TECHNICAL REPORT

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Nanotechnologies — Framework for identifying vocabulary development for nanotechnology applications in human healthcare

Nanotechnologies — Cadre pour le développement d'un vocabulaire d'identification des applications de nanotechnologies en santé humaine

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Foreword

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The committee responsible for this document is ISO/TC 229, *Nanotechnologies*.

Introduction

Terminology related to the use of nanotechnologies in human healthcare is on the rise as research in the field continues to intensify. The heightened focus in medical research on nanotechnologies is reflected by the number of medical and related scientific journals that are reporting on this research. The number of publications mentioning both nanotechnology and biology or medicine has increased logarithmically since approximately the year 2000.[1]

This Technical Report explains current concepts related to human healthcare in the clinical setting and identifies pertinent and timely categories most likely to be advanced by nanotechnologies. Certain aspects of human healthcare are expected to be advanced by nanotechnologies more than others, and standardization needs unique vocabulary to support the development of applications of nanotechnologies within it. It is recognized, for example, that physical chemists use the term "substrate" to describe a material surface supporting adsorption processes; this differs from a biologist's use of the term "substrate" to describe a substance that an enzyme acts upon.

Due to the keen public interest in the advancement of human healthcare, a common vocabulary is particularly relevant to the development of research proposals to gain funding and to communicate findings and results. This Technical Report provides a taxonomic framework to serve as the basis for the development of terminology related to the application of nanotechnologies in human healthcare. The framework identifies categories associated with the clinical value chain most likely to be advanced by nanotechnologies and describes some of the promising technologies being developed and utilized within the clinical workflow. It is intended that terms will be identified and harmonized definitions will be developed for them within the framework offered by this Technical Report.

Nanotechnologies — Framework for identifying vocabulary development for nanotechnology applications in human healthcare

1 Scope

This Technical Report will not attempt a formal, comprehensive definition of “nanomedicine”. Instead, it will provide a taxonomic framework for the development of vocabulary for clinical applications of nanotechnologies in human healthcare. While it is understood that the origins of nanotechnologies for healthcare applications emerge from pre-clinical and translational research, the interest of this Technical Report is to determine where these technologies will impact the clinical value chain and the practice of medicine.

This Technical Report is intended to facilitate communications between developers and users of nanotechnologies, deliverers and users of medicine including the pharmaceutical, research and medical communities, regulatory professionals, and additional organizations and individuals who might interact with these groups, including biotechnology, diagnostic, and medical device companies, the life sciences, patent attorneys and patent offices, institutional review boards, ethics review boards, and accreditation organizations.

2 Symbols and abbreviated terms

nm nanometer

3 Framework

3.1 General

The term “nanomedicine” is used by the scientific community and government agencies to describe a field that is relatively undefined in terms of the affected health care segments and the specific advances in nanotechnologies for biomedical applications.

In addition, the relevant mechanisms currently associated with diagnosis and treatment in biological processes can be larger than approximately 100 nm (e.g. endocytosis). Several participants from the biological sciences work with 400 nm diameter particles as drug carriers, while others consider <1 000 nm or <500 nm as pertinent in exploring emerging applications. Overall, the products currently enabled by nanotechnologies that are available for commercial clinical use are characterized by *in vitro* bulk properties or systemic effects. Examples of nanosize objects of interest in healthcare applications are depicted in Figure 1.

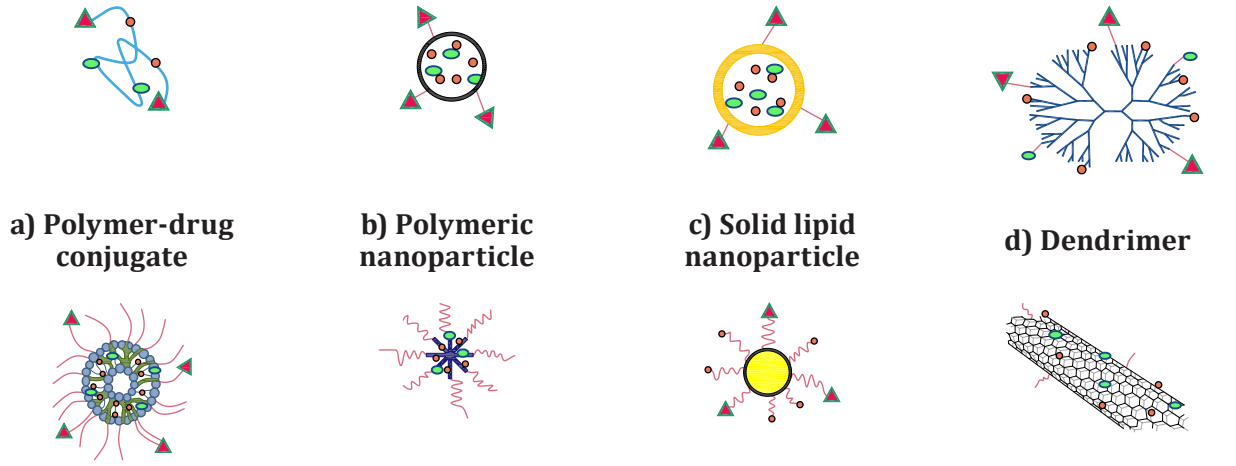

Figure 1 — Examples of nanosize objects of interest in healthcare applications[2]

In contrast, the current ISO definition of the term "nanoscale" stems from materials science and expresses in part the size range associated with quantum effects. The broad, enabling nature of nanotechnologies means that convergence with the biological sciences will continue to intensify. However, this Technical Report does not seek to suggest that current definitions in nanotechnologies, such as the approximately 100 nm upper boundary found in the ISO definition of the term "nanoscale",[3] be normalized to account for all size relationships in biological systems.

3.2 The clinical value chain

3.2.1 General

In recognition of the advancements that are anticipated in the clinical practice of medicine associated with nanotechnologies, relevant applications of nanotechnologies in human healthcare can be identified by their location in the clinical value chain (see Figure 2).

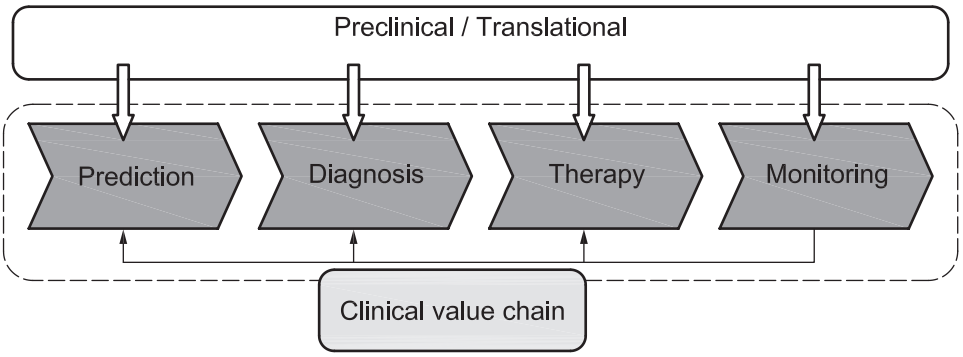

Figure 2 — The clinical value chain

The clinical value chain suggested for use in this Technical Report consists of 4 segments. The prediction and prevention segment includes nanotechnologies that are used to predict, or prevent

disease, conduct disease screening, and which are used in disease surveillance. The diagnosis segment includes nanotechnologies that are used for *in vitro* and *in vivo* detection, classification, grading, etc. of disease. The therapy segment includes nanotechnologies that are associated with therapy for disease. This includes drugs and other medicines (e.g. biopharmaceuticals), surgical implants, materials, devices, and surgical aids, and alternative therapies (e.g. stem cells). The monitoring segment includes nanotechnologies that are used to monitor disease after therapy to evaluate the efficacy of treatment and the progression or remission of disease, recurrence, side effects, etc.

Underlying these segments are pre-clinical and translational activities. That is, fundamental nanotechnology developments in academia, life science, and the biopharmaceutical industry are undertaken with the objective of having an eventual impact or application in one or more of the clinical value chain segments. These might be nanotechnologies used to understand basic life processes or nanotechnologies that support products used in a clinical setting (see Figure 3).

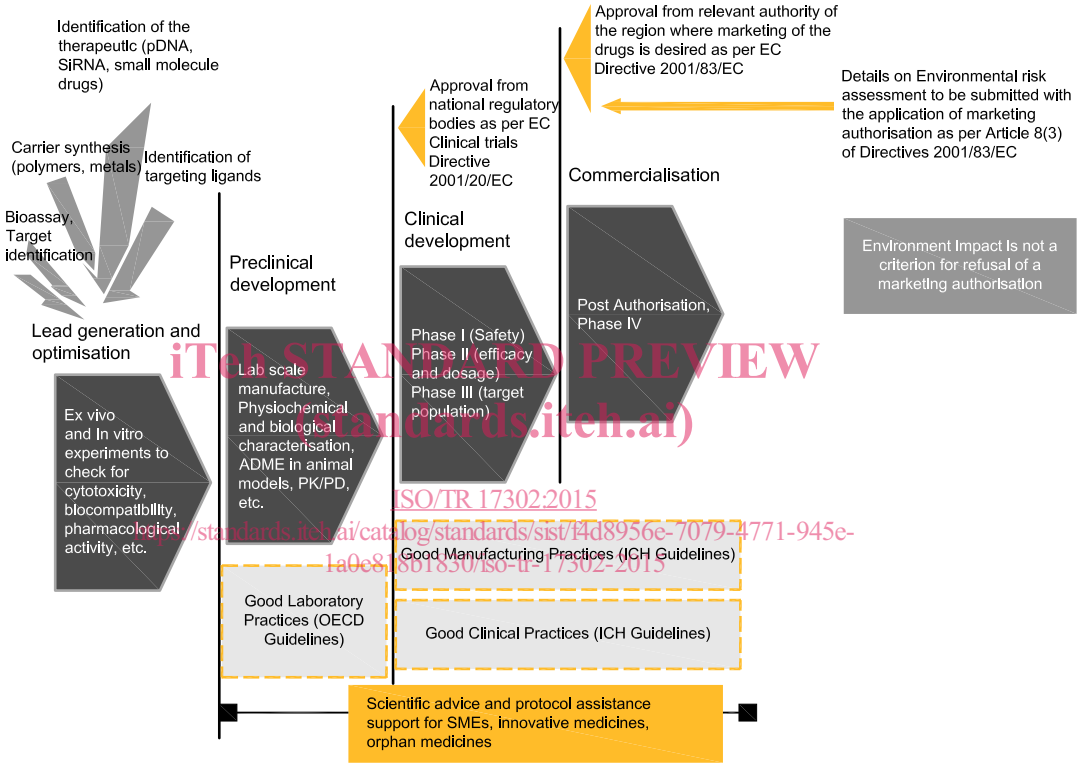

Figure 3 — Illustrative example of the general stages of development for nanotechnologies used in medicine, which highlights the European Union's approach[4]

3.2.2 Prediction and prevention

Prediction and prevention inlcudes technologies that permit accurate screening to identify the risk or susceptibility to disease or disease recurrence, prognosis based on one or more indicators, public health surveillance of disease and immunization to prevent disease. Products enabled by nanotechnologies in this value chain segment include sprays, coatings, antiseptics and vaccines.

Two application areas that are useful to highlight the contribution of nanotechnologies to this segment of the clinical value are the prevention of surgical site infections and the use of informatics to predict and reduce drug side effects by identifying patients at risk. Surgical site infections encompass inadvertent infections occurring inside the hospital or physician's office, the prevention of which can include the use of disinfectants, sterile surfaces, protective gowns, air handling, and appropriate waste disposal. The use of nanotechnologies for preventing adventitious infections might be the source of new terms, e.g. "nanotextured surface" to describe a product designed by the coating industry to ensure a sterile environment. Bioinformatics and nano-informatics might be used to evaluate disease prevalence, drug design, acceptable test protocols, dose metrics, and toxicity.

3.2.3 Diagnosis

Nanotechnologies for diagnostics encompass *in vivo* as well as *ex vivo/in vitro* evaluations. Nanotechnologies can be used to advance sensing systems to improve the accurate and early detection and diagnosis of disease. There are multiple components in the diagnostic process ranging from the manufacturing setting (e.g. reagent and detection systems) to the selection of target analytes (e.g. cells, proteins, tissue structures) and the organism setting (*in vitro/ex vivo* or *in vivo*) (see Figure 4).

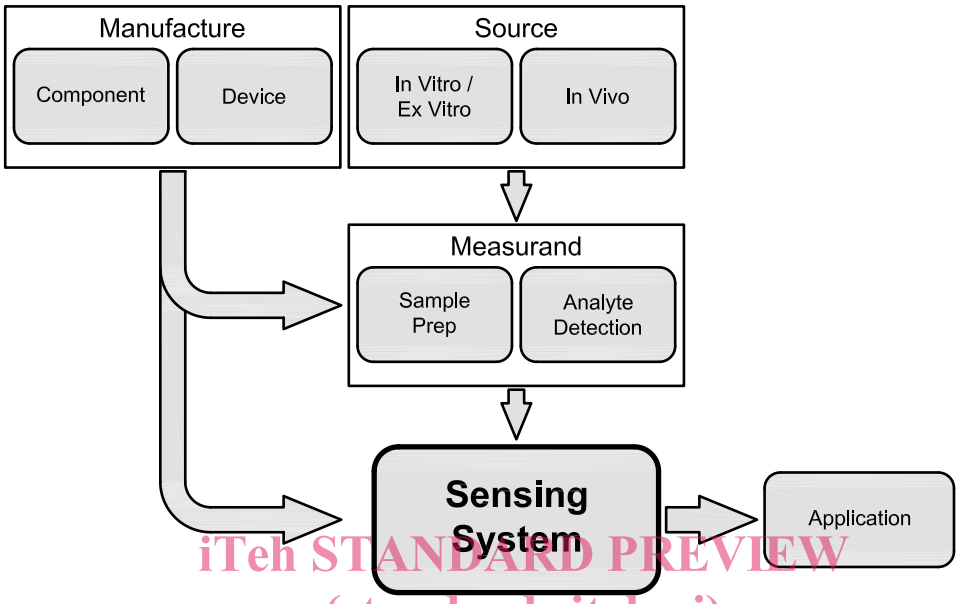

Figure 4 — Overview of nanotechnologies in diagnostics

For example, when a new nanoparticle is developed for *in vivo* imaging, this diagram approach could be applied to understand the application area and technology as follows (Figure 5):

— **Manufacture** — Method of synthesis of the nanoparticle. Further details could be added, such as additional nanotechnology that is required for the manufacturing process.

— **Source** — Context of use of the nanoparticle. In this case, the nanoparticle is designed to image a living patient.

— **Measurand** — This nanoparticle is designed to be delivered into and enhance the visualization of the patient's lymphatics.

— **Sensing System** — The actual diagnostic action occurs with placement of the patient in the MRI device and detecting the nanoparticles with the lymphatics.

— **Application** — The goal of the use of the nanoparticle is for the detection of metastatic cancer in the patient's lymphatics.

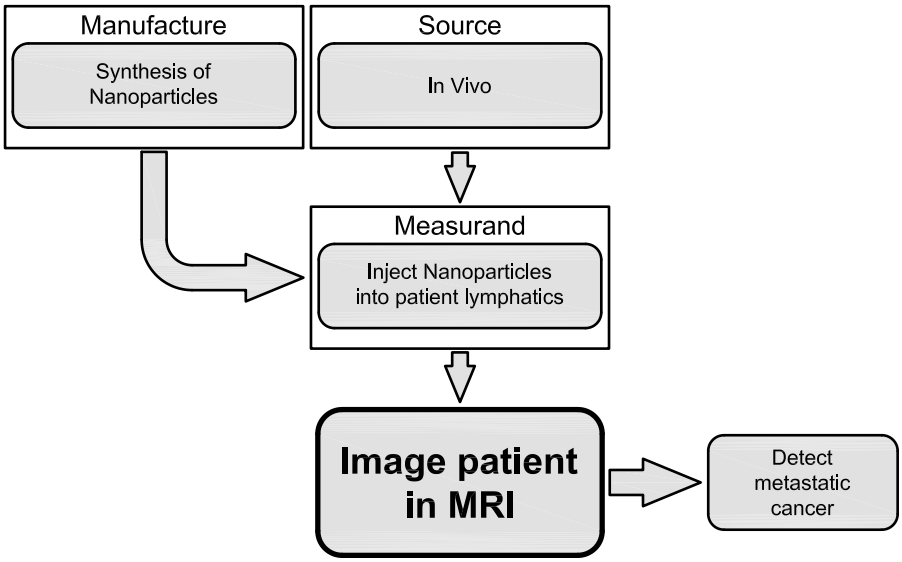

Figure 5 — Example of understanding a diagnostic application for terminology development

3.2.4 Therapy

Applications of nanotechnologies in the therapy segment of the clinical value chain include the delivery selective and targeted drug therapies, material modifications, and medical devices. Specific areas of therapy that could be advanced by the use of nanotechnologies in this clinical value chain segment include clinical indication tools, understanding of route of administration, reduced inter and intra-subject variability, improved dose-response relationship(s), faster achievement of maximum amount of drug in blood stream, and limiting the effect on pharmacokinetics of a drug once absorbed.

Cancer therapy is a dominant field that leverages advancements in nanotechnology. In this area, nano-objects of interest include nanowires, gold (functional metallic), magnetic nanoparticles, viral nanoparticles, polysaccharide nanocarriers, nanobiosensors, nanomicelles, nanoscale liposomes, nano-arrays, nanobioconjugates, nanochannels, stealth nano-objects, nanomembranes, DNA complexes, molecular motors, and protein coronas.

For material modification and manufacture applications, key classes of nano-objects include synthetic nanoparticles, dendrimers (e.g. hyperbranched polymers, dendigrafts, and dendronised polymers), nanogels, nanosuspensions, solid lipid nanoparticles, nano shells, nanopores, nanocapsule, nanoneedle, nanoporous membrane, and nanofilms.

In the area of medical devices, applications of nanotechnologies include the development of artificial muscles, nanoscale knee and lymph sleeves, nanowire and needle scaffolds, tissue and vessel re-enforcement, dental applications, drug delivery devices, and nano-coatings on medical devices, such as ball and socket joints in hip joint replacements.

3.2.5 Monitoring

Post-therapy applications being advanced with nanotechnologies show promise regarding the ability to accurately monitor the progress of disease treatment, recovery, and recurrence. Nanotechnologies of interest can fall into the categories of microchip sensors or nanoparticles, ligands, and reagents that, depending on the intended use, can interact with human systems *in vivo* or *ex vivo* (see Figure 6).