledge of nanoparticle certified reference materials and access to information about them are crucial in developing experimental research algorithms for nanoparticles and further work on their practical applications. However, it is not always easy to find information about available CRMs, especially for researchers working in small laboratories or developing countries. Information about nanomaterials may be presented in various formats and structures, making it difficult to compare and utilize. Additionally, nanomaterials possess many characteristics that can be complex to describe and standardize, complicating the selection of the most suitable reference material for a specific task. There are numerous standards and measurement methods for nanomaterials and choosing the appropriate one can be challenging for researchers, especially beginners.

### **Research Objective**

This analytical study aimed to conduct an information search for accessible and user-friendly resources that enable the rapid acquisition of nanoparticle certified reference materials based on experimental tasks, considering potential practical applications and nanosafety issues.

### **Main Materials of the Study**

Given the growing interest in standardizing nanomaterials for biomedical research, online resources such as the International Organization for Standardization (ISO), ASTM International, the International Electrotechnical Commission (IEC), and the Nanotechnology Standards Database (ANSI) were analyzed. Information on the most frequently used CRMs in scientific research was analyzed using open-access scientific literature databases such as PubMed, Web of Science, Scopus, ResearchGate, and IEEE Xplore.

### **Results**

Nanotechnology finds applications in various fields such as medicine, energy, and information technology, and is considered a key factor in the economic and innovative development of many countries. Analysis of literature data shows that in recent years, new emphasis has been placed on the standardization of nanomaterial research for biomedical applications, particularly concerning the safety and quality of nanomaterials. Consequently, active efforts are underway to search for new nanoparticle certified reference materials (CRMs).

CRMs are well-characterized and certified samples of nanomaterials used as benchmarks for comparing and evaluating the physicochemical and biological properties of other materials. Among the well-characterized CRMs, the following can be highlighted:

- Silver nanoparticles (NIST SRM 8011): This reference material, provided by the National Institute of Standards and Technology (NIST) of the United States, is used for calibrating and evaluating silver nanoparticles.

- Titanium dioxide nanoparticles (NIST SRM 1898): Another reference material provided by NIST, used for calibrating and evaluating titanium dioxide nanoparticles.

- Carbon nanomaterials (NIST SRM 2483): This standard material includes various types of carbon nanomaterials, such as single-walled carbon nanotubes, multi-walled carbon nanotubes, and graphene.

- Gold nanoparticles (NIST SRM 8012): Another reference material provided by NIST, used for calibrating and evaluating gold nanoparticles.

- Zinc oxide nanoparticles (NIST SRM 1899b): Another example of a reference material provided by NIST, used for evaluating and calibrating zinc oxide nanoparticles.

These and other CRNs are developed to ensure accuracy and consistency in the measurements of nanomaterials and serve as important tools for standardization and comparison of research results in the field of nanotechnology.

One of the tasks of our research was to identify the most frequently mentioned CRMs in scientific articles in high-impact journals. The most commonly CRMs in articles and studies include:

- Silver nanoparticles (NIST SRM 1109): Widely used for calibrating nanoparticle size measurement methods and evaluating their properties.

- Silicon nanoparticles (NIST SRM 640): Monodisperse spherical silicon nanoparticles used for calibrating nanoparticle size measurement methods and evaluating their properties.

- Calcium carbonate (NIST SRM 915a and 915b): Crystalline calcium carbonate nanoparticles used for calibrating nanoparticle size measurement methods and evaluating their properties.

- Silicon dioxide (NIST SRM 1963b): Monodisperse spherical silicon dioxide nanoparticles also used for calibrating nanoparticle size measurement methods and evaluating their properties.

- Gold colloids (NIST RM 8012): Colloidal gold used for calibrating methods for measuring the concentration and size of gold nanoparticles.

- Multi-walled carbon nanotubes (NIST SRM 2483): Multi-walled carbon nanotubes used for calibrating methods for their characterization and evaluating their properties.

- Polystyrene dispersion (NIST SRM 1961): Polystyrene dispersion used for calibrating nanoparticle size measurement methods and evaluating their properties.

- Silicon (NIST SRM 640d): Crystalline silicon also used for calibrating nanoparticle size measurement methods and evaluating their properties.

As literature analysis shows, these nanomaterials also form the basis for many studies and analysis methods in the field of nanosafety. Nanoparticle certified standard materials are used for conducting comparative toxicity analysis of different types of nanoparticles and identifying potentially hazardous

materials for living organisms. CRMs serve as a benchmark for creating new nanomaterials with improved properties and minimizing potential risks to health and the environment.

### **Conclusions**

The necessity of developing and utilizing CRMs for biomedical research stems from the need to establish a reliable foundation for comparative analysis of nanoparticle physicochemical and biological properties. This will contribute to the development of safe and effective diagnostic and therapeutic methods and enable the assessment of potential risks associated with using nanotechnology in medical applications.

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### **References**

1. Modi, S., Prajapati, R., Inwati, G.K., Deepa, N., Tirth, V., Yadav, V.K., et al. (2022) Recent Trends in Fascinating Applications of Nanotechnology in Allied Health Sciences. *Crystals.*, 12, 39. URL: <https://doi.org/10.3390/cryst12010039>.