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Emerging Discipline Nanotoxicology: Sources, Challenges and Strategies for Addressing Risk

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Abstract: ***Nanomaterials are now being manufactured and used in many products. However, our knowledge of the human health effects and environmental concentrations of engineered nanomaterials or nanoparticles is incomplete. A number of international research projects on toxicologically relevant properties of engineered nanoparticles has increased greatly, nourishing the expectation that more relevant technical and toxicological data will be explored. The intrigue in nanomaterial research for healthcare applications is wide spread with growing concerns about their unintentional health and environmental impact. This article gives a toxicologists perspective, outlining possible routes of uptake by humans, environmental concentrations, known or suspected toxic effects, and the practical implication for human health risk assessments and public perception. When looking at possible exposure routes for manufactured Nanoparticles, inhalation, dermal and oral exposure are the most obvious, depending on the type of product in which Nanoparticles are used. In this regard, pulmonary toxicity studies reported in various research reports indicated that lung exposures to nanoparticles produce enhanced adverse inflammatory responses which may play important roles in nanoparticle toxicity. Data on exposure is also needed for risk calculations. Current legislation does not specifically address nanoparticles or nanomaterials, and there are concerns about nomenclature, defining nanomaterials as new substance under chemicals regulations act, and the appropriateness of current test methods. The success of nanotechnology will require assurances that the products being developed are safe from an Environmental, Health, and Safety (EHS) standpoint. The key factors for discussion herein include the importance of nanoparticle toxicology; entry routes into the body and possible hazard effects related to nanoparticle exposures, characterization of the nanomaterial, development of a nanomaterial risk framework; dose impact in hazard identification and risk assessment of nanotechnologies as well as corresponding hypothesis on appropriateness of current test methods and factors influencing future legislation.***

Index Terms: **nanotechnology, nanoparticles, nanomaterials, toxicity, risk calculations.**

I. INTRODUCTION

Toxicology traditionally addresses adverse poisoning effects of chemicals to humans, animals and the environment. Nanotechnology, which is about controlling matter at near-atomic scales to produce unique or enhanced materials, products and devices, is now maturing rapidly with more nanotechnology products each and every day on the market. Yet concerns have been raised that the very properties of nanostructured materials that make them so attractive could potentially lead to unforeseen health or environmental hazards.[1]. Depending on the type of product in which Nanoparticles are used the most obvious possible exposure routes are inhalation, dermal and oral exposure. Research reports indicate that nanoparticles can deposit in the respiratory tract after inhalation that can affect the immune system defense ability to combat infections, oxidative stress-related inflammatory reactions have also been observed. However, more research is required to understand mechanisms and pathways in the body. Skin penetration studies also need to be studied so that dermal applications of metal oxide nanoparticles used in sunscreens that lead to systemic exposure can be found out . Uptake of nanoparticles in the gastrointestinal tract after oral uptake is a known phenomenon, of which use is intentionally made in the design of food and pharmacological components.

Emerging technologies in nanoparticles offer opportunities to develop smart drug delivery vehicles that can move through the body to target sites, or sensor and diagnostic systems operating inside cells. Nanomaterials could also be used to synthesis structures for implant into the body that have properties that closely resemble the properties of natural materials. Scientific knowledge about nanoparticle cell interaction mechanisms indicate that the mechanisms and pathways are more difficult to understand. Even particles of the same material can show completely different behavior due to, for example, slight differences in surface coating, charge or size. This makes the categorization of nanoparticle behavior, when in contact with biological systems, intricate and thus nanoparticle hazard identification is not straightforward.

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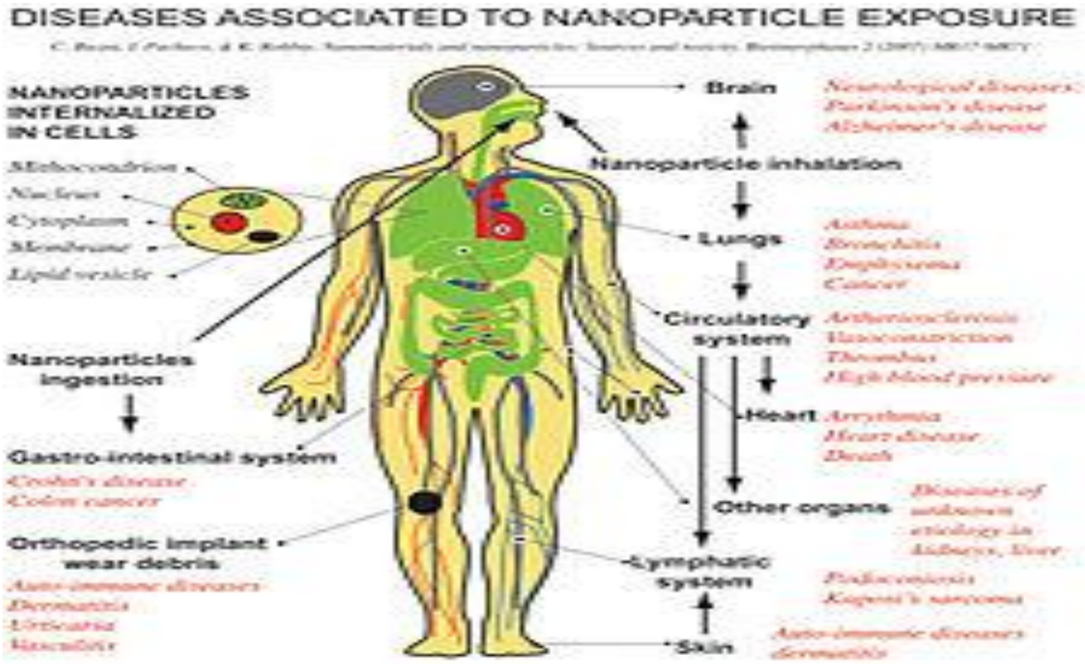

Fig 1. Adverse Effects of Nanoparticles on Human Health

Tissue scaffolds that use biocompatible nanomaterials to control cell growth and adhesion are under development, and in the future artificial organs that mimic the porosity and capillary structure of natural organs such as the heart and liver may become reality. Nanomaterials constitute by far the most significant market opportunity in the foreseeable future. Now is the time for the scientific community, industry and the government to act together for a rational science-based approach to minimize harm caused by these materials, while supporting continued study and appropriate industrial development.

A. Adverse Effects of Nanoparticles on Human Health

Adverse effects of nanoparticles on human health depends on individual factors such as genetics and existing disease, as well as exposure, and nanoparticle chemistry, size, shape, agglomeration state, and electromagnetic properties. In Fig. 1, a detail view of the possible adverse health effects associated with inhalation, ingestion, and contact with nanoparticles were shown. It must be known that not all nanoparticles produce these adverse health effects—the toxicity of nanoparticles depends on various factors, including size, aggregation, composition, crystallinity, surface functionalization, etc. Animal and human studies show that inhaled nanoparticles are less efficiently removed than larger particles by the macrophage clearance mechanisms in the lungs, causing lung damage, and that nanoparticles can translocate through the circulatory, lymphatic, and nervous systems to many tissues and organs, including the brain. The key to understanding the toxicity of nanoparticles is that their minute size, smaller than cells and cellular organelles, allows them to penetrate these basic biological structures, disrupting their normal function. Toxic effects include such as tissue inflammation, and altered cellular redox balance toward oxidation, causing abnormal function or cell death. Diseases associated with inhaled nanoparticles are asthma, bronchitis, emphysema, lung cancer, and neurodegenerative diseases, such as Parkinson’s and Alzheimer’s diseases. Nanoparticles in the gastrointestinal tract have been linked to Crohn’s disease and colon cancer. Nanoparticles that enter the circulatory system are related to occurrence of arteriosclerosis, blood clots, arrhythmia, heart diseases, and ultimately cardiac death. Translocation to other organs, such as liver, spleen, etc., may lead to diseases of these organs as well. Exposure to some nanoparticles is associated with the occurrence of autoimmune diseases, such as systemic lupus erythematosus, scleroderma, and rheumatoid arthritis.

II. NANOPARTICLE CHARACTERIZATION

Nanoparticles are generally classified based on their dimensionality, morphology, composition, uniformity, and agglomeration. An important additional distinction should be made between nanostructured thin films or other fixed nanometer scale objects such as the circuits within computer microprocessors and free nanoparticles. The motion of free nanoparticles is not constrained, and they can easily be released into the environment, leading to human exposure that may pose a serious health risk.

A. Dimensionality
As shape, or morphology, of nanoparticles plays an important role in their toxicity, it is useful to classify them based on their number of dimensions. This is a generalization of the concept of aspect ratio. One-dimensional (1D) nanomaterials. Materials with one dimension in the nanometer scale are typically thin films or surface coatings, and include the circuitry of computer chips and the anti-reflection and hard coatings on eyeglasses. Thin films have been developed and used for decades in various fields, such as electronics, chemistry, and engineering. Thin films can be deposited by various methods,[2] and can be grown controllably to be only one atom thick, a so-called monolayer. Two-dimensional (2D) nanomaterials. Two-dimensional nanomaterials have two dimensions in the nanometer scale. These include 2D nanostructured films, with nanostructures firmly attached to a substrate, or nanopore filters used for small particle separation and filtration. Free particles with a large aspect ratio, with dimensions in the nanoscale range, are also considered 2D nanomaterials. Asbestos fibers are an example of 2D nanoparticles. Three-dimensional (3D) nanomaterials. Materials that are nanoscaled in all three dimensions are considered 3D nanomaterials. These include thin films deposited under conditions that generate atomic-scale porosity, colloids, and free nanoparticles with various morphologies.[3]

B. Nanoparticle Morphology
Morphological characteristics to be taken into account are flatness, sphericity, and aspect ratio. A general classification exists between high- and low-aspect-ratio particles. High-aspect-ratio nanoparticles include nanotubes and nanowires, with various shapes, such as helices, zigzags, belts, or perhaps nanowires with diameter that varies with length. Low-aspect-ratio morphologies include spherical, oval, cubic, prism, helical, or pillar. Collections of many particles exist as powders, suspension, or colloids.

C. Nanoparticle Composition
Nanoparticles can be composed of a single constituent material or be a composite of several materials. The nanoparticles found in nature are often agglomerations of materials with various compositions, while pure single composition materials can be easily synthesized today by a variety of methods

D. Nanoparticle Uniformity and Agglomeration
Based on their chemistry and electromagnetic properties, nanoparticles can exist as dispersed aerosols, as suspensions/ colloids, or in an agglomerate state. It is only through knowledge of the properties of the particles under study that meaningful toxicological evaluation is possible. This is of equal importance for industrial and environmental particles as well as for nanoparticles designed for nanomedical applications.

III. TOXICOLOGY OF NANOPARTICLES

A. Respiratory tract
After inhalation, nanoparticles deposit throughout the entire respiratory tract, starting from nose and pharynx, down to the lungs.[4] Due to their large surface area, the lung is the primary entry portal for inhaled particles. The nasopharyngeal region captures mainly micro particles and nanoparticles smaller than 10 nm, while the lungs will receive mainly nanoparticles with diameters between 10 and 20 nm.[5]. The adverse effect of inhaled nanoparticles on the lungs depends on the lung burden (determined by the rate of particle deposition and clearance) and on the residence time of the nanoparticles in the lungs.[6] For example, carbon nanotubes are not eliminated or very slowly eliminated from the lungs. The persistent presence within the alveoli of inhaled particles especially those with mutagenic potential, increases the risk of lung cancer.[6] Smaller particles have a higher toxicity than larger particles of the same composition and crystalline structure, and they generate a consistently higher inflammatory reaction in the lungs. Smaller nanoparticles are correlated with adverse reactions such as impaired macrophage clearance, inflammation, accumulation of particles, and epithelial cell proliferation, followed by fibrosis, emphysema, and the appearance of tumors. .[6] Particle uptake and potential health effects may be dependent on genetic susceptibility and health status. There are also a few reports that indicate nanoparticles of various compositions are able to modulate the intrinsic defensive function of macrophages, affecting their reactivity to infections. It was found that several types of nanoparticles such as ZrO_2 enhance the expression of some viral receptors, making macrophages exposed to nanoparticles hyper-reactive to viral infections and leading to excessive inflammation. On the other hand, exposure to other nanoparticles SiO_2 and TiO_2 leads to a decrease in the expression of some other viral and bacterial receptors, leading to lower resistance to some viruses or bacteria.

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B. Cellular interaction with nanoparticles

- ***Cellular uptake***

Cellular uptake, sub cellular localization, and ability to catalyze oxidative products depend on nanoparticle chemistry, size, and shape.[7] The mechanism by which nanoparticles penetrate cells without specific receptors on their outer surface is assumed to be a passive uptake or adhesive interaction. This type of uptake and free movement within the cell makes them very dangerous by having direct access to cytoplasm proteins and organelles. Upon nonphagocytic uptake, nano particles can be found in various locations inside the cell, such as the outer-cell membrane, cytoplasm, mitochondria, lipid vesicles, along the nuclear membrane, or within the nucleus [8]. Depending on their localization inside the cell, the nanoparticles can damage organelles or DNA, or ultimately cause cell death

- ***Oxidative stress, Inflammation, and Genotoxicity***

Oxidative stress generation, Both in vivo and in vitro studies have shown that nanoparticles of various compositions (fullerenes, carbon nanotubes, quantum dots, and automobile exhaust) create reactive oxygen species [9]. The oxidative stress induced by nanoparticles may have several sources such as reactive oxygen species can be generated directly from the surface of particles when both oxidants and free radicals are present on the surface of the particles; Transition metal (iron, copper, chromium, vanadium, etc.) nanoparticles acting as catalysts in Fenton-type reactions; Altered functions of mitochondrion; and Activation of inflammatory cells. Inflammation, is the normal response of the body to injury. When generated in moderation, inflammation stimulates the regeneration of healthy tissue; however, when in excess, it can lead to disease[10]. In vitro and in vivo experiments demonstrate that exposure to small nanoparticles is associated with inflammation, with particle size and composition being the most important factors [11], DNA damage, generation of reactive oxygen species to the point that they overwhelm the antioxidant defense system shifting the redox balance of the cell can result in oxidation, and therefore destruction, of cellular biomolecules, such as DNA, leading to heritable mutations [11].

- ***Health Effects***

Nanoparticles, due to their small size, can influence basic cellular processes, such as proliferation, metabolism, and death. Many diseases can be associated with dysfunction of these basic processes. For example, cancer results from uncontrolled cell proliferation, while neurodegenerative diseases are caused in part by premature cell death [12]. Oxidative stress has been implicated in many diseases, including cardiovascular and neurological diseases, pancreatitis, and cancer. Severe inflammation is assumed to be the initiating step in the appearance of autoimmune diseases (systemic lupus erythematosus, scleroderma, and rheumatoid arthritis) that can sometimes be associated with exposure to some nanoparticles.

IV. PHYSICOCHEMICAL CHARACTERISTICS DEPENDENT TOXICITY

From previous knowledge of toxicological properties of fibrous particles , it is believed that the most important parameters in determining the adverse health effects of nanoparticles are dose, dimension, and durability[13]. However, recent studies show different correlations between various physicochemical properties of nanoparticles and the associated health effects, raising some uncertainties as to which are the most important parameters in deciding their toxicity: mass, number, size, bulk or surface chemistry, aggregation, or all together. will emphasize what we believe are the most important nanoparticle characteristics associated with their toxicity.

A. Dose-dependent toxicity

Dose is defined as the amount or quantity of substance that will reach a biological system. The dose is directly related to exposure or the concentration of substance in the relevant medium multiplied by the duration of contact. Generally, the negative health effects of nanoparticles do not correlate with nanoparticle mass dose. The main health concerns with nanomaterials will be with chronic low dose exposures over a life time possibly leading to increased incidences of degenerative diseases. Because of the particulate nature of nanoparticles, a logical dose metric [14] will be related to the number of particles reaching each cell or cellular sub-compartment of relevance. While mass alone cannot predict surface area, the number of nanoparticles within a certain size and shape range is predictive of surface area and is therefore likely to be a dose metric which is more predictive of harm than simple mass [15].

B. Nanoparticle surface dependent toxicity

Research reports indicate that the inflammatory effect may be dependent on the surface area of nanoparticles, suggesting a need for changes in definitions and regulations related to dose and exposure limits. Indeed, smaller

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nanoparticles have higher surface area and particle number per unit mass compared to larger particles. The body will react differently to the same mass dose consisting of billions of nanoparticles compared to several micro particles. Larger surface area leads to increased reactivity and is an increased source of reactive oxygen species. The higher surface area of nanoparticles causes a dose dependent increase in oxidation and DNA damage, much higher than larger particles with the same mass dose [10].

C. Size-dependent toxicity
Toxicological studies have demonstrated that small nanoparticles (100 nm) cause adverse respiratory health effects, typically causing more inflammation than larger particles made from the same material. Various research articles indicated that the smaller particles had a significantly prolonged retention, increased translocation to the pulmonary interstitium and pulmonary persistence of nanoparticles, greater epithelial effects, and impairment of alveolar macrophage function.

D. Concentration-dependent toxicity
There are many contradictory results related to the toxic effects of nanoparticles at different concentrations. It has been reported that a high concentration of nanoparticles would promote particle aggregation,[16] and therefore reduce toxic effects compared to lower concentrations. Most aggregates are observed to be larger than 100 nm, a size that seems to be a threshold for many of the adverse health effects of small particles. Therefore, experiments performed with high concentrations of nanoparticles will lead to the formation of nanoparticle aggregates that may not be as toxic as lower concentrations of the same nanoparticles.

E. Particle chemistry-dependent toxicity
Particle chemistry is critical in determining nanoparticle toxicity. Particle chemistry is especially relevant from the point of view of cell molecular chemistry and oxidative stress. Namely, depending on their chemistry, nanoparticles can show different cellular uptake, sub cellular localization, and ability to catalyze the production of reactive oxygen species.

F. Aspect-ratio-dependent toxicity
It was found that the higher the aspect ratio, the more toxic the particle is. Long-aspect-ratio engineered nanoparticles, such as carbon nanotubes (CNTs), are new materials of emerging technological relevance and have recently attracted a lot of attention due to their possible negative health effects, as suggested by their morphological similarities with asbestos.[17] However, there is no consensus in the characterization of CNT toxicity. The contradictory reports on CNT toxicity could be associated with the multitude of morphologies, sizes, and chemical functionalizations of their surface or ends. Carbon nanotubes can be single walled (SWCNTs) or multiple walled (MWCNTs), with varying diameter and length, with closed capped sections or open ends. In addition to the many forms of nanotubes, they can also be chemically modified. CNTs are oxidized to create hydroxyl and carboxyl groups, especially in their ends, which makes them more readily dispersed in aqueous solutions.

V. ENVIRONMENTAL IMPACT OF ENGINEERED NANOMATERIALS
With the increased presence of nanomaterials in commercial products, a growing public debate is emerging on whether the environmental and social costs of nanotechnology outweigh its many benefits. To date, few studies have investigated the toxicological and environmental effects of direct and indirect exposure to nanomaterials and no clear guidelines exist to quantify these effects. Recent studies examining the toxicity of engineered nanomaterials in cell cultures and animals have shown that size, surface area, surface chemistry, solubility and possibly shape all play a role in determining the potential for engineered nanomaterials to cause harm. The unique properties of various types of intentionally produced nanomaterials give them novel electrical, catalytic, magnetic, mechanical, thermal, or imaging features that are highly desirable for applications in commercial, medical, military, and environmental sectors. These materials may also find their way into more complex nanostructures and systems. As new uses for materials with these special properties are identified, the number of products containing such nanomaterials and their possible applications continues to grow. The four types of Intentionally Produced Nanomaterials are Carbon Based Materials, Metal Based Materials, Dendrites, and Composites.

A. Carbon Based Materials
These nanomaterials are composed mostly of carbon, most commonly taking the form of a hollow spheres, ellipsoids, or tubes. Spherical and ellipsoidal carbon nanomaterials are referred to as fullerenes, while cylindrical ones are called nanotubes. These particles have many potential applications, including improved films and coatings,

stronger and lighter materials, and applications in electronics.

B. Metal Based Materials
These nanomaterials include quantum dots, nanogold, nanosilver and metal oxides, such as titanium dioxide. A quantum dot is a closely packed semiconductor crystal comprised of hundreds or thousands of atoms, and whose size is on the order of a few nanometers to a few hundred nanometers. Changing the size of quantum dots changes their optical properties.

C. Dendrimers
These nanomaterials are nanosized polymers built from branched units. The surface of a dendrimer has numerous chain ends, which can be tailored to perform specific chemical functions. This property could also be useful for catalysis. Also, because three-dimensional dendrimers contain interior cavities into which other molecules could be placed, they may be useful for drug delivery.

D. Composites
Composites combine nanoparticles with other nanoparticles or with larger, bulk-type materials. Nanoparticles, such as nanosized clays, are already being added to products ranging from auto parts to packaging materials, to enhance mechanical, thermal, barrier, and flame-retardant properties.

Source: United States Environmental Protection Agency

VI. ANSI-NSP NANOTECHNOLOGY STANDARDS FOR NANOMATERIAL EXPOSURES
Every day, nanotechnology becomes more commercially viable across an expanding range of industry sectors. The properties and functions of novel new structures, devices and systems are directly tied to their nanoscale dimensions. As progress in nanotechnology processes and the manufacture of nanomaterials continues to accelerate, a growing list of stakeholder needs has arisen. At the top of that list is the fundamental building block for any emerging industry—consistent and globally-accepted nomenclature and terminology. Following closely are specifications and tests needed to support nanoscale measurement and characterization; and methods for evaluating how nanomaterials could potentially impact human health and safety, as well as the environment. The American National Standards Institute's Nanotechnology Standards Panel (ANSI-NSP) serves as the cross-sector coordinating body for the purposes of facilitating the development of standards in the area of nanotechnology including, but not limited to, nomenclature/terminology; health, safety and environmental aspects; materials properties; and testing, measurement and characterization procedures. The purpose of ANSI-NSP Nanotechnology Standards Database is to capture information about standards and associated documents (standards, best practices, guidelines) that directly relate to nanomaterials and nanotechnology-related processes applications and products.

A. Objectives of the ANSI-NSP
Coordinate and provide a forum for academia, individual industries, standards developing organizations, and governmental entities to define needs, determine work plans and establish priorities for updating standards or creating new standards.

- Solicit participation from nanotechnology-related sectors and academia that have not traditionally participated in the voluntary standards system, and work cooperatively to achieve the mission of the ANSI-NSP.
- Facilitate the timely development and adoption of standards responsive to identified needs in the area of nanotechnology in general and nomenclature/terminology specifically.
- Facilitate and promote cross-sector collaborative efforts between standards developing organizations to establish work plans and develop joint and/or complementary standards.
- Where standards do not exist, obtain agreement from a standard developer to initiate development of the standard in a timely manner.
- Establish and maintain liaison with other national, regional and international standards efforts addressing nanotechnology issues so as to create identical or harmonize existing standards.
- Establish and maintain a database of nanotechnology standards, accessible from the Internet, and capable of generating updates, notices, and reports.
- Identify any impediments preventing the timely adoption of needed American National Standards.
- Make widely available the results of the ANSI-NSP's work.

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VII. NANOPARTICLES AND THE ENVIRONMENT

While nanoparticles occur naturally in the environment and have been intentionally used for centuries, the production and use of engineered nanoparticles has seen a recent spike, which makes environmental release almost certain. The risk of nanoparticles entering atmosphere, soil or water environment could occur from waste streams from industrial plants being discharged into streams and rivers, accidental releases from production and during transportation of nanoproducts into streams, rivers and the atmosphere and domestic nano waste discharge from the use of nanotechnology in cosmetics, toiletries and sun creams. The risk of environments needs to be assessed and researched in the following areas [18]:-

A. The Detection of the Particles in the Environment

Because nanotechnologies are diverse and exposures to nanomaterials will vary widely, assessing exposure and potential impacts on health or the environment will require multiple sensor types operating under different conditions. Three issues stand out as fertile ground for innovative research:

- monitors for airborne exposure,
- detectors for waterborne nanomaterials, and
- Smart sensors that can measure both exposure and potential hazards.

B. The Measurement of Emissions of Nano-Particles

There are many aspects to evaluating nanomaterial toxicity. But there are three that we consider crucial for stimulating high-quality research and preventing the unnecessary use of hazardous nanomaterials:

- validated screening tests,
- developing viable alternatives to in vivo tests, and
- Determining the toxicity of fibre-shaped nanoparticles.

C. The Impact on the Immediate and Longer Range Environment

- First, to develop validated models capable of predicting the release, transport, transformation, accumulation and uptake of engineered nanomaterials in the environment.
- Second, validated models must be developed that are capable of predicting the behavior of engineered nanomaterials in the body, including dose, transport, clearance, accumulation, transformation and response. These models should: relate the physical and chemical characteristics of nanomaterials to their behavior; allow an integrated approach to predicting potential impact of engineered nanomaterials and nanoproducts; and estimate impact within susceptible populations.
- Third, to use predictive models for engineering nanomaterials that are safe by design. This might include engineering the nanomaterials in ways that enhance desired properties while suppressing hazardous ones, or creating fail-safe mechanisms that ensure a transition to benign materials upon disposal.

D. The Toxicity of the Particles to the Environment

- The main concern will be if any of the nanoparticles entering the environment are toxic or could become toxic to living species in the environment. Nanoparticles entering the environment may not initially be toxic to living species in the environment, but they could in their lifecycle become toxic. The nanoparticles could react to other substances in the environment, break-down in the environment, provide a catalyst (speeding up) for the reactions already taking place, or prevent essential reactions taking place. Measuring these effects would require a complete understanding of the nanoparticles themselves, the reactions taking place in the environments encountered by the particles, and the lifecycle of the nanoparticle. Mechanisms on the nano-bio interface can be either chemical or physical
- Chemical mechanisms include the production of reactive oxygen species (ROS) , dissolution and release of toxic ions, disturbance of the electron/ion cell membrane transport activity , oxidative damage through catalysis , lipid peroxidation or surfactant properties. ROS is considered as being the main underlying chemical process in nanotoxicology, leading to secondary processes that can ultimately cause cell damage and even cell death. Moreover, ROS is one of the main factors involved in inflammatory processes. This is believed to happen via up-regulation of genes involved in the pro-inflammatory response triggered by the activation of certain transcription factors. However, free radical formation can also have direct impacts on cell integrity.
- Physical mechanisms at the nano-bio interface are mainly a result of particle size and surface properties this includes disruption of: membranes, membrane activity, transport processes, protein conformation/folding and protein aggregation/ fibrillation.

E. The Life-Cycle of the Particles in the Environment

- Developing robust ways of evaluating the potential impact good or bad of a nanoproduct from its initial manufacture, through its use, to its ultimate disposal
-

F. Develop strategic programmes that enable relevant risk-focused research

- The first challenge is identifying mechanisms that enable collaborative research programmes whether interdisciplinary, between government and industry, or between different stakeholders.
- Developing communication activities that enable technical information to be summarized, critiqued and ultimately synthesized for various interested parties, including decision-makers and consumers. The advent of the Internet provides an ideal venue for such activities and we encourage its use in communicating with the end-users of risk-based science.

VIII. SUMMARY, OUTLOOK AND FUTURE NEEDS

The fate, behavior and toxicity, of different class of nanomaterials in environment is discussed. Research on humans and animals indicates that some nanoparticles are able to enter the body, and rapidly migrate to the organs via the circulatory and lymphatic systems. Subjects with preexisting diseases such as asthma and diabetes, among others may be more prone to the toxic effects of nanoparticles. Genetic factors may also play an important role in the response of an organism to nanoparticle exposure. There are still huge gaps in knowledge about the nature of interaction of nanoparticles with the environmental system. Further studies on kinetics and biochemical interactions of nanoparticles within organisms are imperative. These studies must include, at least, research on nanoparticle translocation pathways, accumulation, short- and long-term toxicity, their interactions with cells, the receptors and signaling pathways involved, cytotoxicity, and their surface functionalization for an effective phagocytosis. Existent knowledge on the effects of nanoparticle exposure on the lymphatic and immune systems, as well as various organs, is sparse. In order to clarify the possible role of nanoparticles in diseases recently associated with them such as Crohn’s disease, neurodegenerative diseases, autoimmune diseases, and cancer, nanoscale characterization techniques should be used to a larger extent to identify nanoparticles at disease sites in affected organs or tissues, and to establish pertinent interaction mechanisms. Other important research topics to be pursued include nanoparticle aging, surface modifications, and change in aggregation state after interaction with bystander substances in the environment and with biomolecules and other chemicals within the organisms. Much more studies are needed to evaluate the stability of these matrices in a variety of test systems to fully determine the potential for human exposure to the nanoscale components of commercially available products, as well as future products. Importantly, analytical techniques are needed that permit real-time, in situ monitoring to optimize production processes, thus minimizing waste and energy costs as well as providing mechanistic information. Once the biomedical community embraces nanoparticles as new tools for in vivo imaging, for longer time scales, we speculate that new knowledge of how cells and organs work, both internally and externally with others, will be obtained. With increased knowledge, and ongoing study, we are more likely to find cures for diseases associated with nanoparticle exposure, as we will understand their causes and mechanisms. We foresee a future with better-informed and, hopefully, more cautious manipulation of engineered nanomaterials as well as the development of laws and policies for safely managing all aspects of nanomaterial manufacturing, industrial and commercial use, and recycling.

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Sai Chaitanya Hanmanthu has completed his B.Tech in Electrical and Communication Engineering from JNTU Hyderabad in 2013. He is in the final semester of MS program from the Department of Electrical and Computer Science and Engineering at, NYIT, Old Westbury, NewYork. Since August 2014 until August 2015 he was engaged in several research projects undertaken in the Electrical Engineering department and Nanotechnology lab, at NYIT in the capacity of research assistant. He is working on towards his MS thesis on a topic titled “A Novel Highly Selective, Ultrafast, Reliable And Wide Linear-Range Biosensors For The Detection Of Glucose In Urine" . He is in the process of submitting to get a patent for his invented biosensor to the United States Patent and Trademark Offic**e**. He is having nine international conference papers to his credit and one journal under advanced stage of revision. He has worked on various projects from August 2011 till date on topics involving Carbon Nanotube's, Biosensors for Telemedicine, Nanobiosystems, and R.F Magnetron sputtering techniques relevant to Thin Film Fabrication. After his graduation from NYIT IN December 2015, he will be pursuing a PhD in Electrical Engineering and Computer Science at MIT with research focus on Nanofabrication. Mr. Hanmanthu is a member of IEEE (Institute of Electrical and Electronics Engineers, Inc), Eta *Kappa* Nu, Institute of Electrical and Telecommunication Engineering (IETE), and also a volunteer of STEM program and REACH HIGHER program (Initiative of the First Lady Michelle Obama) at the NYIT, Old Westbury Campus. As an active volunteer in STEM program he was involved in various community and school programs as well as submitted a Paper on” Next Generation Innovative Initiatives and Technologies for STEM Education within Asian American and Pacific Islanders(AAPI) Community” to AAPI community on 4-14-2014 at the U. S Department of Interior. He has volunteered with many organizations in organizing educational programs for underserved and rural communities.