MANUAL ON CRITICAL ISSUES IN NANOTECHNOLOGY R&D MANAGEMENT

AN ASIA-PACIFIC PERSPECTIVE

CHAPTER 1
Nano-safety, Standardization and Certification

Prepared for

Asian and Pacific Centre for Transfer of Technology of the United Nations – Economic and Social Commission for Asia and the Pacific (UNESCAP)

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Manual on Critical Issues in Nanotechnology R&D Management: An Asia-Pacific Perspective

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Nano-safety, Standardization and Certification

1. Introduction

Nanoscience and nanotechnology has seen an exponential growth over the past decade. This is largely due to the advances in nanomaterial synthesis, sophisticated and improved imaging/analysis tools and funding from numerous agencies to pursue research and innovation in this emerging area.

Nanotechnology is a 'converging technology', which amalgamates various scientific disciplines, such as physics, chemistry, information technology, medicine and biology for providing new and innovative solutions. It is also referred to as 'enabling technology', since it opens new avenues in various disciplines of science and technology. Nanotechnology is considered as the next logical step in science (Lehn, 2002). This is due to the fact that size reduction leads to increased surface area imparting new optical, magnetic, quantum properties to the material. These properties cannot be explained with the conventional assays used to understand the biological effects. This has led to the development of a new branch of science to unravel the uncertainties linked to engineered nanomaterials (ENMs). Due to their size, it is now well established that ENMs exhibit unique physical and chemical properties different from those of the same material in bulk form. Thus, engineered nanoparticles (ENPs) could be defined on the basis of length scale, change in properties and new functionalities. The report by the Royal Society and Royal Academy of Engineering (Royal Society, 2004) gives the following definitions of 'nanoscience' and 'nanotechnologies':

"Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macromolular scales, where the properties differ significantly from those at a larger scale". And, *"nanotechnologies are the design, characterisation, production and application of structures, devices and systems by controlling shape and size at nanometre scale".*

Other definitions are more specific, such as by Nanoforum: *Nanotechnology is made up of areas of technology where dimensions and tolerances in the range of 0.1 nm to 100 nm play a critical role.*

International Organization for Standardization (ISO) has defined it as follows:

- *Understanding and control of matter and processes at the nanoscale, typically, but not exclusively, below 100 nanometres in one or more dimensions where the onset of size dependent phenomena usually enables novel applications.*
- *Utilizing the properties of nanoscale materials that differ from the properties of individual atoms, molecules, and bulk matter, to create improved materials, devices, and systems that exploit these new properties.*

In conclusion, we can define nanotechnology, as the *manipulation, precision placement, measurement, modelling or manufacturing of sub-100 nanometre scale material where a size dependent modulation in the physicochemical properties leads to novel functionalities.*

1.1 Application of nanotechnology

Nanotechnology has found application in diverse sector such as energy, electronics, food and agriculture, biomedical devices, imaging, bio-sensing and chips, high-density data to detecting DNA sequence, environmental cleanup, house hold products, paints, consumer products and sports (PEN, 2013).

In biomedical area, nanotechnology has been applied for development of colorimetric assay to measure enzyme activity using bioconjugated gold nanoparticles and quantum dots; nanoscale sensors for pathogen detection; nanodevices for disease diagnosis, and others (Fadeel and Garcia-Bennett, 2010;

Jyoti *et al.*, 2010). It has also been used for rapid mapping the genetic information in DNA and RNA molecules, including detection of mutations and measurement of expression levels. This technology uses DNA microchip arrays that adapt some of the lithographic patterning technologies of the integrated circuit industry. This microchip (nanofabricated structure) serves as molecular sieve to separate nucleic acid according to size (Fadeel *et al.*, 2007).

Nanomedicine is another important area which has revolutionized the health care sector by enhancing the bioavailability of drugs and gene into the living cells through novel delivery systems. This has been achieved due to the fact that surface functionalization of the nanoparticles permits conjugation with insoluble chemicals, proteins, antibodies, DNA molecules and tracking dyes, thereby facilitating their cellular internalization and detection (Gajewicz *et al.*, 2012). The distinct advantage of such therapy has been exploited in cancer and AIDS where the major drawback of therapeutics drugs is their side effects and toxicity. The nanoformulation of anticancer and anti HIV drugs coupled with targeted delivery systems has enabled the medical fraternity to administered far less amount of drugs with similar efficacy in plasma levels thereby reducing the overall toxicity and hence increasing the lifespan and quality of life of the patients. US FDA has approved 34 nanobased drug formulations for use in cancer, HIV, cardiovascular disease and other patient as the benefit outweighs risk. In Asia including Indian context liposomes based antibiotics are in market. This has reduced the drug burden in patients as well as their side effects. More recently, silver nanoparticles, due to their antimicrobial properties, are being exploited for developing wound dressings to avoid excessive use of antibiotics. DeMuth et al (2013) have come up with a novel vaccine delivery system using multilayer polymer (Demuth *et al.*, 2013). The efficacy and speed of drug action in the human body can thereby be dramatically enhanced because of their higher bioavailability and hybrid or synergistic properties. The development of new polymers and nanoparticles, have improved the *in vitro* and *in vivo* transfection efficiencies that has made a significant impact on new drug development (Singh, 2009). Application of ENMs in the area of medicine has been summarized in (Table 1).

Table 1: Application of nanoparticles in medical technology

Category	Product	Application
Surgical tools	Surgical scalpels and the composition of surgical suture needles	• Diamond - coated surgical scalpels (surface roughness 20-40 nm). • Surgical suture needles containing steel nanoparticles (1-10 nm). • Operating room textiles containing nano silver.
Medical imaging techniques	Contrast media	• Super paramagnetic iron oxide nanoparticles (50-500 nm) for magnetic resonance imaging (MRI). • Micro and nano bubbles for ultrasonic imaging.
Implantable materials	Bone cement / bone replacement materials	• Hydroxyapatite and tricalcium phosphate: nanoparticles which facilitate rapid integration with the bone of the patient.

	Surface coatings of conventional implants with ENMs	• Joint prosthetics (hip, knee) with nano hydroxyapatite coating. • Coronary stents with a diamond-like nano composite coating made of ultrathin polymer.
Wound treatment	Wound dressings	• Wound treatment products containing nano crystalline silver particles which are used for improved antibacterial and anti-fungal activity.
Biochips	DNA/protein microarray chips	• lab-on-a-chip devices for molecular in vitro diagnostics, point-of-care applications
	Bio-sensors	• Bio-detection for the diagnosis of diabetes, cancer, bacteria and viruses
Nano therapeutics	Anticancer agents	• Heat therapy with super paramagnetic iron oxide nanoparticles • Heat ablation with gold nanoparticles • Light therapy • Boron neutrons capture therapy.

In the area of agriculture and food production, nanotechnology is playing major role in improving the product shelf-life, storage, processing and packaging (Maynard, 2007; Handy *et al.*, 2008). This is being achieved throughout the process of food processing, such as use of nano-sieves during industrial processing, increasing food values by introducing nutrients in nano form into the product for increased bioavailability (Table 2). Besides this, with the use of nanotechnology, healthy food could be developed and introduced for preventive healthcare.

More than 1300 consumer products have already been released in the market, majority of these are personal care products (PEN, 2013).

In the areas of sports, aviation, automobiles, construction etc. nanotechnology is being used to strengthen the product by enhancing their quality and reducing the weight.

Nanotechnology has also helped in environmental cleanup of contaminated sites using different kind of ENMs (PEN, 2013). This technology is also being used in house hold products such as air conditioner, fridge, washing machine etc. to prevent microbial contamination.

Table: 2 Application of nanoparticles in food production

Nanoparticles type	Application	Property/function
Colloidal metal nanoparticles	Food additive	Desired better gastro-intestinal uptake claimed
Metal oxide nanoparticles (silver, zinc oxide)	Food colorant	Attractive and better representation
	Packaging materials/ storage	Prevent from contaminant and extending shelf life
	Equipment for food preparation	Cleaning of surfaces
	Fridges, storage containers	Anti-bacterial coating of equipment for storage and handling of food
	Water treatment/soil decontamination	Removal of contaminants /catalyse the metabolism of toxicant
	Sprays	Anti-bacterial

Complex structures on nanoscale	Nanosensors in packaging	Detection of food spoilage and food poisoning

There has been a significant impact on the global economy due to the advent of nanotechnology in science and engineering since more products containing nanomaterials are moving from research and development to industry.

1.2 Scope

According to the US National Nanotechnology Initiative (NNI), thousands of tons of silica, alumina and ceria, in the form of ultrafine coarse particle mixtures including nanoparticles are used each year in slurries for precision polishing of silicon wafers. More than 300 companies around the world are producing in excess of 1.2 million tons of ZnO nanoparticles per year. The production rate of metal oxide nanoparticles for cosmetics is estimated to be a thousand tons per year (Kumari *et al.*, 2011). Due to the large production and widespread use in consumer products, it is likely that ENMs will be released into aquatic, terrestrial, and atmospheric ecosystems throughout their life cycle i.e. from raw material production to end of use (Figure 1) (Kumar *et al.*, 2011f).

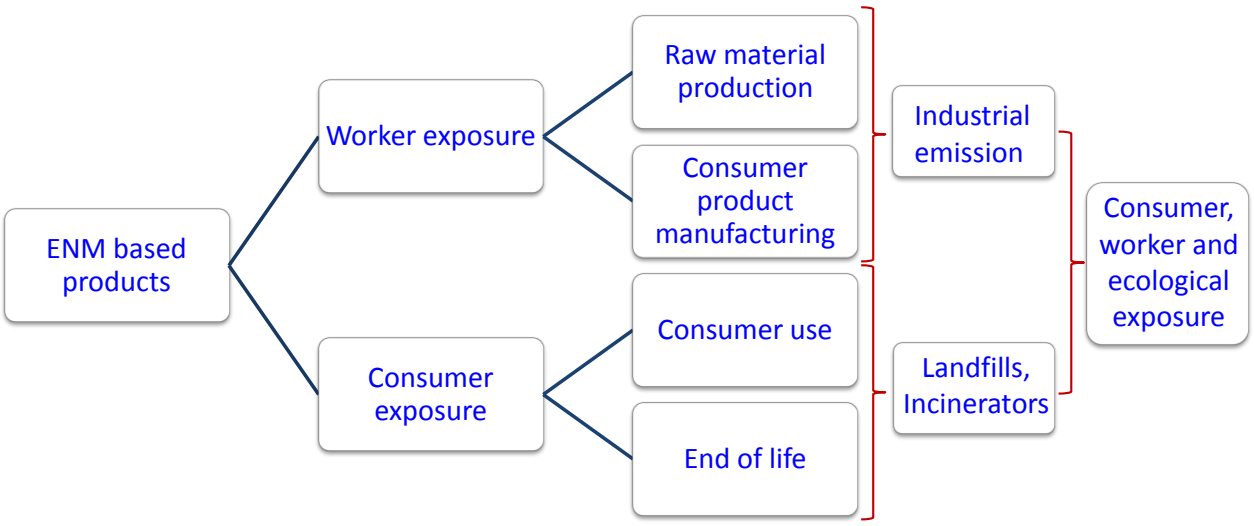

Figure 1: Human and environmental exposure paradigm of ENMs

The development of numerous products in diverse sectors using nanotechnology has raised concern regarding the fate of ENMs in human and the environment.

The unique size-dependent properties of ENMs, such as increased surface area, higher surface-to-volume ratio, abundant reactive sites, large number of atoms at the surface and increased mobility could make them a special class of pollutant (Navarro *et al.*, 2008). The concern that the ENMs could be hazardous to the ecosystems is partly fuelled by examples in the history that illustrate the unintentional environmental release of "beneficial" chemicals, such as DDT (Dichlorodiphenyltrichloroethane), which was used to control malaria but was later found to be toxic to non-target species such as humans and birds. Endosulfan, an organochlorine insecticide was used in agriculture around the world to control insects and pests. It was earlier considered safe but is now banned in 74 countries due to severe human health implications including deformities in limbs, loss of motor nervous control, brain damage, delayed

puberty, cancer and teratogenicity. The residues of these pesticides were persistent in the environment and were detected in places where there were never used. This was due to the fact that they were transferred through air and water globally.

Currently, ENMs are being incorporated into commercial products at a faster rate than the development of knowledge and regulations to mitigate potential health and environmental impacts associated with their manufacturing, application and disposal (Kumar *et al.*, 2012). Variety of ENMs with different chemical compositions, synthesized through different methods, differing in size, shape, surface coatings, etc. have been shown to be genotoxic and cytotoxic in different models such as prokaryotes (Brayner, 2008; Simon-Deckers *et al.*, 2009; Kumar *et al.*, 2011b; Kumar *et al.*, 2011c; Kumar *et al.*, 2011d), plants (Kumari *et al.*, 2011; Vajpayee *et al.*, 2011), human cell lines (Sharma *et al.*, 2009; Shukla *et al.*, 2011a; Shukla *et al.*, 2011b; Sharma *et al.*, 2012a), primary human cells (Sharma *et al.*, 2011), *in vivo (*Wang *et al.*, 2008*;* Xie *et al.*, 2011*;* Sharma *et al.*, 2012c*)* and aquatic models (Allen *et al.*, 2011; Fabrega *et al.*, 2011). There are several *in vitro* reports that have demonstrated the genotoxic, carcinogenic and apoptotic properties of ENMs to human (Sharma *et al.*, 2009; Shukla *et al.*, 2011a; Sharma *et al.*, 2012a). There is considerable evidence that ENMs cause toxicity to bacteria which play a major role in maintaining the homeostasis in human. Studies have shown that ENMs also adversely affect the microbes (*Escherichia coli*, *Pseudomonas aeruginosa* and *Streptococcus aureus*) which are responsible for maintain the environmental health. (Brayner *et al.*, 2006; Wahab *et al.*, 2010; Wu *et al.*, 2010; Premanathan *et al.*, 2011) is also available. This also raises the possibility that the release of ENMs may be detrimental to important bio-geochemical processes in soil such as carbon or nitrogen cycling. Therefore, organisms, especially those that interact strongly with their immediate environment, are expected to be affected as a result of their exposure to ENMs. It is also likely that the ENMs can directly interact with the food web at different trophic levels and affect the ecological sustenance. The bio-magnification of ENMs across the genera is also a big concern.

Humans get exposed to ENMs at various steps of its synthesis (laboratory), manufacture (industry), use (consumer products, devices, medicines etc.) and the environment (through disposal). The lack of regulatory guidelines, reference standards and certification processes for ENMs (from manufacture to product development) is a major stumbling block in hazard identification through risk and exposure assessment. This is compounded by the lack of equipment for accurate and sensitive measurement of ENMs with respect to their number, mass and surface area in the environment. Hence, it is prudent to address the issues of risks associated with ENMs and develop ethical, legal and regulatory framework to mitigate their exposure.

Hence, the present document is intended to address the need for: (1) Environmental, health and safety impact of nanomaterials; (2) Social, ethical and legal issues of nanomaterials and nanoproducts; (3) Safe production, handling, use and disposal of nanomaterial – Risk assessment/analysis, Risk monitoring/management; (4) Current regulatory landscape – nanosafety policies, risk governance, regulatory and institutional mechanism; (5) Guideline for the best practices for testing, standardization and certification of nanoproducts.

2. Environmental, health and safety impact of nanomaterials

The applications of nanotechnology in diverse areas will lead to their inadvertent release in surface and sub-surface environments through landfills and other waste disposal methods. It is likely that some of these ENMs may induce adverse/toxic effects in both lower and higher trophic organisms (Handy *et al.*, 2008; Kumar *et al.*, 2011a). At the safety level, it is well known that the high surface area to volume ratio of ENM leads to increased surface reactivity and associated risk. However, the mechanisms involved in

reactivity and toxicity are not well understood yet. There is also a great deal of uncertainty about the environmental fate, behaviour and bioavailability of ENMs in the ecosystem. Also, lack of reliable and validated schemes for assessing the ecotoxicological risk is a big concern (Wen-Che Hou *et al.*, 2013). The major constraints in risk assessment of ENM are the lack of appropriate methods for characterization in exposure media, bioavailability, mobility, biopersistance, and bioaccumulation (Farre *et al.*, 2009; Kumar *et al.*, 2012). The impact of ENMs on various ecosystems will be significant because their distribution depends on a number of factors such as Brownian motion, inertia, gravitational influences, thermal influences, pH, and ionization. As the ENMs have high mobility, they can easily move in the air, water and soil and can contaminate the flora and fauna. This may also result to the transfer of ENMs in the food chain, leading to the creation of non-biodegradable pollutants (Mahapatra *et al.*, 2013). Also, ENMs can affect the bioavailability of the other toxicant/pollutant by facilitating their transportation (Navarro *et al.*, 2008). ENMs may also elicit a negative physical, chemical and biological impact on different strata of the ecosystem (air, water and soil). Hence, to minimize the exposure to ENMs and thereby its adverse effects on the environment and human health, it is imperative to consider the following points: (a) the behaviour of ENMs in the environment (air, water, and soil) and their exposure to humans (b) methodological and metrological approaches for the detection/quantification of ENMs in environmental samples (c) approaches and knowledge gaps in ecotoxicity studies.

2.1 Behaviour of ENMs in the environment (air, water, and soil) and their exposure to humans

The behaviour and bioavailability of ENMs in freshwater/marine ecosystem depends on their interaction with the aquatic colloids, such as natural organic matters (NOMs), humic substances, and salt ions (Navarro *et al.*, 2008). NOMs usually get adsorbed on the surface of the ENMs by different electrostatic, hydrogen bonding and hydrophobic interactions, which affects their dispersity and bioavailability. NOMs are classified into three major classes; (1) rigid biopolymers, such as polysaccharides and peptidoglycans produced by phytoplankton or bacteria (2) fulvic compounds, mostly from terrestrial sources, originating from the decomposition products of plants (3) flexible biopolymers, composed of aquagenic refractory organic matter from a recombination of microbial degradation products (Buffle *et al.*, 1998). ENMs in aqueous suspension are dispersed due to the electrostatic and steric repulsion of the surface charge (positive/negative) present on the particle. Apart from NOMs, salt ions, protein content, presence of molecular clusters enable nucleation leading to agglomeration/aggregation thereby modulating the bioavailability of ENMs in the environment (Figure 2). Also, the biomolecules such as proteins or polymers present in the ecosystem form a layer over the ENMs, named as “corona” which plays important role in their biological fate. It has also been shown that it is not only the ENMs alone but the “corona” govern the properties of the “particle-plus-corona” compound in the biological system (Lynch and Dawson, 2008; Elsaesser and Howard, 2011).

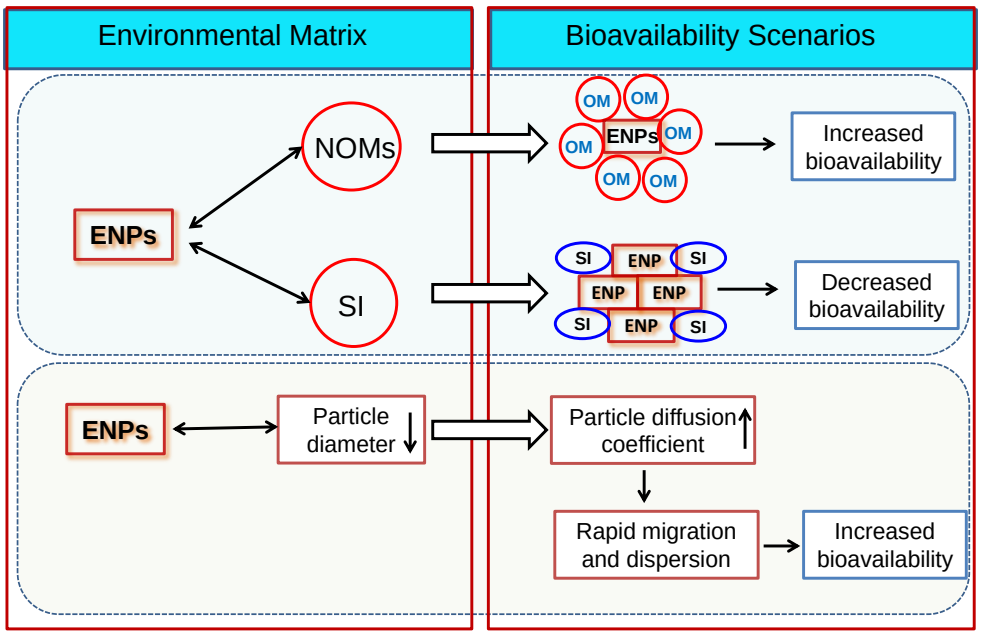

Figure 2: Availability of engineered nanoparticles after interaction with different environmental matrixes

The behaviour of ENMs in air is majorly governed by diffusion, agglomeration and potential re-suspension of aerosol from deposited nanomaterials. It is also reported that in traditional aerosol science, particle size, inertia, gravitational and diffusion forces govern aerosol behaviour in the environment. As the particle size decreases, diffusional forces become increasingly important and nanoscale particles are thus likely to behave in a manner more alike to a gas or vapour (Aitken *et al.*, 2004; 2008). Particle diffusion coefficient is inversely proportional to the particle diameter. Particle with a high diffusion coefficient such as ENMs have high mobility and mix rapidly in an aerosol. After their release in the environment, atmospheric diffusion facilitates the ENMs to migrate rapidly from a higher to a lower concentration, thus resulting in rapid dispersion and potential for particles to travel a great distance from the source (Feliu and Fadeel, 2010).

European Commission's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) evaluated the risk assessment of products of nanotechnologies (SCENIHR, 2009). SCENIHR evaluated the knowledge base on the release of ENMs into the environment and the subsequent exposure to humans through inhalation. It was reported that "*Examples of the exposure routes for ENMs via the environment are inhalation by human and other air breathing species, and uptake by aquatic organisms from water and sediments. Assessment of exposure concentrations of dispersed nanomaterials requires detailed insight into the process that act on these materials in the environment. However, currently available knowledge of these processes is insufficient to allow quantitative prediction of the environmental fate of nanomaterials*" (SCENIHR, 2009).

The critical questions in relation to ENM exposure are how much (intensity/concentration), how long (duration/frequency) and how many (number). The main routes by which one can get exposed to the ENMs are inhalation, ingestion and dermal (Figure 3). Inhalation is considered to be the primary route by which air breathing species including humans get exposed to the ENMs suspended in air. Once these ENMs are inhaled, they are likely to get deposited in different regions of the respiratory tract. However, the location and the extent of the deposition depend on the particle size (Oberdorster *et al.*, 2004). Ingestion exposure of ENMs may arise through hand to mouth contact or by consuming contaminated

water/food (Chau *et al.*, 2007; Gruere, 2012). It may also be caused by swallowing mucous which contains deposited particle cleared from the lungs. Dermal exposure of the ENMs can occur by handling or touching the materials or surfaces coated with ENMs. It also occurs by the use of cosmetics and other personal care/protective equipment containing ENMs.

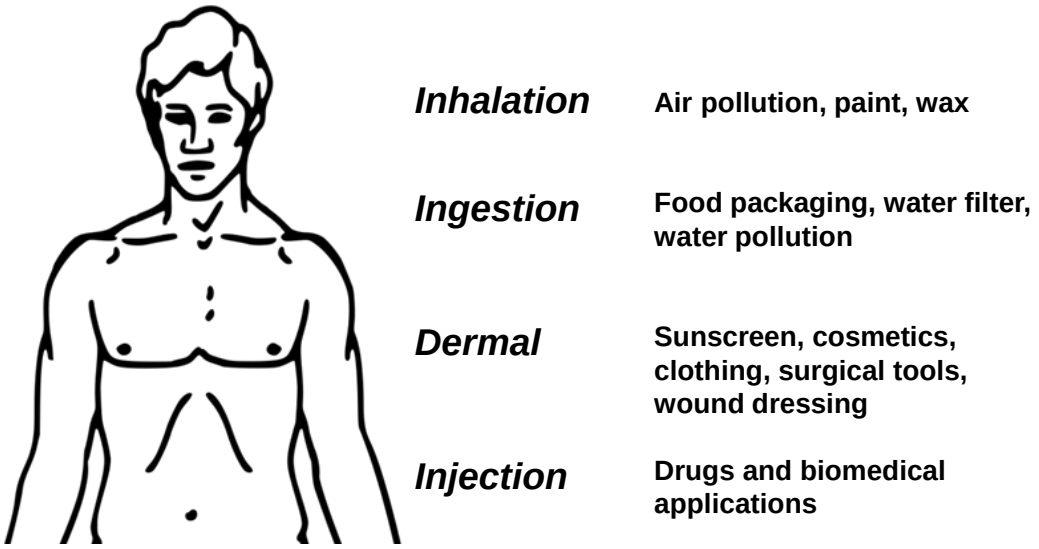

Figure 3: Schematic for the possible routes of exposure to engineered nanomaterials in humans

2.2 Methodological and metrological approaches for the detection of ENMs in environmental samples

Lack of methodological and metrological approaches for the detection of ENMs in environmental samples is one of the major hurdles in mitigating their adverse health impact. The first uncertainty in the measurement of ENMs is the metric(s) used to represent the concentration. The exposure metric for ENMs could be expressed, based on mass, number or surface area, whereas, it is represented only as surface area for other hazardous materials such as fibrous aerosol and asbestos. It is also recommended by The National Institute for Occupational Safety and Health (NIOSH) that "*exposure metrics other than airborne mass concentration may be a better predictor of certain lung diseases, but it was decided that existing sampling methods will report in mass concentration because the toxicological effects observed are based on a mass dose*" (NIOSH, 2010). The issue of the proper metric for enumerating nanoparticles in workplaces is still a debatable issue. As mentioned, surface area concentration has been found to correlate well, regardless of particle size, with pulmonary response. However, this may not be true for all particle types and may also be a function of the agglomeration state.

Hence, the development of ENM measurement methods and instrumentation in an occupational exposure scenario is focused on the measurement of mass concentration, surface area and number count. These instruments fall into two general categories: "time-integrated" and "direct reading". Time-integrated measurements involve those which require the completion of a sampling duration after which an analysis is made to determine aerosol concentration, whereas direct-reading instruments provide concentration values in "real time" and typically employ a digital memory device to store the measurements taken for subsequent display and mathematical analysis (O'Shaughnessy, 2013). The time-integrated devices work on the principle of filter based collection and have been used for decades to determine the threat caused by dusts containing asbestos, silica and others, whereas direct-reading devices is more accurate and therefore more frequently used for the past two decades (Pui, 1996). Direct-reading instruments work on

optical particle counter (OPC), condensation particle counter (CPC), which measure a count concentration, the surface area monitor (SAM), which measures surface area concentration, and the aerosol photometer measures the mass concentration. An OPC provides a count concentration in the size range of 300 – 20000 nm. This instrument sizes and count particles to allow for the determination of both a number concentration and particle size distribution (Kulkarni *et al.*, 2011). As a particle passes through a viewing volume of the detector illuminated by a laser, it scatters light which is then detected by a photo detector. The electrical pulses generated by the photo detector are converted to counts and the pulse height is related to particle size.

These "time-integrated" and "direct reading" based instruments can only measure the ENMs from the air. However, the major constraint in these instruments is that they can only measure ENMs of size ≥300nm. Additionally, the detection of ENMs from the aquatic/colloidal system is a big challenge. Filtration and centrifugation of large amount of the water or sediment and electron microscopy analysis of the pellet is the only viable option for the qualitative and quantitative measurement of ENMs.

2.3 Approaches and knowledge gaps in ecotoxicity studies

The frequent release and interaction of ENMs with different components of the ecosystem, necessitates the development of certain strategies to test the possible hazards of ENMs. The fate, behavior and detection of different of ENMs in the ecosystem have been critically discussed above (1.2). It can be inferred from the above discussion that interactions of cells with ENMs are dependent on their size, shape, chemical composition, surface charge, surface structure, area, solubility and aggregation state. Thus, it is essential to study these physiochemical properties of ENMs while assessing their biological hazards.

Among these physiochemical characteristics, surface properties of the ENMs are the most important factor that govern the stability and mobility of ENMs in aqueous suspension (Dhawan *et al.*, 2009). The agglomeration tendency of the ENMs is determined by the surface properties, which are mainly dependent on temperature, ionic strength, pH, concentration, size and the solvent. However, it is difficult to measure the surface properties of ENMs at nano to pico gram range due to the limitations of the commercially available analytical instruments. On the other hand, the concentration of ENMs in suspension is also a crucial step in designing the experiments, since the ENMs have the tendency to agglomerate/aggregate which results in a change in their physicochemical properties, and hence modified cellular concentration (Donaldson and Borm, 2004). Thus, the experimental design should also consider the concentration induced aggregation effects of the ENMs.

It may also be speculated that at lower concentration range ENMs will tend to show less aggregation that lead to increased uptake and response than that expected at high concentrations. However, different surface modifications in ENMs (particle coating, dispersant /surfactant, sonication) stabilize the particles and avoid agglomeration which may result in exacerbated biological response. The durability of surface coating in cellular/biological environment and the effects of cellular metabolites on the ENMs are the other key issues that need to be addressed in order to understand the adverse health effects of ENMs. Other possible effects of ENMs uptake could be the interaction with other (toxic) substances and their mobilisation and bioavailability.

The environmental fate, behavior and bioavailability of ENMs are not well understood; therefore their persistence and the possible interaction/impact, bio magnification in food webs at different trophic levels are of immediate concern. Hence, to study the ENMs effect in ecosystem, the study design should address the ENMs interaction/impact directly with different trophic level organism as well as the perturbations

induced by the ENMs biomagnification (Kahru and Dubourguier, 2010). ENMs effect on other toxicant/pollutant also needs to be examined, because the transportation of the contaminant could be facilitated through their adsorption to ENMs which may have a negative impact on useful bacteria for natural remediation and other water bodies (Navarro *et al.*, 2008). The presence of impurities in the ENMs also influence the toxicity, thus the purity of the ENMs should also be considered in the study design. Elemental analysis using different analytical techniques could be helpful in analysing the purity of ENMs (Nowack, 2009).

Some of the metal oxide nanoparticles are known to release ions in the aqueous suspension which could alter the toxicity outcomes. Hence, the quantitation of soluble metal ions in the exposure medium is also a prerequisite in nanotoxicology studies (Baun *et al.*, 2008; Handy *et al.*, 2008; Fairbrother and Fairbrother, 2009). Lack of reference materials, appropriate methods to monitor ENMs behaviour, dose dilemma and exposure methods, ENM behaviour in environmental matrices, regulatory toxicology test methods are certain other hurdles that need to be addressed properly. Therefore, prior to use the ENMs based consumer products in daily life activities, it is important for nanotoxicology research to understand their fate in environment, so that their undesirable effects can be avoided.

In summary, in order to develop a full understanding of the potential risks posed by ENMs, further examination of their environmental transport and fate within air, soil and water bodies is necessary. Also, different approaches such as particle characterization, uptake, computational modelling, ecotoxicity studies and others can be helpful in improving the contextual knowledge (Figure 4). Although the current lack of quantitative exposure data hampers the prediction of the environmental fate and thus concentration. The knowledge base in this area continues to grow and develop rapidly. The attention should be given to extrapolate the evidences/data from laboratory studies and from knowledge obtained with industrial chemicals.

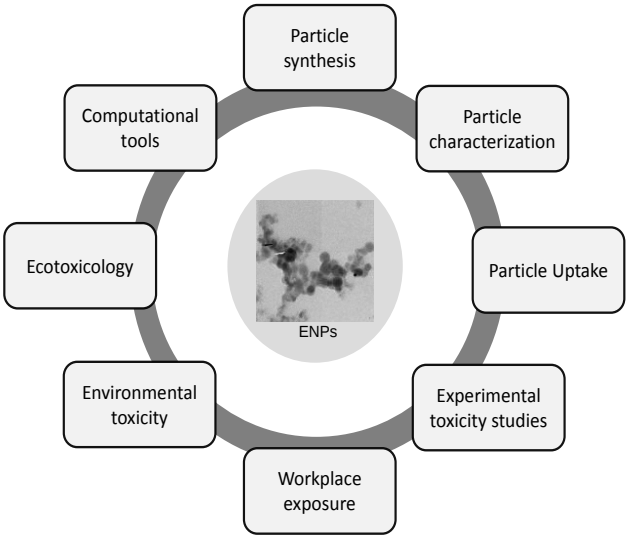

Figure 4: Risk assessment strategies for engineered nanomaterials

3. Social, ethical and legal issues of nanomaterials and nanoproducts

Recent studies have demonstrated that ENMs can be found in air, water, soil, plants, and, subsequently, human and animal bodies; therefore, there is enormous public debate about the toxicological and environmental effects of ENMs after direct or indirect exposure (Sharma *et al.*, 2012b). ENMs can bring risk during their fabrication, transportation, handling, usage, waste disposal and recycling (Nel, 2006;

Stone and Donaldson, 2006; Oberdarster *et al.*, 2007; Stebounova *et al.*, 2012). Some ENMs can enter into the body using a variety of routes, such as inhalation, ingestion, injection and through skin, and can persist in the system for longer periods (**Figure 1**). Several kinds of sicknesses can be expected from exposure to ENMs, including asthma, bronchitis, lung and liver cancer and others (Borm *et al.*, 2006; Wardak *et al.*, 2008). Nanoethics is the area of ethics that relates to the study of nanotechnology and its products, and provides guidelines for training, prohibition, and limitation in the use of these materials. This ensures that the overall risk factors and public concerns can be minimized before the use of ENMs in different applications.

The need of nanoethics can easily be linked with the development in nanotechnology and the doubts about their misuse. The advent of biotechnology not only resulted into the beneficial products such as transgenic plants and fruits, recombinant proteins, organ culture and many others but has raised some new ethical issues that were not aroused previously. Examples of such ethical issues are pre-determination of the sex of human offspring via various technical means, the development of recombinant protein, multi drug resistance, creation of new forms of plant and animal life via r-DNA techniques, human reproductive cloning via somatic cell nuclear transfer. There are strong disputes over the acceptability of such issues, because of difference in the purpose of applications of these developed technologies.

Likewise, ENMs have several unique physiochemical properties which are getting exploited for the development of novel materials/products with diverse application but also posed harmful effects to the living organism due to the way they are manipulated on an atomic scale. They are also new materials produced by entirely new manufacturing techniques. Hence, there are no specific rules and regulations to cover their manufacturing processes. Also, the concerns about the health implications of ENMs have been widely reported (Donaldson *et al.*, 2004; Schins *et al.*, 2004; Borm *et al.*, 2006; Service, 2008). Oberdorster *et al*. (2004) showed in animal experiments that inhaled ultrafine particles (smaller than 100nm) can be translocated from the olfactory nerve to the olfactory bulb in the brain (Oberdorster *et al.*, 2004). However, the significance of this study for humans still needs to be established. The translocation of ENMs along nerve fibers could provide a portal of entry into the central nervous system. Thus the effect of the inhaled ultrafine particles on central nervous system needs to be explored in future studies. Also, the incorporation of ENMs in the sunscreen cream and other personal care products have been questioned by different scientific groups, because of their ability to induce cytotoxic and genotoxic effects after short term exposure (Hardman, 2006; Singh and Nalwa, 2007; Ahamed *et al.*, 2008; Sharma *et al.*, 2009; Singh *et al.*, 2009). Long term exposure studies are still necessary to understand the fate of ENMs in the biological system. Carbon nanotubes (CNTs) have been extensively used in basic science research and development worldwide because of their extraordinary physical, chemical, physicochemical and biological properties. It is also reported that CNTs can induce genotoxicity, immunotoxicty, cytotoxicity in human as well as ecotoxicity /environmental toxicity in the ecosystems (Dhawan *et al.*, 2006; Singh *et al.*, 2006; Maynard, 2007). However, there are no defined rules and regulations regarding the manufacturing and marketing of CNTs.

ENMs involve wider societal issues and pose several social challenges such as environmental pollution, workplace exposure, water contamination, genetic alteration and carcinogenicity etc. Predicted adverse consequence about different ENMs reiterates the need of nanoethics in research, development, production and manufacturing as well as social, economical, moral, health, and other human applications. The implication or knowledge of nanoethics will be very useful for training and protecting the academia (undergraduate/graduate/research students), scientists, industries, policymakers and user for the health and safety, social and philosophical, environmental, educational, and other legal issues associated with the ENMs.

Social scientists and organization workers in this field recommend that the social issues related to ENMs should be well understood and all risks and impacts of the ENMs should be well defined for the public. It is also suggested that the public participation should be there in every decision made by scientists and government (Spagnolo and Daloiso, 2009; Kermisch, 2012). Hence, the universities, research institutions, industries and government should take initial step to avoid the exposure of ENMs to students, researchers and workers. Furthermore, the social desirability of the safe use of ENMs based products can be avoided by the particular labelling of the nanoparticles constituents on the products or by printing the adverse effects of the ENMs on the products. Hence, even at the individual level, the citizen will able to make a choice while purchasing the nanoproducts. It is also suggested that using participatory mode of risk prevention, the ENMs associated risk can be minimized (Figure 5).

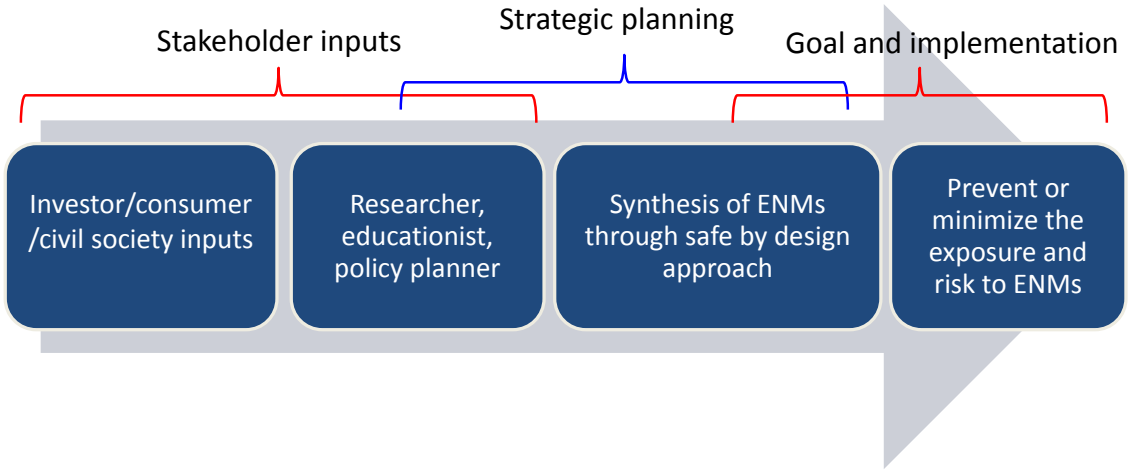

Figure 5: Participatory mode of risk prevention of engineered nanomaterials

There are some suggestions that need to be considered while formulating the ethical guidelines for nanotechnology are given below:

- Nanosystems can be useful in solving the problems of disease and aging, pollution and scarcity. It can create revolutionary changes in the social life, unlike any ever seen.
- The potential harmful uses (intentional and unintentional) of ENMs need to be studied well in advance.
- The debates over nanotechnology, including chat room discussions, researchers, policy makers, industrialist and NGO members view should be documented, published and accessible to all. The debate should also be focused on the merits of the arguments rather than personal attacks, such as questioning the intentions of researcher.
- The regulating bodies should consider the preventive rule for the misuse of ENMs such as: nano weapons; intelligence-gathering devices.
- All published research and development, discussion, methodology used in nanotechnology should be accurate as much as possible and elaborative. As the methods used in the ENMs testing are having much confusion about their interference with the test methods, it will be very much helpful in data interpretation and methods validation.
- Labelling of the products should be clear and accurate, the promotion services for the ENMs, including consulting, should disclose any conflicts of interest.
- Industries should be collaborative and self-regulating. They should also support the public

- awareness programme for the dissemination of science and reasonable legislation to deal with legal and social issues associated with nanotechnology.
- Scientists working in the field of material sciences in developing new ENMs should have a compact training of ecology/ecotoxicology and public safety or they should consult someone for the risk assessment of newly synthesized ENMs.
- The research institutions, scientists, industries should be accountable for the fraudulent or irresponsible misuse of the nanotechnology.
- The research institutions, industries should have preventive measure to minimize the work place exposure of the researcher and worker.
- The research institutions, industries should have a proper storage and disposal guideline for ENMs to avoid the contamination and risk.

4. Safe production, handling, use and disposal of nanomaterial – risk assessment/analysis, risk monitoring/management

According to actual state of knowledge available with regard to the properties of ENMs, it is established that the factors such as surface area, surface properties, elemental composition, tendency to aggregate, the form of the particles and surface charge of ENM plays a critical role in their distribution through the environment, ecosystem and human body. Due to having high mobility they may gain access into the human body through skin (dermal exposure), lungs (inhalation) and gastrointestinal tract (ingestion). Also, ENMs may penetrate deep into tissues through fine capillaries, readily travel throughout the body and interact with organs, tissues, cells and/or sub-cellular structures. The pharmacokinetic studies show that different types of nanoparticles can be found in various cells such as mitochondria (Li *et al.*, 2003; Xia *et al.*, 2006), lipid vesicles (Penn *et al.*, 2005), fibroblasts (Tian *et al.*, 2006), nucleus (Chen and von Mikecz, 2005; Shukla *et al.*, 2011a; Shukla *et al.*, 2011c) or macrophages (Yokoyama *et al.*, 2005; Tian *et al.*, 2008). Moreover, *in vivo* and *in vitro* studies demonstrated that ENMs in contact with the cell surfaces and cellular proteins may lead to:

i. formation of reactive oxygen species (ROS), which results in oxidative stress and inflammation, leading to infection and exacerbation of asthma and chronic obstructive pulmonary disease (Nel, 2005; Oberdarster *et al.*, 2005; Nel, 2006)
ii. DNA damage, lipid peroxidation of cellular membranes, resulting in cell damage (Sharma *et al.*, 2009; Shukla *et al.*, 2011a)
iii. the up/down regulation of genes encoding a specific protein involved in inflammatory processes/ apoptosis/carcinogenicity (Cui *et al.*, 2005; Dobrovolskaia *et al.*, 2009)

Several *in vitro* and *in vivo* studies have also shown that ENMs can be cytotoxic (Thill *et al.*, 2006; Warheit *et al.*, 2007; Kumar *et al.*, 2011d), neurotoxic (Long *et al.*, 2006; Win-Shwe and Fujimaki, 2011; Wu *et al.*, 2011), genotoxic (Singh *et al.*, 2009; Xu *et al.*, 2009; Shukla *et al.*, 2011a), ecotoxic (Colvin, 2003; Vajpayee *et al.*, 2011) or bactericidal (Brayner *et al.*, 2006; Brayner, 2008; Kumar *et al.*, 2011d; Kumar *et al.*, 2011e). The perturbations induced by ENMs in human and environment might significantly affect ecological balance and the carrying capacity of the ecosystem. In general, ENMs tend to be toxic due to chronic exposure, when a sufficient amount of an ENM has accumulated. In other words, the potential adverse health effects of ENMs have been associated with dose, dimension, and durability. However, reduction of particle's size to the nanoscale level results in display of unanticipated physical and chemical properties that do not occur at the micro or macro scales (Auffan *et al.*, 2009). According to Oberdorster et al. (2005), particle size is not the only possible factor inducing toxicity, other factors such

as size distribution, agglomeration state, shape, porosity, surface area, chemical composition, structure-dependent electronic configuration, surface chemistry, surface charge, and crystal structure plays vital role (Oberdarster *et al.*, 2005) . It is still largely unknown that for a specific ENM, which property/properties influence their toxicity. It is hard to generalize a common mechanism of the potential toxicity of ENMs. Also, lack of current knowledge about the toxicity of ENMs, methods to assess ENMs toxicity and the current safety data sheets do not adequately reflect the hazardous nature of ENMs. It is, therefore, suggested that all ENMs should considered potentially hazardous unless sufficient information to the contrary is obtained and should be treated as same as a radioactive substance. Therefore, a comprehensive risk characterization (size, size distribution, agglomeration state, shape, porosity, surface area, chemical composition, structure-dependent electronic configuration, surface chemistry, surface charge, crystal structure, interaction with the DNA, protein cellular organelles, and others) should be performed whenever a novel ENMs is designed/produced and then introduced into the market. Additionally, the precaution should also be taken while handling, use, storage and disposal of ENM containing products. Moreover, safety precautions while working with ENMs in laboratory/industry and the general approach to managing risks from nanoparticles are also important to avoid the exposure/contamination or to mitigate the exposure (Dhawan *et al.*, 2011).

4.1 Safe production, handling and use of ENMs

As the adverse effects of ENMs have shown a close relationship with their size, atomic structure, elemental composition and others, it is prudent to monitor the exposure assessment of ENMs at the level of production, handling and use.

The preparation of ENMs at the laboratory and industrial scale offers several challenges as there is no uniform process for the synthesis of ENMs. It varies considerably in different research institutions and industrial scale laboratories. Sol gel technique, spray-drying process, microemulsion processing are few of the commonly used methods. Sol gel technique is one of the most commonly used for the synthesis of ENMs, due to its simplicity and flexibility in controlling the properties of the final products at various stages (Brinker and Scherer, 1990; Fadeel and Garcia-Bennett, 2010). However, the disadvantage with this method is in difficulties to control the kinetics of crystal growth precisely when large batches of ENMs are prepared, which may lead to particle agglomeration and large particle size distributions. Overall, this is a suitable method for laboratory-scale preparations.

Spray-drying process is another method for ENMs synthesis which involves spraying a homogenized precursor solution composed of the inorganic compounds and relevant additives within a specially designed chamber at temperatures at or above the boiling point of the solvent (Vasiliev *et al.*, 2008). The precursor solution is first atomized through a nozzle into droplets using flowing gas and then the droplet is sprayed into a chamber through which a flow of hot air or nitrogen is introduced. This leads to the quick evaporation of the droplets and the formation of the inorganic particle. The droplet size is the limiting factor for the particle size and hence the type of nozzle and atomizer unit determines the possibilities of using this technique for the production of ENMs.

There is a debate about the identification of the safe methods for the synthesis of the ENMs. Some of the ENMs synthesized by the above mentioned methods are known to induce the perturbation in human and environment, whereas few of them are nontoxic for the ecosystem. The probable reason for the conflict could be the size limit of the ENMs synthesized by different methods as well as the internal properties of the chemicals used in the precursor solution. Hence, we should adopt an approach that can be used to produce the safe ENMs.

4.2 Storage of nanoparticles

A suitable system for storing ENMs is one that:

- minimizes the dangers to personnel
- prevents the breaking of containers and contaminating the working environment
- protects the ENMs from external contamination

These conditions may be achieved by dedicating specific areas and equipment for this purpose. The storage cabinets must carry appropriate danger labels, and inside the doors, there should be lists showing the contents, quantities, expiry dates of the products and the material safety data sheet of the nanoparticle. Storage criteria should also take account of the potential incompatibility of chemically different products (considering the fact that, in their dry state, ENMs constitute an explosion risk that is far greater than the same materials with larger dimensions). The ENMs should be stored in suitable cabinets, separately, according to their type, with proper labeling (Dhawan *et al.*, 2011).

4.3 Disposal procedures

The waste management guidance for the disposal of hazardous materials applies to ENMs-bearing waste streams (solid and liquid waste), including:

- pure ENMs;
- items contaminated with ENMs, such as containers, wipes, biological tissues, culture wares and disposable personal protection equipment (PPE); and
- liquid suspensions containing ENMs

A plan for storage and disposal of ENMs or ENMs contaminated waste should be developed, taking account of the hazardous nature of the particles and the quantities involved. Any material that has come into contact with dispersible manufactured ENMs should be considered as belonging to an ENM-bearing waste stream. This includes PPE, wipes, blotters and other disposable laboratory materials used during research activities. Material from ENMs-bearing waste streams should not be put into the regular waste or down the drain. Equipments used during ENMs handling should be decontaminated before it is disposed of or reused. Wastes (cleaning solutions, rinse waters, rags, disposable PPE) resulting from decontamination should be treated as ENMs-bearing waste.

4.3.1 Storage of ENM waste prior to disposal

4.3.1.1 **Storage in waste containers:** Package ENM-bearing wastes in compatible container that is in good condition and afford adequate containment to prevent the escape of the ENMs. Label the waste container with a description of the waste and include available information characterizing known and suspected properties.

4.3.1.2 **Storage in plastic bags:** Collect paper, wipes, PPE and other items with loose contamination in a plastic bag or other sealable container stored in the laboratory hood. When the bag is full, close it and carefully place it into a second plastic bag or other sealing container, avoiding outside contamination. Take it out of the hood and label the outer bag with an appropriate waste label.

4.3.2 Disposal of nanoparticle waste

It is reasonable to assume all ENM waste as potentially hazardous. It can therefore be disposed of as hazardous waste. The ENMs in solvent should be disposed by immobilizing them in agar/agarose made in distilled water. All other solutions coming in contact with the ENMs should be collected in containers and

disposed at the hazardous waste disposal site.

4.4 General approach to managing risks from nanoparticles

Treat ENMs/NPs as highly toxic till enough data is generated on the contrary. Following safety measures may be undertaken to mitigate and manage the risks arising from handling of nanoparticles:

- Designate the area where nanomaterials are to be used in the laboratory.
- Instruct the personnel involved, about the specific physical properties of free nanoparticles, the need for special measures, and potential long term effects of nanoparticles. Include relevant information in the operating instructions. Furthermore, deny unauthorized persons access to the relevant work areas. There should be a documentation of the training imparted with the signature of the staff.
- Perform activities in contained installations (laminar flow/ chemical hoods), wherever this is possible. If this cannot be done, avoid the formation of dusts or aerosols.
- Ensure clean work wear. Work wear must be stored separately.
- Ensure the regular cleaning of workplaces.
- Wear protective gloves, protection goggles with side protection and protective clothing depending on substance properties.
- Inside a laboratory, the ENMs will behave in a similar way to a gas; furthermore, if not completely restricted, they will spread quickly and remain in the surrounding air for a long time. Therefore, the specifications of control systems designed for ENMs, such as fume hoods, glove box, and ventilation, should be like those typical to gases, rather than that of powders.
- Appropriate containers properly labelled should be used for transporting bottles containing ENMs safely, from the storage room to the testing laboratories.

4.5 Safety precautions

- Laboratories and rooms, where nanoparticles are handled, must be labeled. In particular, when nanomaterials are handled openly e.g. as dry powder, appropriate protective measures (lab coat, gloves, respiratory mask) must be adopted.
- Regular training for staff members should be implemented.
- Staffs who work temporarily or for short periods of time have to be instructed, according to their place of work and the tasks they have to undertake (once before commencement of work, further training sessions 1 per year).
- Cleaning of all working surfaces potentially contaminated with nanomaterials (e.g. glassware, apparatus, exhaust hoods, support equipment) at the end of each day with a HEPA vacuum and/or wet wiping. Do not dry sweep or use compressed air.
- Trainees, doctoral students and scientific guests have to discuss their work with the head of the laboratory, and obtain permission from their supervisor for tasks outside the regular working hours.
- Permanent employees should, in the framework of an informative session, be instructed about new findings in connection with nanoscaled materials.
- It can be assumed that nanoparticles in aqueous suspension, in solution or embedded in a solid matrix (composite) or contained in completely tight vessels pose a minimal risk – low hazard!
- Nanoparticles in free form, or as dry powder (during weighing) or even as aerosol pose a higher
- risk and have to be dealt carefully and with a high degree of responsibility – high hazard! In such

cases, additional precautions are to be taken: If possible, the work should be undertaken in a separate room fitted with negative pressure. The chemicals should only be handled in a fume hood or in a closed glove box to provide containment and avoid contaminant release.

- In this case, mouth protection breathing mask and protective eye wear should be made mandatory.
- In nanoparticle laboratories, sufficient facilities (clothes racks, wardrobes) must be made available so that the safety clothing in use can be deposited / stored inside the laboratory. It is not permitted to wear safety clothing outside the laboratory (due to danger of contamination in corridors, offices and to co-workers).
- Laboratories, where nanoparticles are handled are to be marked (advisory signs: protective clothing must be worn, limited entry: for trained staff only") and are to be furnished with an emergency plan.
- In the case that nanoparticles are accidentally spilt, the work place must be cleaned immediately with a damp towel. Under no circumstances may residual materials be blown off the surface particularly in the case of metallic or explicitly toxic nanomaterials.
- If it is suspected that even the smallest amounts of substances that may be potentially dangerous for an unborn child and lactating mothers, it is advisable to forbid such women personnel from carrying out any operations that entail handling these substances.
- Personnel should be provided with suitable masks when there are NPs in the dry state, or in aerosols.
- Whenever possible NPs are to be used for *in vivo* experiments in animals housed in isolated ventilated cages. Isolated cages should be assigned for *in vivo* experimentation to avoid any transfer of material from one animal to the other, especially in case of dermal application.
- Assessment should be made of whether, in addition to the danger characteristics already indicated, it is possible to include an indication of the average quantities of products used, their location, the loaded quantity, the loading date, and the name of the person who performed this.
- Other important considerations for effective risk management of nanomaterial exposure include fire and explosion control. Some studies indicate that nanomaterials may be more prone to explosion and combustion than an equivalent mass concentration of larger particles.
- Provide laundry service for contaminated work clothing.
- Do not eat or drink in the areas where nanomaterials are handled.

5. Current regulatory landscape – nano-safety policies, risk governance, regulatory and institutional mechanisms

Development of new technologies is usually associated with both benefits & risks, and nanotechnology obeys the same rule. A lot of emphasis has been given to develop nanomaterial based products since last decade. Various studies have underscored the potential risks and concerns associated with the ENM based products. It has also underlined that ENMs based risks and concerns are not simple to identify or to determine. Even if there were a clear-cut cause and effect connections, it is hard to predict the exact reason of the effect and the extrapolation of the results toward their behaviour and fate in human and environment. Hence a governance system which addresses the potential risks and concerns associated with ENM, in a time manner, is of high importance.

It is also necessary to develop a clear idea of the risks and concerns associated with nanotechnology to build a proper level of trust amongst stakeholders and the consumer. This will be helpful in differentiating

the real and perceived risks associated with ENMs and will also define the risks and benefits graph for using the nanotechnology based products. The lessons from previous emerging technologies (such as, the use of genetically modified organisms; GMOs, asbestos, pesticides), where the information disseminated by industry alone is often seen as biased, and as a consequence, it is perceived as unreliable. Interactive, industry and research/ academic collaborative research, expert opinions, workers view and bidirectional communication between the industries and public can be employed in gaining reliable data and consumer confidence.

Currently there are many scientific uncertainties and regulatory challenges associated with the nanotechnology. Different regulatory authorities of the nanotechnology using nations have a broad consensus that as of now no new nanotechnology-specific regulatory framework is needed (Breggin *et al.*, 2009). In United States regulatory authority for nanomaterials and nanotechnology based products is divided between several federal agencies. The Environmental Protection Agency (EPA) regulates any chemical substances or pesticides that are, or contain, nanomaterials. The Food and Drug Administration (FDA) considers the risks of nanomaterials used in drugs, medical devices, food, food additives and cosmetics. The Occupational Health and Safety Administration (OSHA) deals with workplace safety dimensions while the Consumer Product Safety Commission (CPSC) is concerned with protection against risks from consumer products. Finally, the Department of Agriculture deals with food and feed safety dimensions.

Later in 2000, US launched the National Nanotechnology Initiative (NNI) to coordinate the nanotechnology-related research, development and policy activities of different federal agencies. They pointed out many issues related to the ENMs based products and has taken a number of decisions in response to the newly emerging risks. For example, in reaction to the marketing in 2006 of a washing machine that uses nanosilver as an antimicrobial, the EPA decided to regulate such equipment as a pesticide and to require registration accordingly (EPA, 2007b). Also, in 2008, EPA decided that carbon nanotubes should be treated as new rather than existing chemicals under the Toxic Substances Control Act (TSCA), with the consequence that stricter regulatory requirements apply, including premanufacture notice (EPA, 2008). EPA and FDA have also examined the regulatory challenges that nanotechnologies pose. FDA's nanotechnology taskforce concluded in 2007 that nanomaterials are having unique health risks and a number of uncertainties but the demand for the introduction of nano-specific labelling requirements cannot be accepted because "the current science does not support finding that classes of products with nanoscale materials necessarily present greater safety concerns than classes of products without nanoscale materials" (FDA, 2007). Although, US regulatory agencies have also acknowledged the knowledge gaps and scientific uncertainty with regard to nanomaterials risk. EPA, for example, has identified research needs on the toxicology and ecotoxicology of nanomaterials and recommends bigger collaboration with different research agencies and stakeholders (EPA, 2007a).

Like the US, European government also rely on the existing laws and regulations mostly at EU level, in the fields of chemicals, food, cosmetics, drugs, etc. They have also opted for a sector and product-specific regulatory approach, in contrast to its technology-focused regulatory system. As the nanomaterials enter the market as chemical substances, the EU has formed a new chemicals law REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals), in 2007 to look the nanotechnology oversight in Europe. Once REACH will be fully implemented, it will be one of the most advanced and comprehensive chemicals laws in the world. European regulators have also taken the first regulatory decisions on specific nanomaterials. The EU decided in 2008 not to exempt carbon and graphite from registration under REACH due to safety concerns about certain carbon nanotubes (European Commission, 2008). In the food safety area, the European Food Safety Authority (EFSA) has produced scientific assessments of the safety of nanosilver for use in food supplements and of nanostructured silicon dioxide and titanium nitride

in food contact materials. In both cases, EFSA pointed out the knowledge gaps that prevent in determining the safety of nanosilver in food products (EFSA, 2007; EFSA, 2008b; EFSA, 2008a).

In India different government agencies, publicity funded research institutes, universities as well as private academic or research institutes are involved in research & development as well as in formulation of guideline for safe use of nanomaterials. Under the Ministry of Science and Technology, Government of India, Department of Science and Technology (DST), Department of Biotechnology (DBT) and Council of Scientific and Industrial Research (CSIR) are the primary agencies involved with nanotechnology. DST is the nodal department for coordinating activities of nanoscience and technology in India through the Nanoscience and Technology Mission (NSTM). DBT on the other hand is primarily involved in promoting the field of biotechnology in India and therefore has been involved in the nanobiotechnology. CSIR which is constituted by a network of 38 laboratories undertakes research in areas of scientific and industrial importance and also supports R&D in the area of nanoscience and technology in its laboratories. Other agencies supporting nanotechnology in India include Indian Council of Medical Research (ICMR) under the Ministry of Health and Family Welfare for developing applications in the context of health as well as Ministry of Renewable Energy that is encouraging nanomaterial research for energy production and storage. Also, Department of Atomic Energy (DAE) and Defence Research and Development Organisation (DRDO), a network of 50 laboratories under the Ministry of Defense have also been sponsoring research in the area of nanoscience and technology. These agencies are involved in development of the safe nanoparticles and are also investigating the potential risks associated with them using the existing environmental health and safety (EHS) regulations.

It is now becoming now apparent that various international initiatives are being undertaken to address the safety concerns of the nanoparticles using novel strategies. It can also be assumed that the regulatory debate in nanotechnologies is also now well underway. International governance of nanotechnology risk is still very much limited to scientific and technical standardization and coordination efforts by the leading nanotechnology countries in the OECD and some other international forums. No deeper structures for global governance of nanotechnology have been created despite the rapid globalization of nanotechnologies.

6. Guideline for the best practices for testing, standardization and certification of nanoproducts

It is now well established that the properties of ENMs are the combined function of their size, shape, surface area, surface to volume ratio, chemical composition, solubility and others. Hence, to study the ENMs' effect in human and ecosystems, the study design should be multipronged, which address the ENM characterization, validated protocols, hazard identification in human and environment (Figure 6). It is also important to mention that surface properties of the ENMs affect their biological behaviour in the ecosystem. In order to measure the risk/toxicological endpoints associated with the ENMs, the material should needs to be fully understood and characterised. Otherwise, the possible risk/toxic effects cannot be easily attributed to a certain property of the ENMs or even the ENM itself because, for example, impurities and other components could be responsible (Dhawan and Sharma, 2010). Therefore, a critical assessment of the biological behaviour of ENMs without a careful physicochemical characterization is not meaningful. Apart from this the interference/interaction of ENMs with the testing methods/reagents also creates the possibilities of wrong interpretation of the results (Howard, 2009; Stone *et al.*, 2009). It has also been reported that ENMs can bind with the active sites of the enzyme and made them inactive as well as it can bind with the substrate and inhibit the binding sites of the enzyme (Kain *et al.*, 2012). Hence, the ENMs characterization and the activity testing should be done using array of methodologies.

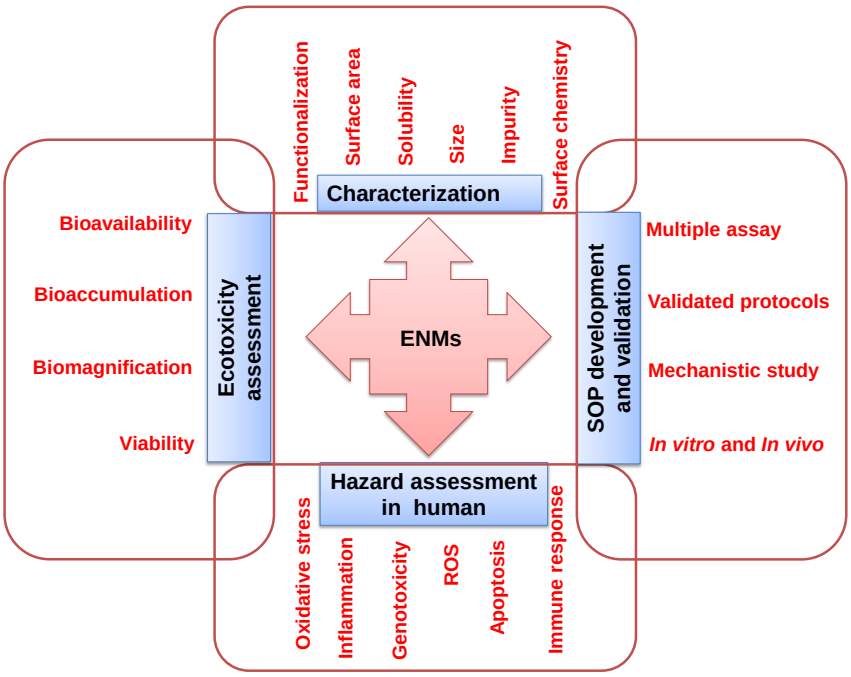

Figure 6: Multipronged approach for hazard identification of engineered nanomaterials

The physicochemical properties characterization of ENMs includes the analysis of purity, crystallinity, solubility, chemical composition, surface chemistry, reactivity, size, shape, surface area, surface porosity, roughness, morphology etc. A nanoparticle with a radius of 2.5 nm and a density of 5 g/cm^3 has a surface area of 240 m^2/g, when the shape is considered like a ball (Borm *et al.*, 2006). At this stage around 20% of the particle atoms are at its surface. However, the surface of a nanoparticle is never "naked". Due to high energetic adhesive forces close to the surface, the particles are either agglomerated to their neighbors, glued to the next available surface or work like an activated charcoal filter towards other small molecules. Changing in the elemental composition, size or surface properties of ENMs can result into the transformation in physical and chemical properties:

• *Size*: based on the material used in precursor solution to produce ENMs, the properties like solubility, transparency, absorption or emission wavelength, conductivity, melting point, colour and catalytic behaviour are changed by varying the particle size of ENMs.

• *Composition effects*: it is clear that different particle compositions lead to a different physical and chemical behaviour of the material.

• *Surface effects*: smaller the diameter of a spherical particle, more is the surface-to-volume ratio and specific surface area. This is accompanied by the properties like dispensability, conductivity, catalytic behavior, chemical reactivity and optical properties. Therefore greater attention has to be paid to the surface material of a nanoparticle rather than its core material. When bare ENMs come in contact with the heterogeneous environment, the smaller structures such as atoms, molecules or macro molecules attach to the surface of the ENMs either by strong or weak interaction forces. In a biological environment with biomolecules such as proteins and polymers present, this surface layer has been named the “corona”. It has also been shown that it is not the ENMs alone but the “corona” mainly defines the properties of the “particle-plus-corona” compound (Lynch and Dawson, 2008; Elsaesser and Howard, 2011). This makes it

necessary to understand not only the behavior of ENMs but also the environment where they are going to interact with biological system.

Hence, it can be summarized that to assess the risk/toxicity of ENMs, the primary criterion is to have full knowledge of the ENMs to be tested. Considering the novel characteristics of ENMs, unlike their chemical counterparts, it is imperative to undertake their comprehensive characterization prior to risk/toxicity evaluation.

6.1 Characterization

The behavior and activity of ENMs is largely dependent on a number of physical and chemical properties. Therefore, a complete characterization is essential for interpreting the results. The characterization of ENMs should be carried out, to know about the specific physiochemical properties such as purity, crystallinity, solubility, chemical composition, surface chemistry, reactivity, size, shape, surface area, surface porosity, roughness, morphology etc (Table 3). Determination of the hydrodynamic size, size distribution, zeta potential, dispersity and the concentration and time at which agglomeration occurs should be done in the biological medium.

Table 3: Significance of measuring the physicochemical properties of engineered nanomaterials

S. No.	Nanomaterials property	Significance
1.	Size	Nanomaterials possess a unique physicochemical property due to their size; it also affects the mobility and transport behaviour of the materials.
2.	Shape	Nanomaterials with different shapes (e.g. spherical, tubular, and cubical) have different affinities and accessibilities towards the cell wall. Toxicity of nanomaterials has also been reported due to their shape and size.
3.	Structure	The structure of the nanomaterials can influence the stability and behaviour of the ENMs (e.g. rutile and anatase are the possible crystal structures of TiO_2 NPs).
4.	Surface area	As the size of nanomaterials reduces, the corresponding surface area increases leading to higher reactivity and sorption behaviour.
5.	Agglomeration tendency	Agglomeration affects the surface properties of nanomaterials and their bio-availability to the cells.
6.	Solubility	Some of the nanomaterials are reported to produce ions in soluble form which may be toxic to the cells e.g. ZnO, CuO.
7.	Elemental composition	Elemental composition shows as to whether the nanomaterials have contamination that may lead to false positive results or nanomaterials behaviour.

8.	Size distribution	Size distribution of the nanomaterials gives an idea of the size range and helps in interpreting the results.
9.	Surface charge and dispersity	Surface charge of the nanomaterials affects the particle solubility in suspension, whereas the dispersity of nanomaterials provides information about their tendency to agglomerate.

Different microscopic and spectroscopic techniques have been used to characterize the ENMs. Microscopy-based methods include optical approaches, i.e. confocal microscopy, as well as electron and scanning probe microscopy. The dimensions of ENMs are below the diffraction limit of visible light; hence they are beyond the range of optical microscopy. However, near-field scanning optical microscopy (NSOM) is a kind of scanning probe microscopy (SPM) technique that can achieve a spatial resolution of 50–100 nm through the use of a sub-wavelength diameter aperture. It is better than the conventional optical microscopes to visualize the agglomeration of ENMs. The diffraction of light is also the limiting factor for the conventional confocal microscopy. However, confocal laser scanning microscopy (CLSM) has higher resolution (up to 200nm) hence the fluorescent ENMs (natural and labelled) can be observed. Recently, for non-fluorescent particles, the reflection based study using confocal microscopy has been reported to detect ENMs in cells (Lindfors *et al.*, 2004; Van Dijk *et al.*, 2005; Van Dijk *et al.*, 2006; Zucker *et al.*, 2010).

Electron microscopy (scanning electron microscopy; SEM, transmission electron microscopy; TEM and atomic force microscopy; AFM) is the most popular and extensively used technique to characterize the ENMs. This technique not only gives visual image of the ENMs but also provides the information about the properties such as size, state of aggregation, dispersion, structure and shape (Mavrocordatos *et al.*, 2004). In TEM, electrons are transmitted through a specimen; therefore the specimen needs to be well distributed and spread on the grid (in case of materials) to get a good image, whereas in SEM, scattered electrons are detected at the sample interface for imaging. Analytical tools, mostly spectroscopic, are coupled with electron microscopes for additional elemental analysis. For example, energy dispersive X-ray spectroscopy (EDS) when combined with SEM and TEM provides percentage elemental composition of ENMs (Kumar *et al.*, 2011c). Other analytical tools like electron energy loss spectroscopy (EELS) when coupled with TEM, detect the elements based on the loss of energy of the incident electron through the specimen (Mavrocordatos *et al.*, 2004). Selected area electron diffraction (SAED) can also be combined with TEM to provide information on crystalline properties of particles (Mavrocordatos *et al.*, 2004). Although electron microscopy is a very versatile tool for scientists in the area of nanotechnology, it has certain limitations. A critical limitation is that TEM and SEM are operated under vacuum so, it is difficult to analyse the liquid samples. The sample preparation steps of dehydration, cryo-fixation or embedding usually lead to sample alteration and dehydration artifacts (Dhawan and Sharma, 2010). Another disadvantage of the TEM is that the samples cannot be analysed twice or used for validation of results. Further the charging effects caused by accumulation of static electric fields at the specimen due to the electron irradiation create confusion during imaging (Tiede *et al.*, 2008).

The atomic force microscopy (AFM) is also a kind of scanning probe microscope (SPM) which is a cost effective instrument and has several advantages in the characterization of ENMs. The main advantage of an AFM is that, it images sub-nanometer structures under ambient air and liquid dispersion, and provides data about the size, shape, surface texture and roughness of the particles. In addition, multiple scanning of the sample can also be done to get robust statistics. There are some limitations of AFM for ENMs

visualization; generally the geometry of the probe is larger than the particles which lead to the over estimation of the lateral dimensions of the nanoparticles.

It can be summarised that a combination of microscopic techniques, can be used to analyse the nanoparticles for size, shape, size distribution etc. (Jose-Yacaman *et al.*, 2001; Baatz *et al.*, 2006; Chuklanov *et al.*, 2006). However, the analysis of the microscopic images is a crucial step because only small amounts of samples can be analysed by microscopy which has an impact on the statistical significance of the results. The average particle size of ENMs is a value that depends on the number of particles counted and measured. As the ENMs in aqueous suspension have a tendency to agglomerate, it is important to count and measure enough number of particles to obtain robust statistics on each size fraction.

A wide range of spectroscopic techniques are available for the characterization of ENMs in suspension. Some of the important techniques used for the characterization of ENMs based on the light scattering property are static (SLS) and dynamic light-scattering (DLS) and small-angle neutron scattering (SANS).

Dynamic light scattering (DLS) or photon correlation spectroscopy (PCS) measures time dependent fluctuations in scattering intensity of light produced by particles in Brownian motion and yields the size of the particle by applying the Stokes–Einstein equation. DLS size of the nanoparticle is usually greater than that measured by other techniques, like TEM, Brunauer–Emmett–Teller (BET), etc. DLS is particularly very useful for sizing nanoparticles (based on intensity, volume and number) and determining particle stability/aggregation state in suspensions with respect to time and medium. It is a quantitative technique and gives the statistically relevant data as compared to TEM (Dhawan *et al.*, 2009). Although DLS provides fast, in situ and real-time sizing, it also has certain limitations. For example, interferences can be caused by a range of materials such as dust particles and nanoparticle impurities which influences the scattering intensity and skews the average hydrodynamic diameter towards the larger value. Also, the intensity of the scattered light is proportional to the sixth power of the particle diameter that makes it very sensitive to the presence of large particles and the data obtained from samples containing particles with heterogeneous size distributions are difficult to interpret. DLS is considered an indispensable technique in toxicity studies, as it provides valuable information pertaining to the zeta potential, polydispersity and size range of the ENMs in the biological medium in which the organism is exposed.

Static light scattering, also known as multi-angle (laser) light-scattering [MAL(L)S], provides information about the particle structure and together with dynamic light-scattering provides information about the shape of the particle (Tiede *et al.*, 2008). In small-angle neutron scattering (SANS), a beam of neutrons is focussed on the sample, which can be solid (crystal, powder) or a suspension (aqueous, non-aqueous). These neutrons interact with the nuclei of the atoms and get scattered due to changes in the refractive index. The intensity of the scattered light gives information regarding the radius of gyration of a particle using Guinier's equation.

Therefore, it can be inferred that a combination of analytical methods are required to detect and characterize the nanoparticles in different matrices including air, soil, water and consumer products to which human beings and ecosystems are likely to be exposed. Additionally, this will also provide the broader idea related to the behaviour of the particles which will be helpful for the toxicological and risk assessment of the nanoparticles. Different characterization techniques for ENPs as well as their merits & demerits have been summarized in Table 4.

6.2 Agglomeration and aggregation

ENMs in aqueous suspension are dispersed due to the electrostatic and steric repulsion of the surface charge (positive/negative) present on them. As the surface charges of the ENMs skew towards the zero value, the repulsive forces between the ENMs reduced and ultimately settle down by gravitational forces. The phenomenon of agglomeration involves the adhesion of particles to each other, mainly because of van der Waal's forces, which dominate at the nanoscale due to the increased surface area to volume ratio (Elsaesser and Howard, 2011). Due to agglomeration/aggregation, the physicochemical properties such as surface charge, size, size distribution, surface to volume ratio, surface reactivity of ENMs get altered that affects their bioavailability and toxicological responses (Navarro *et al.*, 2008). In the medium, ENMs can be dissolved or tend to form agglomerates/aggregates, depending on their surface charge (hydrophilic or hydrophobic) and interactions with medium (medium pH, salinity, protein content, etc.). However, in an environmental setup factors such as fulvic compounds, protein content, salt ions and flexible biopolymers modify the ENMs surface charge and affects the aggregation and bioavailability of the ENMs. Earlier report has demonstrated that humic acid coating of hematite reversed their charge from positive to negative leading to decreased attachment efficiencies from 1 to 0.01mg/L to a sandy soil (Kretzschmar and Sticher, 1997). Highly agglomerated ENMs cannot enter the nucleus and mitochondria while ENMs that do not agglomerate can be distributed all over the cell (Ahmed *et al.*, 2008; Dhawan *et al.*, 2009).

TiO_2 NPs were found to be internalized into the human skin epidermal cells or to adhere to the cell membrane, depending on their size. ENMs of 30-100 nm were found in the cytoplasm, vesicles and nucleus, while larger particles (>500 nm) remained outside the cells (Shukla *et al.*, 2011a).

Table 4: Characterization techniques for nanoparticles

Techniques	Parameters analyzed	Remarks
Electron microscopy	Size, shape, agglomeration, Size distribution, elemental composition	• Direct measurement of particle size/shape • Time-consuming • Requires skilled personnel • Analyze dry samples • Sample preparation leads to agglomeration and altered properties • Requires a sufficient number of particles for statistical analysis • Hard to differentiate between particles and artifacts
Brunauer–Emmett–Teller	Size, surface area	• Provides two parameters simultaneously: size as well as surface area • Only provides average size, not size • Distribution • Requires large quantity of sample
Atomic force microscopy	Size, size distribution morphology, surface texture and roughness, agglomeration	• Visualization in three dimensions • Provides information about multiple surface properties • Requires skilled personnel • Cannot differentiate the particles and artifacts • Sample preparation is time consuming • Cannot predict the chemical composition of the particles

Dynamic light scat Dynamic light scattering tering	Size, size distribution, agglomeration, zeta potential	• Provides average hydrodynamic size • Measures size in suspension • Gives information about the stability of particles with respect to time • Polydispersity of the sample can lead to misinterpretation of results • Measures the charge at the slipping plane • Not appropriate for anisotropic particles

6.3 Bioavailability and uptake

Availability of the ENMs to the cell/tissue and their uptake is one of the major factors that can provide important information about their adverse effects on cellular systems. The exponential increase in usage of the ENM containing products in daily life has also enhanced the likelihood of their interaction with the individual cell. The fate of the ENMs largely depends on behaviour, bioavailability and their interaction with the surrounding medium (Kahru and Dubourguier, 2010; Kumar *et al.*, 2011c).

The detection of ENMs internalization in an organism is a crucial step for understanding their behaviour and toxicity. The commonly used methods for assessment of uptake of ENMs in the cells are transmission electron microscopy (TEM), scanning electron microscopy along with backscattered electron and energy-dispersive X-ray spectroscopy (SEM+BSE+EDS), confocal and fluorescence microscopy, reflection based imaging and flow cytometry (Dhawan and Sharma, 2010; Kumar *et al.*, 2011e; Sharma *et al.*, 2011; Shukla *et al.*, 2011c). These techniques have several advantages of tracking the ENMs in the cells as well as cellular organelles. The high resolution of TEM enables the imaging of membrane invagination, mode of ENMs uptake, ultrastructural changes occur in the cells subsequent to ENMs treatment. SEM on the other hand used to study the morphological changes and ENMs interaction with the cell. Whereas, EDS coupled with SEM provides an additional feature to analyze the elemental composition of the specimen based on the released energy by the corresponding element. Although these imaging techniques provide several advantages there are certain drawbacks, for example in TEM and SEM the samples have to be fixed, therefore live cell uptake cannot be monitored. It is also resource intensive, time consuming and confined to imaging of few cells. Furthermore, the staining process introduces electron dense artifacts that may be mistaken for nanoparticles (Dhawan and Sharma, 2010). Confocal and fluorescence microscopy, on the other hand require that the particles be tagged with a probe or be doped with a fluorescence dye for their detection. Since the native nature of ENMs is lost, there is a likelihood that it may lead to their non-bioavailability leading to false/incorrect interpretation of observations.

Flow cytometry is another technique used to assess the uptake of ENMs in the cells. It is rapid, high throughput, cost effective, reliable, easy and sensitive technique that can analyse thousands of events rapidly in three dimensions, leading to the reduction of false negative or type II errors (Shapiro, 2001). In addition, flow cytometry provides a rapid, multi-parametric, single cell analysis with robust statistics, due to large number of events measured per treatment. In this method a laser beam strikes on the stream of fluid containing single cell suspension. The light diffracted, reflected and refracted by the cells is recorded by the photomultiplier tubes and the electronics convert these optical pulses to digital values. These values are then supplied to the computer with data representing the size and granularity of the cells as well as the intensity of the fluorochrome. It is well established that the light diffracted by the cells represent the forward light scatter and is used to measure the cellular size. However, the reflected and refracted light corresponds to the side scatter, which is a combined effect of the granularity and the cellular mass of the cell. ENMs in the host cell serves as granules and reflect/refract the light based on their intrinsic property. As the ENPs enters into the cells, the side scatter intensity of side scatter of the

cell increases proportionately to the concentration of the ENMs. However, a fluorescent particle can give an increased signal of side scatter as well as the fluorochrome intensity in a dose dependent manner.

It is also reported that ENMs are having their own scattering phenomenon, hence the interference of the ENMs scattering phenomenon with the scattering phenomenon of interrogated cells cannot be ruled out.

6.4 Development and validation of standard operating procedure

The development of the methodologies for the assessment of risk associated with the ENMs is in early stage. Most of the studies concerning to ENMs risk have been carried out using the classical in vitro toxicity test methods established for chemicals. However, these established methods cannot be used for assessing the toxicity of ENMs, as ENMs display several unique physicochemical properties. Due to these properties, ENMs interfere with normal test systems, and this interference has been well documented in the literatures (Monteiro-Riviere and Inman, 2006; Doak *et al.*, 2009; Kroll *et al.*, 2009; Monteiro-Riviere *et al.*, 2009; Song *et al.*, 2010; Kain *et al.*, 2012). Examples of such properties include: high surface area, leading to increased adsorption capacity; different optical properties that interfere with fluorescence or visible light absorption detection systems; increased catalytic activity due to enhanced surface energy; and magnetic properties that make them redox active and thus interfere with methods based on redox reactions (reference). Single-walled carbon nanotubes (SWCNTs) interact with a variety of indicator dyes employed in commonly used cytotoxicity assays, such as 3-(4,5-dimethylthiazole-2-yl)-2,5-biphenyl tetrazolium bromide (MTT), 2-(4-iodophenyl)- 3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H tetrazolium, monosodium salt (WST-1), Coomassie blue, alamar blue and neutral red. It is also suggested that these nanotubes bind with formazan crystals and stabilize their chemical structure, meaning that these crystals cannot be solubilized. The same phenomenon can be observed with carbon nanotubes where the unusual rope-like structure of these ENMs binds with the MTT dye and leads to the false positive result (Worle-Knirsch *et al.*, 2006). The high adsorptive capacities of ENMs have also been reported to interfere with annexin V/PI binding and ELISA tests for cytokine responses (Monteiro-Riviere and Inman, 2006). Another example for the ENMs interference with the test system is detection of oxidative DNA damage with formamidopyrimidine DNA glycosylase (FPG) enzyme. The presence of ENMs in the nucleoid has been reported and their possibility to induce additional DNA damage during the assay has been discussed extensively (Karlsson *et al.*, 2004; Stone *et al.*, 2009; Karlsson, 2010). The presence of ENMs close to DNA during the comet assay also increases the probability for the interaction of ENMs with FPG. It has recently been shown that the incubation of the ENMs and ions with FPG enzyme leads to the total loss of the ability of the enzyme to detect oxidatively damaged DNA in the comet assay (Kain *et al.*, 2012). This disturbance is most likely due to the binding of ions to the SH groups at the active site (Kain *et al.*, 2012). Another possible reason could be the physical hindrance by NPs, which prevent the enzyme action at the damaged DNA site.

Hence, it is important to standardize the methods for the physicochemical characterization of nanoparticles; development of appropriate methods/protocols for hazard assessment; safe production, handling, use and disposal methods; methodological and metrological approaches for the detection, bioavailability and uptake; agglomeration and aggregation state; reference materials; modelling and simulations and many more to overcome the limitations of current hazard and risk assessment schemes. It is also recommended to analyze the interaction/interference properties of ENMs prior to the beginning of the experiments. United Kingdom is playing a key role in leading the development of nanotechnology standards through its national committee NTI/1 "Nanotechnologies". They established the technical committee (TC; ISO TC 229) in June 2004 with the motto to (a) formulate a UK strategy for standardization in nanotechnologies through a broad consultation with relevant stakeholders (b) ensure

the UK view is given due consideration within the European Union, CEN, ISO and IEC (c) develop and support formal standards and other standardization documents in the area of nanotechnologies and to promote their use by industry and other stakeholders (d) ensure due consideration of the need for standards and standardization is given by UK nanotechnology networks and organisations, and to coordinate activities and actions in this area (BSI, ; ISO/TC229). Funding agencies such as the European Union; Department of Science and Technology, Department of Biotechnology, Council of Scientific and Industrial Research, Government of India, have focussed on the development & validation of SOPs for ENM preparation and testing as well as their life cycle assessment and fate in ecosystems. India is also participating in the European Union Seventh Framework Programme (FP7/2007-2013) under the project "Development of reference methods for hazard identification, risk assessment and LCA of engineered nanomaterials (NanoValid)". These characterization and standardization process will contribute to a better mechanistic understanding of the behaviour of nanoparticles in various test media, physiological solutions and environmental matrices. This can also be helpful in developing reference material as well as the test schemes for risk management. The first certified reference material was developed by the Institute for Reference Materials and Measurements, Joint Research Centre. The material was prepared with colloidal silica of a spherical diameter of 20nm. Certification of the material was based on a global interlaboratory comparison in which 34 laboratories participated with various analytical methods (DLS, CLS, EM, SAXS, ELS; (Braun *et al.*, 2012).

To maximize the outcomes of the initiatives taken by EU, a NanoSafety Cluster (NanoSafetyCluster, 2013) has been formed between the existing 29 projects of FP6 and FP7 programmes (NANOMMUNE, NanoTEST, NANODEVICE, NanoFATE, MARINA, QNnao NanoValid, NanoLinen, NewIndigo project etc.) addressing all aspects of nanosafety including toxicology, ecotoxicology, exposure assessment, mechanisms of interaction, risk assessment and standardisation.

6.5 Certification of nanoproducts

Certification plays an important role in getting the confidence of the consumer in commercial sector. It also provides an evidence of the existence of agreements between manufacturers and national accreditation testing and certification organisations. With the increasing use of ENM based products in the market, nanocertification will be important to confirm the applicability and technologies to this developing sector. It will also provide a guarantee and adequate quality of nanoproducts both at manufacturing & application stage, and encourage the manufacturers to develop quality products for consumer acceptance. Besides this, the certification system will also promote a favourable public opinion concerning the reliability and safety of nanoproducts and nanotechnologies.

Initially in September 2005, the UK Micro and NanoTechnology Network (MNT), has initiated a MNT Quality Mark for firms involved in the nanotechnology industry. The primary objective of the MNT Quality Mark was the development and implementation of best practice in nanotechnologies and to set a minimum standard of performance and achievement (UKMNT).

Later, in Taiwan, a National Science Council (NSC) was established to develop a "Nano-product Certification System Plan" with the coordination of Industrial Development Bureau (IDB), Ministry of Economic Affairs (MOEA), and Centre for Measurement Standards (CMS). The goal of NSC was to promote the development of nano-industries starting with the different aspects of the nanotechnology and industry. Additionally, the development of nanoMark certification in Taiwan enhances the overall enterprise competitiveness and already 34 companies with 1,215 products have passed the nanoMark certification. From the viewpoint of economy, granting the nanoMark would encourage manufacturers to produce quality products for a sustainable operation (nanoMark).

Further, RUSNANO was established in March 2011 by Russian Corporation of Nanotechnologies, with a mission is to develop the Russian nanotechnology industry through co-investment in nanotechnology projects with substantial economic potential or social benefit. They developed a voluntary certification system (VCS) called "Nanocertifica" for nanoindustry products. It is registered with the Federal Agency on Technical Regulation and Metrology for the quality management systems of companies operating in the nanoindustry under the provision of ISO 9000 and ISO 14000 (RUSNANO).

Recently, National Nanotechnology Center (NANOTEC), National Science and Technology Development Agency, Thailand have also launched the NanoQ mark to set industrial standards for nanotechnology related products (NanoQ, 2013).

It is apparent that different countries are realizing the potential of nanotech based products where standardization leading to certification will play a key role in quality assurance. This will also build confidence amongst the manufacturers and consumers alike regarding the widespread acceptability of nanotech based products.

7. Summary

The increasing use of engineered nanomaterials in various applications has increased the likelihood of their possible interaction with human and the environment. Humans get exposed to ENMs at various steps of its synthesis (laboratory), manufacture (industry), use (consumer products, devices, medicines etc.). Also, there is an almost complete lack of data on bioaccumulation, bioconcentration and biodegradation of ENMs in environmentally relevant species. Currently, the rate of ENM incorporation in commercial products is much faster than the development of regulation and knowledge to mitigate their potential adverse effects. This can be attributed to the lack of regulatory guidelines, reference standards and certification processes for ENMs (from manufacture to product development). This is compounded by the lack of suitable models, problems in experimental protocols and appropriate study design.

Hence, the knowledge regarding the fate and impact of ENMs on human and the environment; social, ethical and legal issues; safe production, handling, use and disposal; nanosafety policies, risk governance and the guidelines for the best practices for testing, standardization and certification of nanoproducts could be helpful in mitigating the risk associated with ENMs.

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References

Ahamed, M., Karns, M., Goodson, M., Rowe, J., Hussain, S. M., Schlager, J. J., and Hong, Y. (2008). DNA damage response to different surface chemistry of silver nanoparticles in mammalian cells.

Toxicology and Applied Pharmacology 233, 404-410.

Ahmed, M., Ramadan, W., Rambhu, D., and Shakeel, F. (2008). Potential of nanoemulsions for intravenous delivery of rifampicin. *Die Pharmazie* 63, 806-811.

Aitken, R. J., Hankin, S. M., Lang Tran, C., Donaldson, K., Stone, V., Cumpson, P., Johnstone, J., Chaudhry, Q., Cash, S., and Garrod, J. (2008). A multidisciplinary approach to the identification of reference materials for engineered nanoparticle toxicology. *Nanotoxicology* 2, 71-78.

Aitken, R. J., Koopman, P., and Lewis, S. E. (2004). Seeds of concern. *Nature* 432, 48-52.

Allen, H. J., Impellitteri, C. A., Macke, D. A., Heckman, J. L., Poynton, H. C., Lazorchak, J. M., Govindaswamy, S., Roose, D. L., and Nadagouda, M. N. (2011). Effects from filtration, capping agents, and presence/absence of food on the toxicity of silver nanoparticles to Daphnia magna. *Environmental toxicology and chemistry / SETAC* 29, 2742-2750.

Auffan, M., Rose, J., Wiesner, M. R., and Bottero, J. Y. (2009). Chemical stability of metallic nanoparticles: a parameter controlling their potential cellular toxicity in vitro. *Environ Pollut* 157, 1127-1133.

Baatz, M., Arini, N., Schape, A., Binnig, G., and Linssen, B. (2006). Object-oriented image analysis for high content screening: detailed quantification of cells and sub cellular structures with the Cellenger software. *Cytometry A* 69, 652-658.

Baun, A., Hartmann, N. B., Grieger, K., and Kusk, K. O. (2008). Ecotoxicity of engineered nanoparticles to aquatic invertebrates: A brief review and recommendations for future toxicity testing. *Ecotoxicology (London, England)* 17, 387-395.

Borm, P. J., Robbins, D., Haubold, S., Kuhlbusch, T., Fissan, H., Donaldson, K., Schins, R., Stone, V., Kreyling, W., Lademann, J., Krutmann, J., Warheit, D., and Oberdorster, E. (2006). The potential risks of nanomaterials: a review carried out for ECETOC. *Particle and Fibre Toxicology* 3, 11.

Braun, A., Kestens, V., Franks, K., Roebben, G., Lamberty, A., and Linsinger, T. P. J. (2012). A new certified reference material for size analysis of nanoparticles. *Journal of Nanoparticle Research* 14, 1021-1033.

Brayner, R. (2008). The toxicological impact of nanoparticles. *Nano today* 3, 48-55.

Brayner, R., Ferrari-Iliou, R., Brivois, N., Djediat, S., Benedetti, M. F., and Fievet, F. (2006). Toxicological impact studies based on Escherichia coli bacteria in ultrafine ZnO nanoparticles colloidal medium. *Nano letters* 6, 866-870.

Breggin, L., Robert, F., Nico, J., John, P., and Read, P. (2009). Securing the promise of nanotechnologies: Towards transatlantic regulatory cooperation. *Report. London: Chatham House.*

Brinker, C. J., and Scherer, G. (1990). The Physics and Chemistry of Sol–Gel Processing,. *Elsevier, The Netherlands*.

BSI http://shop.bsigroup.com/en/Browse-By-Subject/Nanotechnology/BSI-Committee-for-Nanotechnologies/.

Buffle, J., Wilkinson, K., Stoll, S., Filella, M., and Zhang, J. (1998). A generalized description of aquatic colloidal interactions: The three-colloidal component approach. *Environmental Science and Technology* 32, 2887–2899.

Chau, C., Wu, S., and Yen, G. (2007). The development of regulations for food nanotechnology. *Trends in Food Science and Technology*. 18, 269–280.

Chen, M., and von Mikecz, A. (2005). Formation of nucleoplasmic protein aggregates impairs nuclear function in response to SiO2 nanoparticles. *Exp Cell Res* 305, 51-62.

Chuklanov, A., Ziganshina, S., and Bukharaev, A. (2006). Computer program for the grain analysis of AFM images of nanoparticles placed on a rough surface. *Surf Interface Analysis* 38, 679–681.

Colvin, V. L. (2003). The potential environmental impact of engineered nanomaterials. *Nature Biotechnology* 21, 1166-1170.

Cui, D., Tian, F., Ozkan, C. S., Wang, M., and Gao, H. (2005). Effect of single wall carbon nanotubes on human HEK293 cells. *Toxicol Lett* 155, 73-85.

Demuth, P. C., Min, Y., Huang, B., Kramer, J. A., Miller, A. D., Barouch, D. H., Hammond, P. T., and Irvine, D. J. (2013). Polymer multilayer tattooing for enhanced DNA vaccination. *Nature materials*, doi:10.1038/nmat3550.

Dhawan, A., Shanker, R., Das, M., and Gupta, K. C. (2011). Guidance for safe handling of nanomaterials. *J Biomed Nanotechnol* 7, 218-224.

Dhawan, A., and Sharma, V. (2010). Toxicity assessment of nanomaterials: Methods and challanges. *Analatical and Bioanalytical Chemistry* 398, 589-605.

Dhawan, A., Sharma, V., and Parmar, D. (2009). Nanomaterials: A challenge for toxicologists. *Nanotoxicology* 3, 1-9.

Dhawan, A., Taurozzi, J. S., Pandey, A. K., Shan, W., Miller, S. M., Hashsham, S. A., and Tarabara, V. V. (2006). Stable colloidal dispersions of C60 fullerenes in water: Evidence for genotoxicity. *Environmental Science and Technology* 40, 7394-7401.

Doak, S. H., Griffiths, S. M., Manshian, B., Singh, N., Williams, P. M., Brown, A. P., and Jenkins, G. J. S. (2009). Confounding experimental considerations in nanogenotoxicology. *Mutagenesis* 24, 285-293.

Dobrovolskaia, M. A., Germolec, D. R., and Weaver, J. L. (2009). Evaluation of nanoparticle immunotoxicity. *Nat Nanotechnol* 4, 411-414.

Donaldson, K., and Borm, P. (2004). Particle and Fibre Toxicology, a new journal to meet a real need. *Particle and Fibre Toxicology* 1, 1.

Donaldson, K., Stone, V., Tran, C. L., Kreyling, W., and Borm, P. J. A. (2004). Nanotoxicology. *Occupational and Environmental Medicine* 61, 727-728.

EFSA (2007). Opinion of the scientiac panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request related to a 14th list of substances for food contact materials. . *EFSA Journal* 5, 452–454.

EFSA (2008a). Scientiac opinion of the panel on food contact materials, enzymes, fla- vourings and processing Aids (CEF). *EFSA Journal* 6, 888-890.

EFSA (2008b). Scientific opinion: Inability to assess the safety of a silver hydrosol added for nutritional purposes as a source of silver in food supplements and the bioavailability of silver from this source based on the supporting dossier. *EFSA Journal* 6, 884.

Elsaesser, A., and Howard, C. V. (2011). Toxicology of nanoparticles. *Advanced Drug Delivery Reviews* 64, 129-137.

EPA (2007a). Nanotechnology White Paper. EPA 100/B-07/001.

EPA (2007b). Pesticide registration; Clarification for ion-generating equipment. *Federal Register 72(183).*

EPA (2008). Toxic substances control act inventory status of carbon nanotubes. *Federal Register 73(212).*

European Commission (2008). Commission Regulation (EC) No. 987/2008 Official Journal of the European Union L268/14.

Fabrega, J., Luoma, S. N., Tyler, C. R., Galloway, T. S., and Lead, J. R. (2011). Silver nanoparticles: behaviour and effects in the aquatic environment. *Environment International* 37, 517-531.

Fadeel, B., and Garcia-Bennett, A. E. (2010). Better safe than sorry: Understanding the toxicological properties of inorganic nanoparticles manufactured for biomedical applications. *Advanced Drug Delivery Reviews* 62, 362-374.

Fadeel, B., Kagan, V., Krug, H., Shvedova, A., Svartengren, M., Tran, L., and Wiklund, L. (2007). There's plenty of room at the forum: Potential risks and safety assessment of engineered nanomaterials. *Nanotoxicology* 1, 73-84.

Fairbrother, A., and Fairbrother, J. R. (2009). Are environmental regulations keeping up with innovation? A case study of the nanotechnology industry. *Ecotoxicology and Environmental Safety* 72, 1327-1330.

Farre, M., Gajda-Schrantz, K., Kantiani, L., and Barcelo, D. (2009). Ecotoxicity and analysis of nanomaterials in the aquatic environment. *Analytical and Bioanalytical Chemistry* 393, 81-95.

FDA (2007). Nanotechnology. A report of the U.S. food and drug administration nanotechnology task force.

Feliu, N., and Fadeel, B. (2010). Nanotoxicology: no small matter. *Nanoscale* 2, 2514-2520.

Gajewicz, A., Rasulev, B., Dinadayalane, T. C., Urbaszek, P., Puzyn, T., Leszczynska, D., and Leszczynski, J. (2012). Advancing risk assessment of engineered nanomaterials: application of computational approaches. *Advanced Drug Delivery Reviews* 64, 1663-1693.

Gruere, G. P. (2012). Implications of nanotechnology growth in food and agriculture in OECD countries. *Food Policy* 37, 191–198.

Handy, R. D., Owen, R., and Valsami-Jones, E. (2008). The ecotoxicology of nanoparticles and nanomaterials: current status, knowledge gaps, challenges, and future needs. *Ecotoxicology (London, England)* 17, 315-325.

Hardman, R. (2006). A toxicologic review of quantum dots: Toxicity depends on physicochemical and environmental factors. *Environmental health perspectives* 114, 165-172.

Howard, A. G. (2009). On the challenge of quantifying man-made nanoparticles in the aquatic environment. *J Environ Monit* 12, 135-142.

ISO/TC229
http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_tc_browse.htm?commid=381983&published=on&includesc=true.

Jose-Yacaman, M., Marin-Almazo, M., and Ascencio, J. (2001). High resolution TEM studies on palladium nanoparticles. *Journal of Molecular Catalysis A* 173, 61–74.

Jyoti, A., Pandey, P., Singh, S. P., Jain, S. K., and Shanker, R. (2010). Colorimetric detection of nucleic acid signature of shiga toxin producing Escherichia coli using gold nanoparticles. *Journal of Nanoscience and Nanotechnology* 10, 4154-4158.

Kahru, A., and Dubourguier, H. C. (2010). From ecotoxicology to nanoecotoxicology. *Toxicology* 269, 105-119.

Kain, J., Karlsson, H. L., and Moller, L. (2012). DNA damage induced by micro- and nanoparticles--interaction with FPG influences the detection of DNA oxidation in the comet assay. *Mutagenesis* 27, 491-500.

Karlsson, H. L. (2010). The comet assay in nanotoxicology research. *Analytical and Bioanalytical Chemistry* 398, 651-666.

Karlsson, H. L., Nygren, J., and Moller, L. (2004). Genotoxicity of airborne particulate matter: the role of cell-particle interaction and of substances with adduct-forming and oxidizing capacity. *Mutation Research* 565, 1-10.

Kermisch, C. (2012). Do new ethical issues arise at each stage of nanotechnological development. *Nanoethics* 6, 29–37.

Kretzschmar, R., and Sticher, H. (1997). Transport of humic-coated iron oxide colloids in a sandy soil: influence of Ca2+ and trace metals. *Environmental Science and Technology* 31, 3497–3504.

Kroll, A., Pillukat, M. H., Hahn, D., and Schnekenburger, J. (2009). Current in vitro methods in nanoparticle risk assessment: Limitations and challenges. *European Journal of Pharmaceutics and Biopharmaceutics* 72, 370-377.

Kulkarni, P., Willeke, K., and Baron, P. A. (2011). Aerosol Measurement: Principles, Techniques, and Applications. *Wiley, New York.*

Kumar, A., Dhawan, A., and Shanker, R. (2011a). The need for novel approaches in ecotoxicity of engineered nanomaterials. *J Biomed Nanotechnol* 7, 79-80.

Kumar, A., Pandey, A. K., Shanker, R., and dhawan, A. (2012). Microorganism: A varsatile model for toxicity assessment of engineered nanomaterials. *Book Name :- Nano-Antimicrobials: Progress and Prospects, Publisher:- Springer Heidelberg Dordrecht London New York* Edited by Nicola Cioffi, Mahendra Rai, 497-524.

Kumar, A., Pandey, A. K., Singh, S. S., Shanker, R., and Dhawan, A. (2011b). Cellular response to metal oxide nanoparticles in bacteria. *J Biomed Nanotechnol* 7, 102-103.

Kumar, A., Pandey, A. K., Singh, S. S., Shanker, R., and Dhawan, A. (2011c). Cellular uptake and mutagenic potential of metal oxide nanoparticles in bacterial cells. *Chemosphere* 83, 1124-1132.

Kumar, A., Pandey, A. K., Singh, S. S., Shanker, R., and Dhawan, A. (2011d). Engineered ZnO and TiO(2) nanoparticles induce oxidative stress and DNA damage leading to reduced viability of Escherichia coli. *Free radical biology & medicine* 51, 1872-1881.

Kumar, A., Pandey, A. K., Singh, S. S., Shanker, R., and Dhawan, A. (2011e). A flow cytometric method to assess nanoparticle uptake in bacteria. *Cytometry A* 79A, 707-712.

Kumar, A., Shanker, R., and Dhawan, A. (2011f). The need for novel approaches in ecotoxicity of engineered nanomaterials. *Journal of Biomedical Nanotechnology* 7 79–80.

Kumari, M., Khan, S. S., Pakrashi, S., Mukherjee, A., and Chandrasekaran, N. (2011). Cytogenetic and genotoxic effects of zinc oxide nanoparticles on root cells of Allium cepa. *Journal of Hazardous Materials* 190, 613-621.

Lehn, J. M. (2002). Towards self organization and complex matter. *Science* 295, 2400-2403.

Li, N., Sioutas, C., Cho, A., Schmitz, D., Misra, C., Sempf, J., Wang, M., Oberley, T., Froines, J., and Nel, A. (2003). Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage. *Environmental Health Perspectives* 111, 455-460.

Lindfors, K., Kalkbrenner, T., Stoller, P., and Sandoghdar, V. (2004). Detection and spectroscopy of gold nanoparticles using supercontinuum white light confocal microscopy. *Physical Review Letters* 93, 037401.

Long, T. C., Saleh, N., Tilton, R. D., Lowry, G. V., and Veronesi, B. (2006). Titanium dioxide (P25) produces reactive oxygen species in immortalized brain microglia (BV2): implications for nanoparticle neurotoxicity. *Environmental Science & Technology* 40, 4346-4352.

Lynch, I., and Dawson, K. A. (2008). Protein-nanoparticle interactions. *Nano Today* 3, 40-47.

Mahapatra, I., Clark, J., Dobson, P. J., Owenc, R., and Lead, J. R. (2013). Potential environmental implications of nano-enabled medical applications: critical review. *Environmental Science: Processes & Impacts* 15, 123–144.

Mavrocordatos, D., Pronk, W., and Boiler, M. (2004). Analysis of environmental particles by atomic force microscopy, scanning and transmission electron microscopy. *Water Sci Technol* 50, 9-18.

Maynard, A. D. (2007). Nanotechnology: the next big thing, or much ado about nothing? *The Annals of occupational hygiene* 51, 1-12.

Monteiro-Riviere, N., and Inman, A. (2006). Challenges for assessing carbon nanomaterial toxicity to the skin. *Carbon* 44, 1070–1078.

Monteiro-Riviere, N. A., Inman, A. O., and Zhang, L. W. (2009). Limitations and relative utility of screening assays to assess engineered nanoparticle toxicity in a human cell line. *Toxicol Appl Pharmacol* 234, 222-235.

nanoMark http://proj3.moeaidb.gov.tw/nanomark/Eng/.

NanoQ (2013). http://www.nanotec.or.th/en/?p=4014.

NanoSafetyCluster (2013). http://www.nanosafetycluster.eu/eu-nanosafety-cluster-projects/seventh-framework-programme-projects/ennsatox.html.

Navarro, E., Baun, A., Behra, R., Hartmann, N. B., Filser, J., Miao, A. J., Quigg, A., Santschi, P. H., and Sigg, L. (2008). Environmental behavior and ecotoxicity of engineered nanoparticles to algae, plants, and fungi. *Ecotoxicology (London, England)* 17, 372-386.

Nel, A. (2005). Atmosphere air pollution-related illness: effects of particles. *Science* 308, 804-806.

Nel, A., Xia, T., Madler, L., Li, N. (2006). Toxic potential of materials at the nanolevel. *Science* 311, 622-627.

NIOSH (2010). National Institute for Occupational Safety and Health, Occupational exposure to carbon nanotubes and nanofibers, current intelligence bulletin, Department of Health and Human Services, Centers for Disease Control and Prevention.

Nowack, B. (2009). The behavior and effects of nanoparticles in the environment. *Environ Pollut* 157, 1063-1064.

O'Shaughnessy, P. T. (2013). Occupational health risk to nanoparticulate exposure. *Environmental Science: Processes & Impacts* 15, 49-62.

Oberdarster, G., Oberdarster, E., and Oberdarster, J. (2005). Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. *Environmental Health Perspectives* 113, 823-839.

Oberdarster, G., Stone, V., and Donaldson, K. (2007). Toxicology of nanoparticles: A historical perspective. *Nanotoxicology* 1, 2-25.

Oberdorster, G., Sharp, Z., Atudorei, V., Elder, A., Gelein, R., Kreyling, W., and Cox, C. (2004). Translocation of inhaled ultrafine particles to the brain. *Inhalation Toxicology* 16, 437-445.

PEN (2013). http://www.nanotechproject.org/inventories/remediation_map/.

PEN (2013). Project of the Emerging Nanotechnologies (PEN) Available at PEN "http://www.nanotechproject.org/inventories/consumer/browse/products/."

Penn, A., Murphy, G., Barker, S., Henk, W., and Penn, L. (2005). Combustion-derived ultrafine particles transport organic toxicants to target respiratory cells. *Environmental Health Perspectives* 113, 956-963.

Premanathan, M., Karthikeyan, K., Jeyasubramanian, K., and Manivannan, G. (2011). Selective toxicity of ZnO nanoparticles toward Gram-positive bacteria and cancer cells by apoptosis through lipid peroxidation. *Nanomedicine* 7, 184-192.

Pui, D. Y. H. (1996). Direct-reading Instrumentation for workplace aerosol measurements. *The Analyst* 121, 1215–1224.

Royal, S. (2004). The Royal society and the Royal Academy of engineers: Nanoscience and nanotechnologies:oppurtunities and uncertainties.

RUSNANO http://eng.thesaurus.rusnano.com/wiki/article3122.

SCENIHR (2009). (European Commission Scientific Committee on Emerging and Newly Identified Health Risks) Risk Assessment of Products of Nanotechnologies.

Schins, R. P., Lightbody, J. H., Borm, P. J., Shi, T., Donaldson, K., and Stone, V. (2004). Inflammatory effects of coarse and fine particulate matter in relation to chemical and biological constituents. *Toxicol Appl Pharmacol* 195, 1-11.

Service, R. F. (2008). Science policy: Report faults U.S. strategy for nanotoxicology research. *Science* 322, 1779.

Shapiro, H. M. (2001). Optical measurements in cytometry: Light scattering, extinction, absorption, and fluorescence. *Methods in Cell Biology, Vol 63* 63, 107-129.

Sharma, V., Anderson, D., and Dhawan, A. (2012a). Zinc oxide nanoparticles induce oxidative DNA damage and ROS-triggered mitochondria mediated apoptosis in human liver cells (HepG2). *Apoptosis* 17, 852-870.

Sharma, V., Kumar, A., and Dhawan, A. (2012b). Nanomaterials: Exposure, effects and toxicity assessment. *Proceedings of the National Academy of Sciences, India Section B: Biological Sciences* 82, 3-11.

Sharma, V., Shukla, R. K., Saxena, N., Parmar, D., Das, M., and Dhawan, A. (2009). DNA damaging potential of zinc oxide nanoparticles in human epidermal cells. *Toxicology Letters* 185, 211-218.

Sharma, V., Singh, P., Pandey, A. K., and Dhawan, A. (2012c). Induction of oxidative stress, DNA damage and apoptosis in mouse liver after sub-acute oral exposure to zinc oxide nanoparticles. *Mutation Research* 745, 84-91.

Sharma, V., Singh, S. K., Anderson, D., Tobin, D. J., and Dhawan, A. (2011). Zinc oxide nanoparticle induced genotoxicity in primary human epidermal keratinocytes *Journal of Nanoscience and Nanotechnology* 11, 3782-3788.

Shukla, R. K., Kumar, A., Gurbani, D., Pandey, A. K., Singh, S., and Dhawan, A. (2011a). TiO(2) nanoparticles induce oxidative DNA damage and apoptosis in human liver cells. *Nanotoxicology* 7, 48-60.

Shukla, R. K., Kumar, A., Pandey, A. K., Singh, S. S., and Dhawan, A. (2011b). Titanium Dioxide Nanoparticles Induce Oxidative Stress-Mediated Apoptosis in Human Keratinocyte Cells. *Journal of Biomedical Nanotechnology* 7, 100–101.

Shukla, R. K., Sharma, V., Pandey, A. K., Singh, S., Sultana, S., and Dhawan, A. (2011c). ROS-mediated genotoxicity induced by titanium dioxide nanoparticles in human epidermal cells. *Toxicol In Vitro* 25, 231-241.

Simon-Deckers, A., Loo, S., Mayne-L'Hermite, M., Herlin-Boime, N., Menguy, N., Reynaud, C., Gouget, B., and Carriere, M. (2009). Size-, Composition- and Shape-Dependent Toxicological Impact of Metal Oxide Nanoparticles and Carbon Nanotubes toward Bacteria. *Environmental Science & Technology* 43, 8423-8429.

Singh, N. (2009). Conference scene - Nanotoxicology: Health and environmental impacts. *Nanomedicine* 4, 385-390.

Singh, N., Manshian, B., Jenkins, G. J. S., Griffiths, S. M., Williams, P. M., Maffeis, T. G. G., Wright, C. J., and Doak, S. H. (2009). NanoGenotoxicology: The DNA damaging potential of engineered nanomaterials. *Biomaterials* 30, 3891-3914.

Singh, R., Pantarotto, D., Lacerda, L., Pastorin, G., Klumpp, C., Prato, M., Bianco, A., and Kostarelos, K. (2006). Tissue biodistribution and blood clearance rates of intravenously administered carbon nanotube radiotracers. *Proceedings of the National Academy of Sciences of the United States of America* 103, 3357-3362.

Singh, S., and Nalwa, H. S. (2007). Nanotechnology and health safety--toxicity and risk assessments of nanostructured materials on human health. *Journal of Nanoscience and Nanotechnology* 7, 3048-3070.

Song, M. M., Song, W. J., Bi, H., Wang, J., Wu, W. L., Sun, J., and Yu, M. (2010). Cytotoxicity and cellular uptake of iron nanowires. *Biomaterials* 31, 1509-1517.

Spagnolo, A. G., and Daloiso, V. (2009). Outlining ethical issues in nanotechnologies. *Bioethics* 23, 394-402.

Stebounova, L. V., Morgan, H., Grassian, V. H., and Brenner, S. (2012). Health and safety implications of occupational exposure to engineered nanomaterials. *Wiley Interdisciplinary Reviews* 4, 310-321.

Stone, V., and Donaldson, K. (2006). Nanotoxicology: signs of stress. *Nature Nanotechnology* 1, 23-24.

Stone, V., Johnston, H., and Schins, R. P. (2009). Development of in vitro systems for nanotoxicology: methodological considerations. *Critical Reviews in Toxicology* 39, 613-626.

Thill, A., Zeyons, O., Spalla, O., Chauvat, F., Rose, J., Auffan, M., and Flank, A. M. (2006). Cytotoxicity of CeO2 nanoparticles for Escherichia coli. Physico-chemical insight of the cytotoxicity mechanism. *Environmental Science and Technology* 40, 6151-6156.

Tian, F., Cui, D., Schwarz, H., Estrada, G. G., and Kobayashi, H. (2006). Cytotoxicity of single-wall carbon nanotubes on human fibroblasts. *Toxicol In Vitro* 20, 1202-1212.

Tian, F., Prina-Mello, A., Estrada, G., Beyerle, A., MÃ¶ller, W., Schulz, H., Kreyling, W., and Stoeger, T. (2008). A novel assay for the quantification of internalized nanoparticles in macrophages. *Nanotoxicology* 2, 232-242.

Tiede, K., Boxall, A. B., Tear, S. P., Lewis, J., David, H., and Hassellov, M. (2008). Detection and characterization of engineered nanoparticles in food and the environment. *Food Additives & Contaminants* 25, 795-821.

UKMNT http://www.innovateuk.org/deliveringinnovation/micronanotechnologycentres.ashx.

Vajpayee, P., Khatoon, I., Patel, C. B., Singh, G., Gupta, K. C., and Shanker, R. (2011). Adverse effects of chromium oxide nano-particles on seed germination and growth in Triticum aestivum L. *J Biomed Nanotechnol* 7, 205-206.

Van Dijk, M. A., Lippitz, M., and Orrit, M. (2005). Far-field optical microscopy of single metal nanoparticles. *Accounts of Chemical Research* 38, 594-601.

Van Dijk, M. A., Tchebotareva, A. L., Orrit, M., Lippitz, M., Berciaud, S., Lasne, D., Cognet, L., and Lounis, B. (2006). Absorption and scattering microscopy of single metal nanoparticles. *Phys Chem Chem Phys* 8, 3486-3495.

Vasiliev, P. O., Faure, B., Ng, J. B. S., and Bergström, L. (2008). Colloidal aspects relating to direct incorporation of TiO2 nanoparticles into mesoporous spheres by an aerosol-assisted process. *Journal of Colloid and Interface Science* 319, 144–151.

Wahab, R., Mishra, A., Yun, S. I., Kim, Y. S., and Shin, H. S. (2010). Antibacterial activity of ZnO nanoparticles prepared via non-hydrolytic solution route. *Applied Microbiology and Biotechnology* 87, 1917-1925.

Wang, B., Feng, W., Wang, M., Wang, T., Gu, Y., Zhu, M., Ouyang, H., Shi, J., Zhang, F., and Zhao, Y. (2008). Acute toxicological impact of nano- and submicro-scaled zinc oxide powder on healthy adult mice. *Journal of Nanoparticle Research* 10 263-276.

Wardak, A., Gorman, M. E., Swami, N., and Deshpande, S. (2008). Identification of risks in the life cycle of nanotechnology-based products. *Journal of Industrial Ecology* 12, 435-448.

Warheit, D. B., Webb, T. R., Reed, K. L., Frerichs, S., and Sayes, C. M. (2007). Pulmonary toxicity study in rats with three forms of ultrafine-TiO2 particles: differential responses related to surface properties. *Toxicology* 230, 90-104.

Wen-Che Hou, Westerhoff, P., and Posner, J. D. (2013). Biological accumulation of engineered nanomaterials: a review of current knowledge. *Environmental Science: Processes & Impacts* 15, 103-122.

Win-Shwe, T. T., and Fujimaki, H. (2011). Nanoparticles and neurotoxicity. *International Journal of Molecular Sciences* 12, 6267-6280.

Worle-Knirsch, J., Pulskamp, K., and Krug, H. (2006). Oops they did it again! Carbon nanotubes hoax scientists in viability assays. *Nano Letters* 6, 1261–1268.

Wu, B., Wang, Y., Lee, Y. H., Horst, A., Wang, Z., Chen, D. R., Sureshkumar, R., and Tang, Y. J. (2010). Comparative eco-toxicities of nano-ZnO particles under aquatic and aerosol exposure modes. *Environmental Science & Technology* 44, 1484-1489.

Wu, J., Wang, C., Sun, J., and Xue, Y. (2011). Neurotoxicity of silica nanoparticles: brain localization and dopaminergic neurons damage pathways. *ACS Nano* 5, 4476-4489.

Xia, T., Kovochich, M., Brant, J., Hotze, M., Sempf, J., Oberley, T., Sioutas, C., Yeh, J. I., Wiesner, M. R., and Nel, A. E. (2006). Comparison of the abilities of ambient and manufactured nanoparticles to induce cellular toxicity according to an oxidative stress paradigm. *Nano Letters* 6, 1794-1807.

Xie, G., Wang, C., Sun, J., and Zhong, G. (2011). Tissue distribution and excretion of intravenously administered titanium dioxide nanoparticles. *Toxicol Letters* 205, 55-61.

Xu, A., Chai, Y., Nohmi, T., and Hei, T. K. (2009). Genotoxic responses to titanium dioxide nanoparticles and fullerene in gpt delta transgenic MEF cells. *Particle and Fibre Toxicology* 6.

Yokoyama, A., Sato, Y., Nodasaka, Y., Yamamoto, S., Kawasaki, T., Shindoh, M., Kohgo, T., Akasaka, T., Uo, M., Watari, F., and Tohji, K. (2005). Biological behavior of hat-stacked carbon nanofibers in the subcutaneous tissue in rats. *Nano Letters* 5, 157-161.

Zucker, R. M., Massaro, E. J., Sanders, K. M., Degn, L. L., and Boyes, W. K. (2010). Detection of TiO2 nanoparticles in cells by flow cytometry. *Cytometry A* 77, 677-685.

MANUAL ON CRITICAL ISSUES IN NANOTECHNOLOGY R&D MANAGEMENT

AN ASIA-PACIFIC PERSPECTIVE

CHAPTER 2

Protection and Valuation of Nanotechnology Intellectual Property

Prepared for

Asian and Pacific Centre for Transfer of Technology of the United Nations – Economic and Social Commission for Asia and the Pacific (UNESCAP)

By

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Manual on Critical Issues in Nanotechnology R&D Management: An Asia-Pacific Perspective

Asian and Pacific Centre for Transfer of Technology (APCTT) of the
United Nations Economic and Social Commission for Asia and the Pacific (UNESCAP)

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Protection and Valuation of Nanotechnology Intellectual Property

1. Introduction

Nanoscience from the time of its inception has charted an interdisciplinary trajectory. Materials with diverse structures and surprising properties have been constructed progressively at will. Similarly bulk materials have been tailored to Nano levels to exhibit targeted characteristics and functions.

Nanotechnology on the other hand has resulted from the science and art of dexterous manipulation of materials whose applications over the years have only stretched the horizon of human imagination. Man has also discovered and mimicked nanostructures in nature with extraordinary properties.

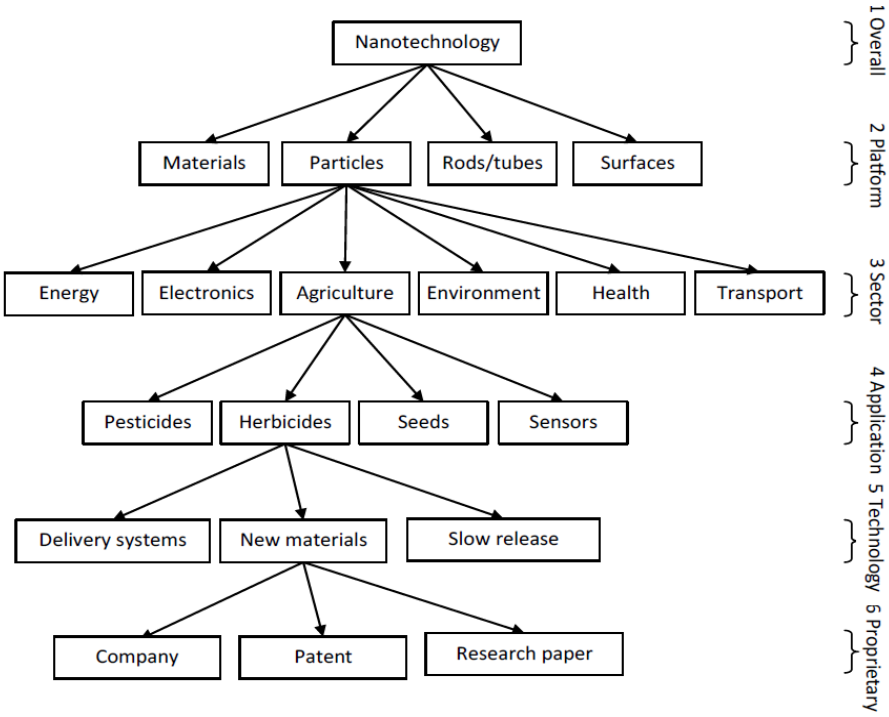


Figure 1: A schematic of nanotechnology

(Source:http://www.oakdenehollins.co.uk/media/225/DEFR01_225_Methodology_full final.pdf)

Figure1 illustrates how over the decades, nanotechnology R&D has experienced a definitive transformation from its conceptual phase of being a path breaking science to reality and more so, into new and commercial products and processes. This trajectory has been dotted with several successes and failures, but the lessons learnt in converting science to technology, and technology to marketables, both with regard to products and processes, have paved the way to development of pragmatic business frameworks for profitable growth and sustainability.

Intellectual Property Rights (IPR) has played an inseparable role in early protection of the knowledge base that showed promises of applications and imminent commercialisation. In view of the importance of IPR, all knowledge transfer processes in nanotechnology have quantitatively and semi quantitatively integrated IPR at all stages of the knowledge nanotechnology value chain.

2. Role of intellectual property rights in nanotechnology

Nanotechnology being strongly science-based initially progressed through conceptualisation followed by validation of concepts. In some cases, concepts have emerged from questioning and explaining discovered properties demonstrated by existing nano materials and in several cases tailoring nano materials for specific end effects or incorporating nano materials as subsystems in integrated systems to produce useful end products.

Diverse aspects of innovations in the field of nanotechnology are protected using tools of Intellectual Property Rights such as:

- Patents,
- industrial design registrations,
- copyright, and
- trademarks

The above IPRs require disclosure of the appropriate aspects to a statutory body for their evaluation for the grant of the intellectual property right applied for. However there are several aspects of an innovation such as know-how, customer portfolio, business process, etc, that may be kept as trade secrets and for which care is taken not to disclose those aspects to the public.

Of the four IPR tools listed above, the role of patents is most significant as it deals with functional aspects of an invention that is so central to nanotechnology R&D and progress. Trademarks plays an important role in the market place in terms of developed “names”, “terminologies”, “logos”, “representations” that help to create associations between the product/service to the manufacturer/distributor/market operators. Industrial Design Registrations (also called design patents in the USA) play a less significant role in nanotechnology as designs deal with the looks of manufactured goods disclaiming functional aspects. We have already noted that in nanotechnology the functional aspects are of paramount importance and those features are protectable by patents. Copyright is also of relative low significance in nanotechnology except for the protection of software associated with nanotechnology products / processes, textual / figurative descriptions, etc. This chapter therefore deals with the relevant aspects of patents related to nanotechnology.

2.1 Patents

Nanotechnology being science-based, progresses substantially through inventions that address changes in functional features in products and processes.

A patent is a legal tool that protects inventions providing technical solutions to problems subject to their satisfying certain defined benchmarks of patentability.

It would be appropriate to set an operations definition of a patent at this stage.

A patent is a grant by sovereign or state to a person giving exclusive right to stop others from making, using, exercising and vending including offering for sale, or selling an invention for a limited period, in exchange for disclosing the invention in a patent specification such that any person trained in the said art can reproduce the invention. The invention must be adequately disclosed and the claims of the application must be clear, concise and supported by the description.

The written description must provide the manner and process of making and using the invention in such concise, exact terms and set forth the best mode of carrying out the invention and must sufficiently disclose the invention as to "enable any person skilled in the art" to make and use it. The specification must conclude with "one or more claims particularly pointing out and distinctly claiming the subject matter" of the invention thereby defining the meats and bounds of the exclusive rights *vis-à-vis* the prior art claimed by the inventor.

Some of the decisions of the European Patent Office (EPO) Board of Appeals illustrate the significance of disclosing the invention adequately in a patent specification. For example:

- In the T 0915/00, June 2002 (Integran Technologies Inc. vs. Atotech Deutschland GmbH) dealing with nanocrystalline metals, the board was satisfied that the process of the claim is disclosed in the patent in a manner sufficiently clear and complete for it to be carried out by the person skilled in the art.

  Excerpts from the EPO decision illustrate the point under discussion (http://www.epo.org/law-practice/case-law-appeals/pdf/t000915eu1.pdf).

  "Claim 1 defines a process for electrodepositing a nonspecified metallic material in nanocrystalline form on a substrate in an electrolytic cell having an anode and a cathode between which a direct current is passed at pulsed intervals. The claim defines ranges for the temperature of the electrolyte, the peak current density and the time periods for which current passes or not, and it specifies that the process shall be so conducted as to deposit the metallic material in nanocrystalline form and having a grain size of less than 100 nm on the cathode. Since such nanocrystalline material is not obtained for each arbitrary combination of parameter values in the ranges set out in the claim as is admitted by both parties and is evident from the prior art documents D1 to D7 which disclose several embodiments in which process conditions within the ranges of claim 1 do not achieve nanocrystalline material, claim 1 shall be construed as meaning that, within the ranges it defines, combinations of parameter values have still to be selected so as to achieve the desired nanocrystalline material.

  To assist the skilled person in selecting an appropriate combination of parameter values for a give material the specification of the patent on the one hand comprises four examples, which all describe the deposition of nanocrystalline nickel from a same electrolyte bath and under the same electroplating conditions and which differ only by the amount of stress reliever and grain refining agent (see column 5, lines 2 to 57). The specification on the other hand provides a series of recommendations as to the proper selection of the electrodeposition conditions: the

quality of the deposit and the nanocrystalline structure thereof are functions of the peak current density in the cell and the rate of pulsing the current, the time off is generally longer than the time on, if the peak current density is too high, there is a risk that the deposited material will burn and, if too low, the grain size will increase (see the paragraph bridging column 4 and 5). Thus, the issue to be decided in respect of the sufficiency of the disclosure is whether the skilled person could on the basis of his general knowledge and of the above indications and without undue burden determine adequate combinations of parameter values allowing the obtaining of nanocrystalline structures also of materials other than nickel. The board in this respect first notes that according to the jurisprudence of the boards of appeal, an objection for lack of sufficient disclosure shall only be raised if there are serious doubts, substantiated by verifiable facts. The mere fact that the claim is broad is not in itself a ground for considering the application as not complying with the requirement of sufficient disclosure under Article 83 EPC (see T 19/90 OJ 1990, 476).

In the present case, however, the respondent in substance only relied upon experimental report D37 to show that applying parameter values in the claimed ranges in three experiments failed to achieve nanocrystalline copper deposits. There is however no doubt that any arbitrary combination of parameter values will not necessarily in the obtaining of nanocrystalline material. The mere failing of three such arbitrary combinations cannot establish that the skilled person could not possibly have devised successful electrodeposition conditions within the claimed parameter ranges, from his normal knowledge and capacity.

The board can in this respect agree to the appellant's definition of the skilled person as a highly qualified scientist well aware of the latest developments in nanocrystalline materials and electrodeposition. This view is indeed consistent with the observation that most of the numerous relevant prior art citations in the file consist of articles from scientific publications, disclosing fundamental research work rather than for instance practical developments in industrial equipment.

The credibility of the numerous experimental reports filed by the appellant to demonstrate that various materials can be deposited in a nanocrystalline form under conditions meeting the parameter ranges of claim 1 (see D18, D27 to D32 and D34) is supported by documents D19 to D22 published after the filing date of the patent in suit. These scientific publications do not in any way suggest the existence of particular difficulties in the selection of proper deposition conditions or bath compositions.

The respondent also questioned the sufficiency of the disclosure in the patent in suit on the ground that the specification did not unambiguously specify how the grain size of less than 100 nm referred to in claim 1 was to be measured, but disclosed instead two distinct procedures which gave different results, namely scanning electromicroscopy and x-ray diffraction. In the board's view, however, the specification clearly indicates that the 100 nm value was referred to merely as a generally recognised grain size limit below which the material was defined as being nanocrystalline (see- 13. column 1, lines 29 to 33). In addition, the results of the two grain size

measurement procedures referred to in the specification are fully consistent, scanning electromicroscopy indicating a grain size less than 100 nm while x-ray diffraction gave grain size values of about 10 to 15 nm with some grain sizes up to about 37 nm (see column 7, lines 43 to 47).

For the above reasons, the board is satisfied that the process of independent claim 1 is disclosed in the patent in a manner sufficiently clear and complete for it to be carried out by the person skilled in the art.

The same conclusion holds true for the nanocrystalline nickel material defined in independent claim 18, the preparation of which is described in details in lines 2 to 57 of column 2 of the specification, with reference to Examples 1 to 4.

Independent claims 19 and 20 as granted, the subject matter of which had also been considered insufficiently disclosed by the opposition division in the decision under appeal have not been maintained by the appellant."

- In T 0288/02, April 2004 dealing with atomic and molecular radicals of nitrogen wherein the applicant was Minnesota Mining and manufacturing company, et. al (http://www.epo.org/law-practice/case -law-appeals/pdf/t020288eu1.pdf). The patent applicant has appealed to the EPO Board of Appeals against a decision by the examining division that the e application did not disclose the invention sufficiently for it to be performed by a skilled person.

  Oral proceedings took place on 22 April 2004. During the oral proceedings, the appellant filed a new main request. The new main request comprises independent claim 1 and dependent claims 2 and 3, and a description adapted to match these amended claims.

Excerpts of the Board decision illustrate the importance of contextual disclosures and claims as follows:

- The original claim 1 claimed an electromagnetic transducer comprising a p-type layer and an n-type layer and the electrical connections to these layers, while claim 1 of the request refers only to the p-type layer and its properties. However, the Board accepts that it is clear both from the description in general and from selected passages of the description in particular (column 2, lines 39 to 43 and column 12, lines 17 to 27 of the application as published), that the invention lies in the provision of a doped p-type IIB-VIA semiconductor layer, and that therefore the reference to the n-type layer and the electrical connections may be omitted without contravening Article 123(2) EPC.
- The application as published discloses without reference to the doping efficiency specified in the originally filed claim 1, that the p-type layer is doped such that the net acceptor concentration is greater than about 5x1015cm-3 and exhibiting an electrical resistivity of less than 15 ohm centimetres (column 2, lines 39 to 43), thereby providing the basis for the amended wording of claim 1.
- It is also disclosed in the description that a free radical source is used to generate atomic nitrogen radicals from gaseous nitrogen (e.g., published application, column 8, lines 24 to 29), that the p-doped film of the transducer has a net acceptor concentration which is greater than

5x1015cm-3 and providing a room temperature (300K) electroluminescent spectrum with an intensity maximum at a wavelength below 550nm (column 3, lines 35 to 42, column 4, lines 9 to 17 and lines 43 to 51), and that it is useful in light emitting diodes and laser diodes (column 7, lines 30 to 34). Accordingly, the subject matter of the corresponding features of claim 1 was already disclosed. The Board is therefore satisfied that the amendments which distinguish claim 1 of the request from claim 1 as originally filed do not introduce subject matter which goes beyond the contents of the originally filed application.

- Claim 1 of the main request is a product claims which, by stating that the film "is obtainable by molecular beam epitaxy using a free radical source to generate atomic nitrogen radicals from gaseous nitrogen", attempts to define some of the features of the product in process terms. The features of the product which are defined by the process features in claim 1 are the electrical and chemical characteristics of the material which are obtained by growing the material by molecular beam epitaxy and by doping the material with atomic nitrogen radicals.
- The Board accepts that material which "is obtainable by molecular beam epitaxy" and in which doping of the material is performed "using a free radical source to generate atomic nitrogen radicals from gaseous nitrogen" displays the verifiable product features that the grown material is free of carbon-based impurities and has the required effective p-type doping concentrations levels to make the transducer useful in light emitting diodes and lasers.
- The Board further accepts that in the present case there is no other concise way of defining the material. As the claimed process features can be associated with identifiable product features, the Board is satisfied that independent claim 1 is clear, as required by Article 84, second sentence EPC. The board concluded that the amended claim 1 was sufficiently and clearly described and hence reversed the decision of the examination board.

The limited period for which the exclusivity is granted is 20 years from the date of the patent application which is called the “term” of the patent. However a granted patent needs to be renewed periodically (the renewal periodicity depends on the applicable patent law in the country). Failure to pay the renewal fee in a country within the prescribed period leads to the lapse of the patent protection in that country.

The invention has to satisfy the benchmarks of patentability, namely:

- Novelty (new),
- Inventive step (non-obvious to a person skilled in the art), and
- Capable of (susceptible to) industrial application (i.e. demonstrate credible utility / usefulness).

This assessment of the invention for its patentability is done by a statutory body such as a patent office based on the applicable patent law in that jurisdiction.

Though the interpretation of the terms novelty, inventive step and utility / capable of industrial application are similar in most jurisdictions, certain inventions may be excluded from patentability in some jurisdiction depending on the law as applicable in that jurisdiction. Article 27 (2) and (3) of the TRIPS Agreement allows for such exclusions:

Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law [Article 27(2)].

Members may also exclude from patentability [Article 27(2)]:

- diagnostic, therapeutic and surgical methods for the treatment of humans or animals;
- plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective sui generis system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO Agreement.

The patent laws in various countries may differ especially depending on the manner in which the flexibilities of Article 27(2) and (3) are built into their respective patent laws.

Further the interpretation of "novelty", "inventive step" and "utility/ capable of industrial application" vis-à-vis an invention may vary from person to person, based on the context and perspective.

Thus, while assessing inventions in nanotechnology for their patentability and drafting patent applications, one ought to take care that the invention as described and claimed in the patent specification, does not fall within the ambit of the exclusions and also satisfies the benchmarks of novelty, inventive step and utility / "capable of industrial application", so that a patent application is appropriately defended during its prosecution in a patent office for its grant and further survives future challenges to its validity in diverse jurisdictions. Another important feature of a patent is its enforcement. In this regard the claims construction and interpretation of the claims in a patent specification would determine whether an invention is infringing the patent or not. Drafting a patent specification is therefore an art that needs to be cultivated.

i. Novelty of an invention for example in the EPO, can be established when there is no evidence that the same invention has ever been described before. With reference to nanotechnology, the mere scaling down in terms of size of an entity (material, device, etc) does not meet the requirement of novelty. For example, a smaller version of a known device is considered new if it shows the same effect as the bigger one, but to a greater extent, such that it is reasonable to assume that the size was selected on purpose. In general, if there is a technical effect that is enhanced in a selected sub-range, the device is new and not just a part of the prior art.

The European Patent Office (EPO) defines nanotechnology as follows:

The term nanotechnology covers entities with a controlled geometrical size of at least one functional component below 100 nanometers in one or more dimensions susceptible of making physical, chemical or biological effects available which are intrinsic to that size [refer to the EPO Brochure "Nanotechnology and Patents",

http://documents.epo.org/projects/babylon/eponet.nsf/0/623ECBB1A0FC13E1C12575AD0035EFE6/$File/nanotech_brochure_en.pdf).

Claims based on the novel properties of nanotechnology inventions often distinguish new claims from prior art due to the different features, characteristics, and properties at the nanoscale that did not exist at the macro scale. Nanotechnology inventions often exhibit unexpected, size-dependent properties that result in the very novelty of the invention.

Article 54 of European Patent Convention (EPC) describes novelty as follows:

"(1) an invention shall be considered to be new if it does not form part of the state of the art; (2) The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application; and (3) additionally, the content of European patent applications as filed, the dates of filing of which are prior to the date referred to in paragraph 2 and which were published on or after that date, shall be considered as comprised in the state of the art."

The EPO developed three criteria which must be fulfilled for a sub-range which is selected from a larger parameter range, to be regarded as novel:

- The selected sub-range must be narrow in comparison to the known range;
- It must be sufficiently far removed from examples that illustrate the known range in the prior art; and
- It must not provide an arbitrary specimen from the prior art (i.e., not a mere embodiment of the prior description but another invention).

In the EPO Board decision T 0006/02 (Photodegradable Cellulose Ester Tow) case, the increased photo degradability of cellulose ester by the inclusion of nano-particle size Titanium Dioxide was regarded as novel since a generic disclosure like plastics materials as laid down in the prior art does not generally take away the novelty of any specific example (cellulose esters) falling within that disclosure.

In the EPO Board decision in the T 0915/00 (Nanocrystalline Metals) Case, the nano-crystal nickel material, taken by electrode position and having crystalline size of less than 11 nm, was considered novel over a distinguishingly identical material disclosed in the literature, constituted by macro crystalline Nickel obtained by electrode position.

In the EPO Board decision T 0509/92 (Dipeptide Crystals) Case, the Board was of the opinion that there was no disclosure in any of the said prior art documents of aspartame type IIa crystals having the given X-ray attributes and moisture content and hence novelty was acknowledged.

An article titled "*Patenting Nanotechnology: Exploring the Challenges*" in WIPO Magazine, April 2011, discusses aspects of nanotechnology and patenting (http://www.wipo.int/wipo_magazine/en/2011/02/article_0009.html). In the section related to novelty it refers to EPO's approach to assessing novelty especially related to "selection inventions", in which it is essential to ensure that the overlap is narrow relative to the larger prior art range, sufficiently far removed from the larger range and indicative of an invention, for example, by exhibiting a new or unexpected effect that occurs only

within the selected sub-range. The new effect does not, of itself, render the sub-range novel; rather, it permits the inference that the sub-range has been specifically selected to provide a technical advantage or resolve a technical issue in the prior art and that it is, therefore, novel. Additionally, the EPO assesses the relevance of the sub-range to prior art documents by asking whether a person skilled in the art would seriously contemplate applying the technical teachings of the prior art in the range of overlap.

When nanoscale inventions exhibit properties that are, in some measure, unanticipated or different from those found in larger scale prior art, exceptions have been made. For example, in BASF vs. Orica Australia, the EPO's Technical Board of Appeals (TBA) held that a prior patent which disclosed polymer nanoparticles larger than 111 nms did not destroy the novelty of a subsequent application by Orica for nanoparticles smaller than 100 nms. Orica's smaller particles exhibited remarkably improved technical properties resulting in a glossier coat compared to the larger particles protected under the prior patent. The difference in properties was held to be sufficient to impart novelty. But does an invention lack novelty if it claims to use particles in a range of sizes that overlap with those disclosed in the prior art? Generally, even the slightest overlap is sufficient to destroy novelty but exceptions have been liberally applied to nanoscale inventions.

The WIPO article also refers to the decision of the technical board of appeals in which the TBA applied this measure in a recent case involving Smithkline Beecham Biologicals vs. Wyeth Holdings Corporation. The question was whether Smithkline's patent application on a Hepatitis B vaccine adjuvant lipid measuring 60-120 nms lacked novelty in light of a prior patent on a similar adjuvant with particles measuring 80-500 nms. The TBA found that Smithkline's patent was novel because the overlap was:

- narrow - only 10% of the larger range in the earlier patent;
- at the extreme lower end of the prior art range; and
- exhibited significantly improved adjuvancy – the smaller particles resulted in an unexpected and favorable shift in immune response.

Moreover, the prior art gave little guidance on how to prepare the smaller particles. A skilled person who followed the vaccine supplier's protocol would have produced particles of between 115 and 951 nms. The technical teachings in the prior art were, therefore, not considered relevant to Smithkline's patent application.

However the German Federal Supreme Court ("BGH") in a series of rulings established the doctrine (contrary to the EPO guidelines) that any parameter range which lies within an already known parameter range lacks novelty and therefore patentability. Specifically, the BGH reasoned that, "[i]n accordance with the rules of arithmetic, the naming of a numerical interval represents a simplified notation of the numerous possible values which lie between the minimum and maximum values." Thus, with the disclosure of a particular range, all values lying between the minimum and maximum values and all sub-ranges are considered to be disclosed as well. Patentees should therefore be aware of both the European and the German patentability criteria when drafting their European claims and, if necessary, introduce additional claims specifically designed for enforcement in Germany ("*The Validity*

of European Nanotechnology Patents in Germany" by S. R. Huebner, *Nanotechnology Law & Business*, 353-357, Fall 2008,

http://www.brainguide.de/upload/publication/0a/o4ey/e73b66792f7f5a8c57301abde76593371366319805.pdf).

In order for a claim to be regarded as novel in Germany,

- It must be delimited against the prior art by an additional feature which does not represent a numerical selection such as by directing the claim not to the nanoproduct itself, but to the use of the nano-product for a certain technical purpose, if this use has not yet been made known to the person skilled in the art; and
- Even if a selected sub-range is regarded as disclosed by the arithmetic doctrine of the BGH, if the person skilled in the art has no way of actually obtaining the product described. For example if an inventor, together with a nanomaterial or nanodevice, also invents a new method of nanofabrication, and substantiates that the product, in the defined size range, can only be produced with this method, the inventor would be entitled to protection for the method as well as for the product, even if the latter is claimed in terms of a numerical selection invention.

This is an example of how even in TRIPS compliant patent systems within a region can vary based on the interpretations of the different institutions involved in the policy and implementation of the patent system in that country / region.

Title 35 of the United States Code and the corresponding rules organized in Title 37 of the Code of Federal Regulations. 35 U.S.C. §§ 101 et seq. and 37 C.F.R. §§ 1.1 et seq. Section 101 of the Patent Laws sets the novelty criteria in terms a few negatives that -

A person shall be entitled to a patent unless:

a. The invention was known or used by others in the USA, or patented or described in a printed publication in the USA or a foreign country, before the invention thereof by the applicant for patent, or
b. The invention was patented or described in a printed publication in the USA or a foreign country or in public use or on sale in the USA, more than one year prior to the date of the application for patent in the United States, or
c. He has abandoned the invention, or
d. The invention was first patented … or was the subject of an inventor's certificate … in a foreign country prior to the date of the application for patent in the USA on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or
e. He did not himself invent the subject matter sought to be patented.

The United States Patent and Trademark Office (USPTO) created a new class for "nanotechnology" inventions…Class 977 (http://www.uspto.gov/web/patents/classification/uspc977/defs977.htm) defining "nanotechnology" as areas "related to research and technology development at the atomic, molecular or

macromolecular levels, in the length of scale of approximately 1–100 nanometer range in at least one dimension, and that provide a fundamental understanding of phenomena and materials at the nanoscale and to create and use structures, devices, and systems that have novel properties and functions because of their size."

Thus, the nanotechnology definition implemented by the USPTO requires size-dependent properties to be included in the 977 Class and therefore patent applicants must include some indicia of inclusion into that size range that results in a novel property exhibited by the claimed invention.

Critical study of prior art is therefore an essential step for the evaluation of inventions for their novelty. One has to identifier and decipher the essential elements of an invention and map them against each of the relevant prior art to establish whether these identified elements are present in any documents / single source in the public domain. A single prior art even without expressly disclosing all of the elements in a claim may come on the way of patentability of an invention. The elements of the claimed invention may be inherent in a disclosed composition or process and is said to anticipate the claimed invention under the doctrine of "inherent anticipation." For this doctrine to be applicable, the anticipatory inherent feature, process, or result must be consistent, necessary, and inevitable in the single prior art and not merely "possible" or "probable". This means that a person skilled in the art would recognise such an anticipatory feature based on his knowledge of the subject and matter disclosed in the prior art. It must be appreciated that one is not allowed to consider a combination of documents (mosaic of documents) in the prior art for purposes of assessing novelty. For novelty consideration only a single prior art must be taken into consideration.

ii. Inventive step

Section 35 U.S.C. § 103(a) of the US Patent Act recites in part:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Unlike in the case of novelty considerations, where a single prior art reference must disclose every element of a claimed invention in order to be anticipatory, the inventive step requirement permits the combination of several references to create the claimed invention if it would have been obvious to a person of ordinary skill at the time the first patent application was made related to the invention (priority date).

The USPTO takes into consideration the following aspects while assessing inventive step (non-obviousness): (1) determining the scope and content of the prior art; (2) ascertaining the differences between the claimed invention and the prior art; (3) resolving the level of ordinary skill in the pertinent art; and (4) evaluating evidence of secondary considerations. 1) the prior art reference (or references, when combined) must teach or suggest all the claim limitations; (2) the combination of references must teach the predictable use of prior art elements according to their established functions; and (3) there must be a reasonable expectation of success in combining the teachings of the references.

The US Supreme Court in KSR International Co. vs. Teleflex Inc. 33 (KSR) with regard to the inquiry as to the determination of obviousness stated that the following errors must be avoided:

- holding that "courts and patent examiners should look only to the problem the patentee was trying to solve";
- assuming "that a person of ordinary skill attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem";
- concluding "that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try"; and
- applying rigid "preventative rules that deny fact finders recourse to common sense"

In Procter and Gamble Company (P&G) vs. Teva Pharmaceuticals USA, Inc. (Teva) the Federal Circuit (though in a case related to nanotechnology), applying KSR's teaching, affirmed that "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound". The Court then added that the patentee, if challenged for obviousness, may rebut relying on unexpected results by demonstrating "that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected".

With specific reference to nanotechnology patents, the Court may be guided by additional consideration, to determine whether, at the time of invention, a person having ordinary skill in the art would have had a "reason to attempt to make the composition" and "a reasonable expectation of success in doing so." The Court then relied on secondary considerations of non-obviousness including the commercial success of the claimed invention, and its satisfaction of long-felt need, and eventually held that the district court correctly found that secondary considerations supported a finding of non-obviousness.

Thus nanotechnology applications can pass the non-obvious test if the invention affords a significant technological advantage over prior art, for example, by enabling a skilled person to practice the previously disclosed invention at the nanoscale for the first time.

The U.S. CAFC held in King Ventilating Co. vs. St. James Ventilating Co., 26 F.2d 357, 359 (8th Cir. 1928) decided that when the only difference between the prior art and its claims was a recitation of relative dimensions of the claimed device, and a device having the claimed relative dimensions would not "exhibit qualitatively different phenomena" from the prior art, the claimed invention was not patentably distinct from the prior art'.

Article 56 of the European Patent Convention (EPC) lays down the guidelines for an invention to satisfy for purposes of arriving at whether an invention has an inventive step. Article 54(2) and (3) EPC defines the state of the art for the purposes of considering inventive step. Thus, according to EPO the question to consider, in relation to any claim defining the invention is whether at the priority date of that claim, having regard to the art known at the time, it would have been obvious to the person skilled in the art to arrive at something falling within the terms of the claim. If so, the claim is bad for lack of inventive step. The term 'obvious' means that which does not go beyond the normal progress of technology but

merely follows plainly or logically from the prior art, that is something which does not involve the exercise of any skill or ability beyond that to be expected of the person skilled in the art. If a range of the sizes is selected that is related to a definite technical effect and if the prior art holds no directions by which a skilled person can presume the selection, and then an inventive step is generally admitted. If however, in comparison the the existing prior art, the invention "would have been obvious for a skilled person to arrive at something falling within the terms of a claim, the unexpected result (would be considered) merely a bonus effect which would not confer inventiveness on the claimed subject matter. Further, when the technical effect is to be found within the selected range a similar effect may be found within a broader known range but with an unexpected degree. Under such circumstances, one has to assess "whether the skilled person would have made the selection or would have chosen the overlapping range in the hope of solving the underlying technical problem or in the expectation of some improvement or advantage. If the answer is negative, then the claimed matter involves an inventive step.

Some of these features have been put to test in the EPO by the Board of Appeals. It has to be noted that when the technical effect is to be found within the selected range a similar effect may be found within a broader known range but with an unexpected degree. In such cases, one has to take into account "whether the skilled person would have made the selection or would have chosen the overlapping range in the hope of solving the underlying technical problem or in the expectation of some improvement or advantage. If the answer is negative, then the claimed matter involves an inventive step.

In Smithkline Beecham Biologicals vs. Wyeth Holdings Corporation case that has already been referred to in the novelty section, the vaccine adjuvant was held to be inventive because of its unexpectedly improved effect and the fact that nothing in the prior art had suggested that a skilled person might consider reducing the particle size to achieve that advantage.

In BASF vs. Orica Australia also referred to in the novelty section, Orica's claimed invention involved manufacturing polymer particles at 100 nos or less by initiating polymerization at temperatures below 40°C. BASF argued that the invention was obvious because a prior patent had disclosed the same manufacturing process using temperatures below 50°C to yield particles averaging 111 nms or more. They argued that a skilled person exercising no inventive effort and repeating reactions on a trial-and-error basis for all temperatures between 0°C and 50°C would have derived sub-100 nm particles at temperatures below 40°C.

The EPO Board of Appeals rejected this argument on the basis that the prior patent suggested using temperatures not exceeding 50°C. While this "did not rule out the use of temperatures below 40°C, it was far from suggesting their use." Moreover, the patent was aimed at manufacturing particles larger than 111nms only. A skilled person following the teachings of the prior patent would not have used temperatures below 40°C or foreseen that lower temperatures would result in particles smaller than 100 nms. The TBA held that Orica's invention provided, for the first time, a method of creating smaller variants of polymer nanoparticles and was, therefore, inventive (Patenting Nanotechnology: Exploring the Challenges, *WIPO Magazine*, http://www.wipo.int/wipo_magazine/en/2011/02/article_0009.html).

A number of cases have been decided by EPO and its Board of Appeals with the question of whether miniaturization can be taken into account as an inventive step (Nanotechnology Patents…..An Overview of Nanotechnology Patents: A European Perspective, http://www.ukdissertations.com/dissertations/employment/nanotechnology-patents.php).

The EPO Board of Appeals case T-610/89, Siemens Ltd vs. Fujistu AG, 1991 related to field-effect transitions which consist of an insulating layer having thickness in the range of a 3 to 18 nm. When examining the contribution to the inventive step of this particular feature, the Board came to the conclusion that the claimed invention was merely a miniaturization to the thickness range of 3 to 18 nm for a dielectric film. Moreover the Appellant was not able to describe any special effects for the dielectric film having a thickness in the specified range. The Board regarded the claim as arbitrary and hence declared it as a non-inventive selection. There is also a similar decision regarding inventive step and miniaturization. In EPO Board of Appleas T-1056/96, Kabushi Kaisha Toshiba ex parte (2001), which related to a semiconductor device consisting of logic and memory components, the Board of Appeal stated that only miniaturization as such in not inventive.

In the EPO Board of Appeals T-70/99 case Affymetrix, Inc. vs. Trustees of University of Pennsylvania, 2003, dealing with fluid handling in micro fabricated analytical devices, the Board held that ‘top-down approach' and miniaturization is a general tendency in the field of biological research tools and inventive step can be characterized to smaller dimension just when a non-expected advantage or technical effects are found from the selected scopes. The board was convinced that the prior art disclosed in the other documents cited by the appellant did not come closer to the invention and that these documents did not contain any more relevant information.

In the T 0915/00 dealing with nanocrystalline metals, the relevant prior art described a continuous electroplating method. The claimed invention differentiated from this prior art in that it comprised passing direct current at pulsed intervals and under peak current density and timing conditions selected in the ranges set out in the claim so as to deposit nanocrystalline material of size less than 100 nm on the cathode, instead of passing direct current in a continuous manner. The EPO Board of Appeals concluded that the skilled person had no obvious reason to foresee that the prior teaching could still be successfully extrapolated to structures smaller by at least two orders of magnitude, if not with the benefit of hindsight.

In the T 0453/97 dealing with antireflective coating for use in photolithography, the technical problem solved was to further reduce the optical reflectance of the antireflective film of titanium nitride disclosed in the prior art. The Board concluded that a skilled person could not be expected to discover the claimed range in an obvious way in the course of routine experiments he would perform when putting into practice the teaching of the prior art.

In the T 0952/01 dealing with method of coating a substrate the patent claimed the use of particles in the claimed size range of 20 to 70 nm as compared to the prior art which recommended a preferred size range of 100 to 500 nm and therefore clearly taught away from the use of particles below 100 nm.

2.2 Capable of industrial application/usefulness/utility/susceptible to industrial application

As mentioned earlier, an invention in addition to being novel and having an inventive step must also be capable (susceptible to) of industrial application (be "useful", show credible utility). Patent laws in all countries has such a requirement and it is mandatory for a patent specification claiming any process, machine, manufacture, or composition of matter, or any improvement to show that the invention has a specific, substantial, and credible utility where credibility is measured from the perspective of one skilled in the art.

In the early days of biotechnology, several gene patents were granted by various patent offices on the basis of potential or "indicated uses". This was subsequently been substituted by the requirement of "credible utility" especially in the USA.

Article 57 of the EPC provides that "An invention shall be considered as susceptible of industrial application if it can be made or used any kind of industry, including agriculture." The EPC requires that to be patentable an invention must be industrially applicable. The industrial application must be particular and substantial, thus general industrial applications alone will not enough. A patent gives a monopoly to the owner of the patent and hence it is to be qualified that the real-world will get benefit from the invention. The invention must be real, not only supposition or science fiction.

Nanotechnology is still in its growth phase and several observations made in this field (especially involving nanomaterials / devices) may have potential applications that patent applicants may like to stake their claim on and therefore demonstration of credible utility could be problematic in some cases.

2.3 Who qualifies as a Person Skilled in the Art……

We have already seen that "the person skilled in the art" is central in the determination of novelty, inventive step and sufficiency of disclosure in a patent system. The issue therefore lies in arriving at a comprehensive definition of "the person skilled in the art". The person skilled in the art need not be "an expert" in the art. He could be an ordinary practitioner with average skill not engaged in creative thinking but aware of what was common general knowledge in the art at the relevant date. This means that if relevant documents from the prior art were made accessible to him at the date of first filing a patent application (priority date) and had at his disposal the normal means and capacity for routine work and experimentation, he would have arrived at the claimed invention without undue experimentation. The skilled person has to be assumed to lack the inventive imagination to solve problems for which routine methods of solution did not already exist.

Nanotechnology is a growing multidisciplinary science and technology cutting across diverse industries and therefore arriving at the perspective of "the person skilled in the art" causes considerable difficulties. Can "a single person" with knowledge in a monodisciplinary field be considered as a person skilled in the art for the purposes of determining the novelty, non-obviousness sufficiency of disclosure, etc in a patent application related to nanotechnology? Should one consider "a multidisciplinary team of persons" be considered as "the person skilled in the art" while dealing with patents / patent application

in nanotechnology? For example if a patent application deals with the use of "nanowires" in complex biotechnological diagnostics should the person skilled in the art be an average person from the field of "nano-materials" or "electronics", or "diagnostics" or should it be looked at from a perspective of "an expert from these fields", or "an expert from a multidisciplinary field combining some of the relevant discipline". The knowledge of the notional person skilled in the art has to be considered as that of a team of appropriate persons who appreciate the difficulties still to be expected when considering solution in the context of the problem. The person skilled in the art in such a case is highly contextual and therefore arriving at conclusions on novelty, non-obviousness (inventive step), "sufficiency of disclosure" in nanotechnology related inventions can become extremely contentious. This is precisely the reason for the variability in decisions on patentability by examiners in diverse patent offices, board of appeals and courts.

Such uncertainties pose severe challenges in the strategic drafting of patent applications in nanotechnology. Questions arise on:

- What is the set relevant prior art to be considered?
- How much to disclose in the patent specification?
- What experiments are adequate to illustrate the inventive step keeping one from not disclosing the "know-how" in a patent specification?
- How much explanation would be necessary in the patent specification to justify the inventive step?

2.4 Prior Art Search in nanotechnology

Due to the multidisciplinary nature of nanotechnology and cross industry utility, searching of relevant information and especially patents from the sea of literature has posed a major problem to researchers.

On March 24, 1971 a hierarchical system of classification of technologies was established in the form of The International Patent Classification (IPC) system. This was amended on September 28, 1979. All fields of technology were divided into eight sections, A to H, which were further subdivided into classes, subclasses, groups and subgroups. Eights sections were broadly classified as: A: Human necessities; B**:** Performing operations; transporting; C: Chemistry; metallurgy; D: Textiles; paper; E: Fixed constructions; F: Mechanical engineering; lighting; heating; weapons; blasting engines or pumps; G: Physics; and H: Electricity.

There were further sub-classifications of the technologies to aid in search of the relevant documents.

Nanotechnology inventions were classed into the B82B subclass of IPC, entitled 'Nano-Structures; Manufacture or Treatment thereof'. However this subclass, B82B did not cover chemical or biological structures per se, as these were dealt with elsewhere in IPC (IPC version 2009.01 available at www.wipo.int).

Interestingly, some of the patent offices in the world created their own classification systems or tagging codes for nanotechnology related patents. The USPTO defined sub class 977, EPO in its European

Classification System (ECLA) defined class Y01N and the JPO created the ZNM class.

The new IPC/ECLA **"B82Y"** scheme superseded **Y01N** codes almost exactly. The **B82Y** nanotechnology sub-class is divided into nine main groups, eight of which relate to specific areas of nanotechnology. Since the beginning of 2011, patent searchers have been able to use the "B82Y"sub-class to find documents relating to nanotechology in the world's patent databases. Table 1 provides the details of the B28Y Nanotechnology subclass.

Table 1: B28Y Nanotechnology subclass in IPC/ECLA

Code	Title
B82Y	NANOTECHNOLOGY
B82Y5/00	Nano-biotechnology or nano-medicine, e.g. protein engineering or drug delivery
B82Y10/00	Nano-technology for information processing, storage or transmission, e.g. quantum computing or single electron logic
B82Y15/00	Nano-technology for interacting, sensing or actuating, e.g. quantum dots as markers in protein assays or molecular motors
B82Y20/00	Nano-optics, e.g. quantum optics or photonic crystals
B82Y25/00	Nano-magnetism, e.g. magnetoimpedance, anisotropic magnetoresistance, giant magnetoresistance or tunneling magnetoresistance
B82Y30/00	Nano-technology for materials or surface science, e.g. nano-composites
B82Y35/00	Methods or apparatus for measurement or analysis of nano-structures
B82Y40/00	Manufacture or treatment of nano-structures
B82Y99/00	Subject matter not provided for in other groups of this sub-class

(Source: Nanotechnology and Patents, European Patent office, www.epo.org)

The USPTO established its own nanotechnology classification as Class 977 which provides patents with disclosures related to Nanostructure and chemical compositions of nanostructure; Device that include at least one nanostructure; Mathematical algorithms, e.g., computer software, etc., specifically adapted for modelling configurations or properties of nanostructure; Methods or apparatus for making, detecting, analyzing, or treating nanostructure; and Specified particular uses of nanostructure. The technology centers (TC) in the Class 977 include: TC 1600- Biotechnology & Organic Chemistry; TC 1700- Chemical and Materials Engineering; TC 2100 - Computer Architecture Software and Information Security; TC 2600 – Communications; TC 2800 - Semiconductor, Electrical, Optical Systems; TC 3600 - Transportation, Construction, Electronic Commerce; and TC 3700 - Mechanical Engineering, Manufacturing and Products.

Class 977 Digest I (Oct. 2004) provides a cross-reference art collection of 263 new subclasses. The creation of cross-reference Class 977 for Nanotechnology and its expanded 263 subclasses provide a consolidated area of search in nanotechnology related fields.

Thus prior art patents in nanotechnology can now be searched and mapped with relative ease both at the time of designing and implementing projects, and identifying the relevant patents for targeted nanotech

based applications for collaborations/ technology transfer via acquisition / licensing routes.

Some available free databases for patents searches are:

- European Patent Office (EPO) provides esp@cenet a network of Europe's patent databases, and access to machine translation of European patents for some languages. Database of the European Patent Office includes European Patents (EP), Patent Cooperation Treaty worldwide patents (WO), Japanese patents (PAJ) and patent applications in their original language. Has information on more than 30 million patents.
- U.S. Patent and Trademark Office (USPTO) provides General Information Concerning Patents and Basic Facts about Trademarks for researchers, inventors, and business people. Printable Patent and Trademark application forms are also available. Search the Patent Databases, and the Trademark Electronic Search System (TESS).
- Japan Patent Office (JPO) provides access to machine translations of Japanese patents.
- World Intellectual Property Organization (WIPO) provides PATENTSCOPE ® Search Service, a full-text search of published international patent applications, machine translations for some documents and a list of international patent databases.
- Korean Intellectual Property Rights Information Service (KIPRIS)
- State Intellectual Property Office (SIPO) of the People's Republic of China and China Intellectual Property Net (CNIPR) provide access to machine translation of Chinese patents.
- Other International Intellectual Property Offices that provide searchable patent databases are: Australia, Canada, Denmark, Finland,France, Germany, Great Britain, India, Israel, Netherlands, Norway, Sweden, Switzerland and Taiwan.
- Free Patents Online - Patents available in PDF format. Offers chemical search, Use the SureChem gateway to do a chemical patent search on full text collections for United States, European and PCT published patents.
- Google Patent Searchcovers patents made available by the USPTO from the 1790s to present date. Search the full text of U.S. patents; use Advanced Patent Search to search by various criteria including patent number, inventor, and filing date. Does not include patent applications, international patents, or U.S. patents issued over the last few months. Patents can be downloaded as PDF.
- Patents Online - A free resource available through Patents Online Pty Ltd.

A search example:

Espacenet (http://www.epo.org/searching.html) offers free searching of its databases Searches more than 80 million patent documents worldwide, containing information about inventions and technical developments from 1836 to today. The EPO brochure describes the various search options such as "smart search", "advanced search" and "classification search" (http://documents.epo.org/projects/babylon/eponet.nsf/0/4E8744EB66E8F944C12577D600598EEF/$File/espacenet_brochure_en.pdf).

Targeted searches in any field including nanotechnology can be conducted using appropriate key words and the nanotechnology classification system to identify the most relevant patent documents related to a defined subject matter.

Thus by putting the keyword "CNT":

- in the "smart search option one obtains 4453 hits,
- Entering the same key word in the field "title and abstract" in the advanced search option one obtains 4476 hits,
- Narrowing the search to the next set of key words "CNT and manufacture" one obtains only 84 hits, and
- Conducting the same search using "CNT" in the "title and abstract" field and the classification number B82Y40/00 in the field "IPC" one obtains 100 hits.

The extra 16 hits in the "D" search as compared to the "C" search option is that the search also captured preparation, treatment in addition to manufacture as one had used the classification system B82T40/00 covering manufacture and treatment of nanostructures.

Similar searches may be conducted in the other online free data bases indicated above.

The brochure titled "Guide to Technology Databases" published by WIPO provides a comprehensive review with details of searching techniques, including the nature of output from each database (free and commercial databases) that can be used to conduct appropriate searches (http://www.wipo.int/export/sites/www/freepublications/en/patents/434/wipo_pub_l434_11.pdf).

2.5 Drafting of patents in nanotechnology

A patent document generally is structured as follows though there may be variations in the contents of each section and the manner in which the contents of each section are drafted depending on the jurisdiction in which the patent application is filed:

- **Title**: related to the invention and subject matter of the patent specification
- **Field of the invention**: the subject matter / field of the technology in the context and invention being described in the specification helping to outline the scope of the invention and its purpose
- **Background of the invention**: statement of the problem, describing the state of art (prior art), the shortcomings of the prior art in the context of the problem being addressed, possible technology gaps and unmet needs with reference to the prior art, identification of new opportunities in terms of applications, uses, adaptions, etc.
- **Objects of the invention**: creates the scope of the subject matter being addressed, provides the options starting with the broad aspects of the invention and then providing various aspects of the invention, its variants within the same inventive concept. These are generally expressed through multiple statements. This section therefore contours the invention.
- **Detailed description of the invention**: Includes description of the invention by way of

disclosures with enabling examples to illustrate the best mode of performing the invention with reference to formulae, figures and tables as appropriate so that the invention can be reproduced by a person skilled in the art without undue experimentation. The essential features and the option features are also described. The disclosures have to be "enabling" though not disclosing knowhow / trade secrets. It is recommended that a section defining the terms used in the specification is advisable especially in the field of nanotechnology (as different people interpret terms differently) without which the usage of the term may be considered to be ambiguous. Putting a term in quotation marks followed by a definition of that term is the safest way to ensure that the term will be interpreted in the manner intended by the applicant. Thus, the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs the interpretation.

- **Claims**: construction of claims is tricky and a lot of care has to be exercised while claiming all the essential features of the invention for effective protection and enforcement. The claims provide the boundary of protection and hence fencing of the invention has to be crafted to survive any future attack of invalidation, narrowing, etc. Generally there are one or more "independent" claims directed to the essential features of the invention. "Add on features" to the "essential features" are claimed as a set of "dependent claims". Dependent claims are appropriately linked to the independent claims (or within themselves). The set of independent claims and their strategic interlining provides the protecting web to the invention. It ought to be appreciated that the claims have to be supported by the disclosures in the patent specification. If the claims are made too broad, then they may encroach into some existing prior art and if the claims are made too narrow, the protection of the invention then gets narrow and it becomes easier for others to work around the claims and avoid falling into the ambit o the claims. As the field of nanotechnology spans across disciplines and integrates diverse aspects of material properties, processes, functions, constructions, applications, software, devices, etc, it is often difficult to construct claims that are most appropriate to protect the invention, simultaneously preserving the unity of invention.
- **Presentation of the table and figures**
- **Abstract with a representative figure** (where appropriate)

In addition to these, a patent document would have the necessary bibliographic information as to the names of the inventors, assignee if any, date of filing, the country in which the application is filed, international patent classification to which the subject matter belongs, the date on which a patent application has been published (after 18 months), date of grant, etc.

2.6 Global scenario in nanopatenting

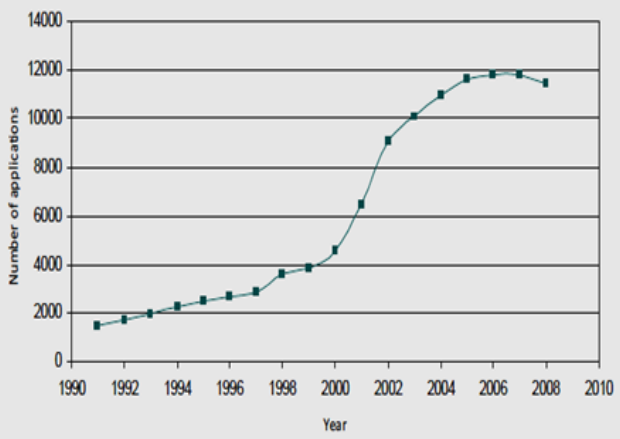
Patenting the inventions in this domain has been an accepted trend as strategic ownership of knowledge and transaction of owned knowledge in nanotechnology development, transfer and commercialisation has played a dominant role. Over the years, densification of the nano patent landscape offers challenges

needing deft handling and management of IPR portfolios, business processes, negotiations, unblocking routes restricted by patent and especially by overlapping claims through planned transactions and pooling of IPR and other resources between the multitudes of stake holders in the nano value chain to enable full exploitation of the available knowledge and technologies to ensure affordable products in the market place for the consumers. In recent times, challenges to patent validity, challenges to patent ownership, infringement related litigations and request for re-examination are also on the rise. These create uncertainties in freedom to operate.

Figures 2-5 present the patenting trends in nanotechnology as reported in Observatory Nano Fact Sheets.(http://www.observatorynano.eu/project/filesystem/files/ObservatoryNANO%20Factsheets%202011.pdf)and in Observatory Nano Briefing No. 20 August 2011 (http://bwcv.es/assets/2011/9/1/Briefing_No.20_Patents__An_indicator_of_nanotechnology_innovation.pdf)

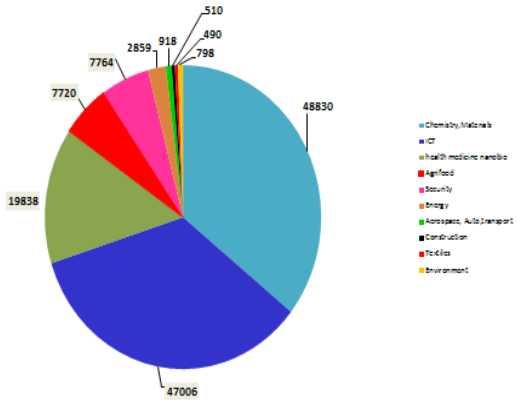
As seen in the figures, the United States, Japan, and the European Union have the largest share of the nanotechnology patent applications, with 47%, 29%, and 20% of the global filings respectively. However the Republic of Korea and China though late starters in this filed are growing rapidly and are expected to soon catch up with the lead nanotechnology nations and are expected to play significant role in the nanotechnology markets.

http://www.observatorynano.eu/project/filesystem/files/ObservatoryNANO%20Factsheets%202011.pdf

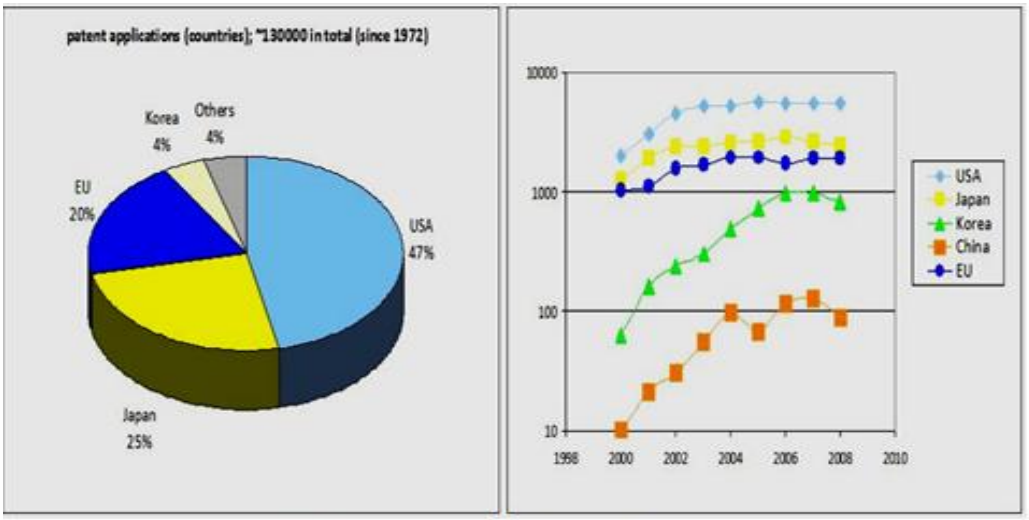


Patent Applications In Nanotechnology

[Observatory NANO Factsheets, March 2011]



http://bwcv.es/assets/2011/9/1/Briefing_No.20_Patents__An_indicator_of_nanotechnology_innovation.pdf



Observatory Nano Briefing No. 20 August 2011
http://bwcv.es/assets/2011/9/1/Briefing_No.20_Patents__An_indicator_of_nanotechnology_innovation.pdf

Figures 2-5: Patents landscape in nanotechnology

However, it may be noted that the number of patent applications have begun to plateau since 2005, possibly due to rising costs, global economic recession, and increased risks. In 2012 the USPTO published some 4000 patents under its class '977 – nanotechnology' as compared to 3439 in 2011, 2770 in 2010 and 1449 in 2009.

It is estimated that about 20% of nanotechnology patents are owned by universities. As patents resulting from upstream research generally have the potential to claim broad patents covering core building blocks needed to implement downstream nanotechnology applications, they have significant ramifications on the development and commercialisation of nanotechnology enabled product, devices, systems, and manufacturing processes. Looking at patent filings in various fields, nanoenabled products dealing with chemistry & materials, ICT, health, medicine, nanobio, agri foods and security are lead areas followed by energy, aerospace, automotive and transport applications, Construction, textiles and environment.

The intense commercial interest in patents is indicated by a significant increase in the number of patent filings by the corporate world with a rapid shift in the ratio (R) of corporate nanotech patent applications to the corporate nanotech publications in a short time domain. "R" of ~0.4 in 1999 grew to ~0.8 to 1.1 in 2003 and further to 1-1.5 in 2006/07 demonstrating definitive corporate interest in commercial implementation of nano-concepts in novel products and processes. It is clear that the corporate world was beginning to consider patents in the nanospace as a valuable tradable asset (Philip Shapirab, Luciano Kayc in http://stip.gatech.edu/wp-content/uploads/2010/09/commercialization-nano-2010-8final.pdf).

As convergent applications based on nanotechnologies evolve, incremental innovations lead to the filing and granting of multiple overlapping patents from competing groups. Such a phenomenon results in regions of high density growth of protected domains in the nanotechnology patent landscape (nanoscape) known as "patent thickets". Traversing through the "patent thickets" is often a very painful exercise as one may have to consider negotiating and settling issues with several patent and patent holders before launching a nano-enabled product in the market.

2.7 IPR transactions including enforcement of IPRs

While conducting a due diligence of the IPR landscape in a particular subject matter, it is advisable to consider all options such as "working around the IPRs" to avoid infringement, licensing of the relevant IPRs from the IPR owner(s), buying off the relevant IPRs, cross-licensing one's IPRs against other's IPRs leading to bartering of rights, challenging the validity of the IPRs that act as barriers to market entry, setting up joint ventures, establishing collaborative R&D, transferring / acquiring manufacturing rights, acquiring / in-licensing the knowhow, etc. It is imperative to give a careful consideration to nanotechnology IPR transactions before embarking on a nanotechnology venture. Many companies find that they cannot successfully manufacture or commercialize a product incorporating nanotechnology without facing overwhelming potential infringement issues from a variety of IPRs.

These aspects are being illustrated using patents as an example of IPR. However the similar approaches have to be followed for the other forms of IPR (Figure 6).

As mentioned earlier, a patent is a grant by sovereign or state to a person giving exclusive right to stop others from making, using, exercising and vending including offering for sale, or selling an invention for a limited period, in exchange for disclosing the invention in a patent specification such that any person trained in the said art can reproduce the invention.

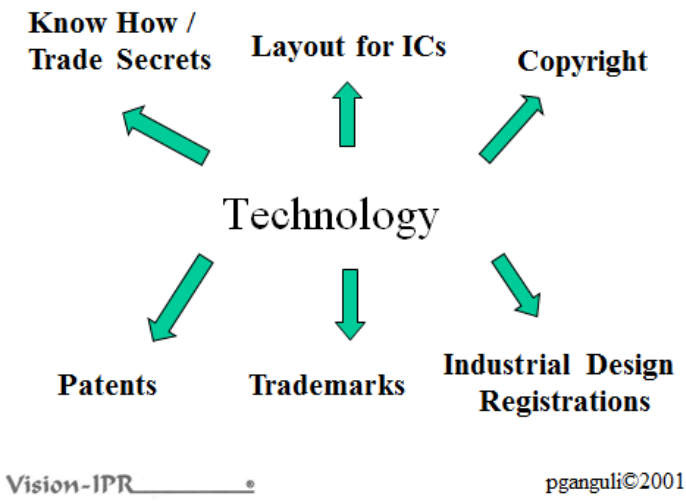


Figure 6: Intellectual property rights associated with technology innovations

A patent is therefore territorial and patent infringement requires a person to indulge in the forbidden activities within the countries in which the patent is granted and valid. Such an activity must fall within the claims of the patent, whether literally, or equivalently. Patent infringement is therefore an area that is dealt with by relevant courts in a country. The court (judge) decides what the claims of a patent mean and whether the alleged infringement falls within the ambit of the claims of the patent in question.

It is customary for a defendant [party who is the alleged infringer] to challenge the validity of the patent(s) of the plaintiff [party who has rights to the patent(s) who is seeking relief in the infringement action]. The plaintiff has to prove that the defendant is infringing the claims and the defendant in addition to denying infringement attempts to prove the invalidity of the patent(s) in suit.

The first problem therefore lies before the plaintiff to detect an infringing activity and mapping the infringement to the claims of the granted and valid patent. This is generally followed by the filing of a suit for infringement against the alleged infringer. The challenge before the defendant lies in the differentiation of the alleged infringing activity vis-à-vis the claims of the patent(s), possibly demonstrate that the alleged infringement is actually disclosed in the prior art and that the patent is invalid on grounds not being novelty, not having an inventive step, not capable of industrial application (no credible utility/ not susceptible to industrial application), not sufficiently described in the patent specification to enable a person skilled in the art to practice the invention.

One of the remedies to the Plaintiffs for patent infringement is injunction, which can restrict the defendant's freedom to operate within a particular field. Other reliefs include claiming damages as a result of the infringement(s) and destruction of the infringing goods. In some countries, patent infringements may even lead to criminal proceedings with reliefs in the form of imprisonment in addition to injunction and destruction of the infringing goods. The defendant may succeed in invalidating the patent or at least some of the claims and / or restricting the width of some or all the claims. In this way the defendant may avoid infringement and create its freedom to operate in the relevant market.

In several cases, the parties in an infringement suit settle their issues "out of court" in which case one has to take care to stay clear of and "anti-competitive" practices.

2.8 Licensing of patents…..an example of IPR transaction in nanotechnology

Licensing is an arrangement in which the owner of the IP (say a patent) retains the ownership of the IP (in this case the patent) and rents the right to someone under mutually agreed terms and conditions. The rent can be exclusive (in which case it is rented exclusively to one party) to non-exclusive (may be rented to many parties).

Licensing is therefore a relationship of co-operation between parties, whereby one party, the licensor, the possessor of IP asset permits the licensee to use his intellectual asset in return of negotiated compensation. The licensing arrangement could include assistance in the form of know-how, technical information or marketing skills. The nature of compensation varies as it is negotiated based on the strength / weakness/ usefulness of the IP. It is therefore imperative that the patent owner before

embarking on a licensing programme with other parties assess the strength his patent portfolio to strategize his bargaining posture. Similarly the potential licensee conducts a due diligence on the concerned IP to assess its usefulness in the context of technology and its relevance to the business. A licensing deal is reflection of the complimentary needs satisfied by a formal contract that appropriately and equitably addresses the mutual requirements within a framework that is enforceable within a specified jurisdiction.

A licensing agreement arrived at by negotiation between the concerned parties (licensor and licensee) broadly includes the following main features:

- Title of transaction
- Table of content
- Identification of parties and signatories to a binding agreement
- Recitals and preamble
- Definitions
- Period of agreement
- Warranties and representations from both sides
- description of rights
- Licensor's and licensee's obligations
- Clauses on IPR
- Confidentiality clauses
- Payments clauses
- Miscellaneous provisions such as non-assignment, good faith and best efforts, waivers, securities and pledges, liabilities, damages, non-performances, breach, force majaure, termination, maintenance, extension, survival clauses (i.e. clauses that will survive beyond the term of the agreement), litigation expenses, Transmission of the rights and obligations, etc
- Dispute settlement, arbitration, jurisdiction of courts, applicable law
- Closing signatures, date & place of signing the agreement, date of effectiveness of the agreement
- Addenda

The commercial considerations of licenses usually involve a combination of some of the features such as down payments, milestone payments, royalty payments, royalty layering, minimum royalty payments, cross-licensing(often free of obligation to pay license fees), etc. Other ways of compensating could be based on deferred returns, profits, successful application of technology, etc.

The IPR related clauses generally include the subject matter under consideration.

If software involved, the licensing agreement should define the accessibility to the source code, outline whether one be allowed to use only the compiled form for the applications indicated, field of use defined and / or will the licensee be permitted to use it for other applications if he develops them or gets them developed by someone else.

Copyright issues related to engineering drawings have to be clearly addressed. For example, who will own any changes to the drawings made during the course of use or if any developments that take place during the term of the agreement. In several cases, such issues are addressed in an annexure to the main agreement or as a separate agreement to deal in detail with the scope of related issues.

A typical licensing agreement related to nanotechnology is included as Annex 1.

3 Evaluation and valuation of nanotechnology

Investors in nanotechnology have been and shall continue to be wary of the risks associated with nanotechnology and therefore spend a lot of time assessing these innate risks.

Whatever the extent of commercialisation of nanotechnology, evaluation and valuation of nanotechnology continues to be an area of concern as none of the traditional modes of valuation of technologies and enterprises meet the spectrum of demands posed by nanotechnology. The nanotechnology value chain due to its peculiar nuances involving dynamic interplay with other technologies, uncertainties in quantitative temporal market demands and risks, evolving environmental and health concerns poses special issues in their realistic valuation. The process of valuation in nanotechnology gets even murkier due to the thickening and densification of the strongly interlinked and cross-correlated patent landscape especially in the fields that have begun to show high commercial potential.

Several technological risks act as risks and barriers to successful translation of the research and developments to the market place. Typical to nanotechnology innovations are tailoring of materials to exhibit specific behaviour in a reproducible manner, and control the properties of a material to ensure

that desired behaviour can be replicated at larger volumes beyond the laboratory and pilot scale. The next round of challenge lies in the successful integration of nanomaterials, devices, components as subsystems to create application specific integrated systems and manufacturing such systems with cost effective reproducibility and minimum or no failure rates.

Uncertain regulatory environments and public perceptions of nanotechnology's environmental, health and safety (EHS) risks and thereby legal and financial liabilities are also parameters that influence evaluation of the technologies investment decisions as it could have major implications on worker's health due to exposure to nanomaterials during their lifecycle.

3.1 Valuation of nanotechnology

Nanotechnology satisfies all the rungs of the IP valuation hirerarchy and hence is an essential and valuable component of the nano-business process.

Nano-enabled products are either a cross-pollination or hybridisation of diverse technologies, it becomes extremely difficult to quantify the contributions of each of the subsystems and therefore valuation of any nano-enabled product becomes extreme complex.

This ubiquitous nature of nanotechnology gets further reflected in granted broad claims in patents taking ownership of a set of technology-intersections and their effects. The tentacles of broad claims generally cover platform technologies and their ramifications. For example emulsions prepared with applications in cosmetic industry may find use in the agro chemical industry for insecticide or fertilizer sprays or as drug delivery systems in nanomedicine.

The patent claims for such inventions generally end up with broad claims on a broad class of emulsions with use cutting across several applications. Such patent claims create barriers for follow-on innovations and therefore become a subject matter for IP transactions such as licensing, cross-licensing, assignments, and legal battles involving challenges to their validity, patent enforcement through injunctions, claiming of diverse forms of royalties, damages, etc. Strategic planning is therefore essential before embarking on any business mission. Valuation of such nano-enabled products becomes an extremely complex process (Figure 7).

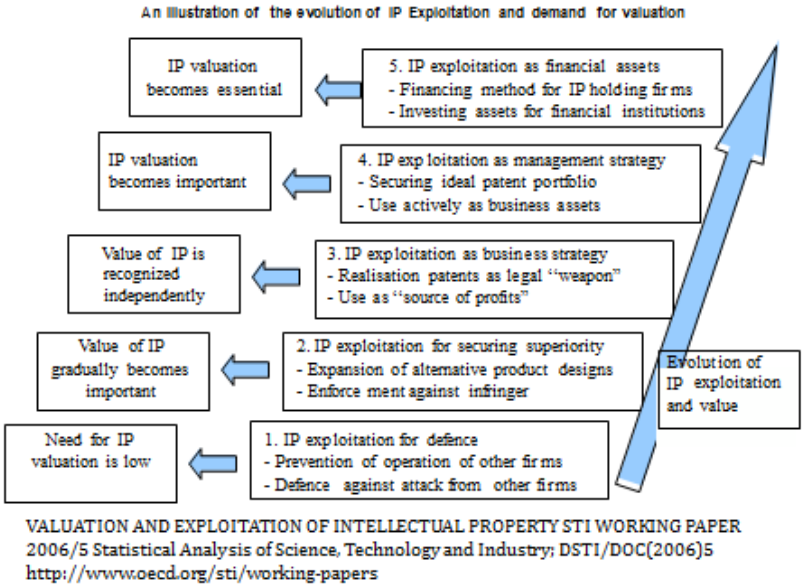


Figure 7: IP valuation hierarchy

3.2 Valuation methods

In a study titled "*The valuation of nanotechnology firms: A Brunswikian approach*" by Carl-Clemens Köhler in April 2009, the value relevance of non-financial variables in the equity valuation of nanotech firms were examined (http://pure.au.dk/portal-asb-student/files/5341/Master_Thesis_Carl-Clemens_Koehler.pdf).

The following key results can be deducted from this empirical study:

- Valuation of nanotech firms strongly depends on risks of non-financial factors.

- Customer loyalty of a firm is of high importance to the prospective development of nanotech firms.
- Prior experience and scientific skills/knowledge of management team members are highly relevant to the further development of a nanotech firm.
- Risks from product-related characteristics play an important role for the equity valuation of nanotech firms.
- Analysts are more successful at applying knowledge of nanotech company's soft factors consistently than at acquiring the information for estimating adequate market values of equity.

Several static and dynamic models for technology and enterprise valuation have been reported in literature.
(http://www.unece.org/fileadmin/DAM/ceci/ppt_presentations/2007/ip/christopher_kalanje.pdf)

Static models estimate value of accumulated intellectual assets at a point in time and neither differentiates temporal differences in the accumulated IP nor do they differentiate the differences among different categories of intellectual assets at the time of valuation.

Dynamic models on the other hand take into consideration the temporal difference in the accumulated intellectual assets (e.g. time value of money and risk of the forecast cash flow) and value of investments in intangibles each at a time.

The most used models in the valuation of intellectual property rights are:

- *Costs approach*: assumes that the value of an asset is based on the cost of constructing a similar asset, at current prices.
- *Market approach*: values an asset by determining the market prices paid for similar assets.
- *Income approach*: values an asset by calculating what the asset will earn in the future.
- *Hybrid approach*: combines any of the above approaches to value an asset.

While preparing a formal reporting of valuation of any technology and associated IP, in addition to the name and qualification of the values and the date of the report, it is essential to include the objective and scope of the valuation and any limitations or restrictions to its scope, description of the identified asset being valued, the date / period that was considered for the value determination, basis, approach and method of valuation with the underlying assumptions and limitations, and a conclusion of value.

3.2.1 Market approach

In this approach as the name suggests attempts are to arrive at a fair market value of the intellectual property / technology under consideration by striking comparison with a similar technology and comparable transactions in the market. The key feature is to try and arrive at a price the technology would attract a buyer in the market. Further, in the case of patents, one may also use indicators such as frequency of citations of the patent in other references (both in patents and journal publications) and royalty rates collected for comparable transactions. Thus one would have to depend on an active market

with documentation on exchange of comparable assets, access to price information at which assets are exchanged, and transactions that reflect market values.

A major limitation of this approach is that credible and reliable information on commercial transactions and their basis are generally not published in literature and hence setting reliable value based benchmarks for comparable transactions become questionable. In several cases, the publicly available market value of comparable transactions may have been influenced by non-value related factors such as the parties to the transaction not being fully informed, having had different negotiating skills, or fundamental differences between the assets being considered thereby resulting in either over-pricing or under-pricing the value of the intellectual property**.** Therefore arriving at a comparable market value of the technology under consideration is done on the basis of certain assumptions and adjustments that may not always be realistic.

Specifically with regard to nanotechnology, due to its unique and ubiquitous nature identifying a set of comparable transactions for purposes of valuation using the "market approach" is even more difficult.

Nevertheless, the process used to apply the market approach to the appraisal of intellectual properties may be summarized as follows (SmartPros, June 19, 2000):

- Research the appropriate market for information on sales transactions, listings, and offers to purchase or license comparable intellectual properties. Comparability is judged in relation to factors such as intellectual property type, intellectual property use, industry in which the intellectual property functions and the date of the sale and/or license.
- Verify the information by confirming that the market data obtained is factually accurate and that the sales or license transactions reflect arm's length market considerations. This verification procedure may also elicit additional information about the current market conditions for the sale and/or license of the subject intellectual property.
- Select relevant units of comparison (e.g., income multipliers or dollars per unit) and develop a comparative valuation pricing analysis for each unit of comparison.
- Compare guideline intellectual property sales and/or license transactions with the subject
- Intellectual property, using the elements of comparison, and adjust the prices of each guideline transaction appropriately to the subject property. If such an adjustment is not possible, eliminate the transaction as a guideline.
- Reconcile the various value indications into a single value indication or range of values wherein two or more value indications that have been derived from the guideline sale and/or license market data must be synthesized into an overall value estimate.

In the final step, the empirical data, the valuation analysis, and the result of each of the value indications needs to be summarized and reviewed in terms of the strengths and weaknesses of each guideline value indication derived and examine the reliability and appropriateness of the market data compiled and of the analytical techniques applied prior to arriving at comparable the market.

3.2.2 Income approach

The "income approach" is based on the calculated "present value" of the projected future income flow arising from the intellectual property (say the patent or a set of patents covering the technology) during its economic productive term. In general the economic productive term is less than the "term of the said intellectual property rights"

Various formalisms are used for this purpose that may be grouped into the following two analytical categories:

1. Direct Capitalization; and
2. Discounted Future Economic Benefits (DCF)

In a direct capitalization analysis, the appropriate measure of economic income for one period (i.e., one period future to the valuation date) is estimated and divided by an appropriate investment rate of return. The appropriate investment rate of return is called the capitalization rate. The capitalization rate may be derived for a perpetual period of time or a specified finite period of time, depending upon the expectations of the duration of the economic income stream.

In discounted future economic benefits analysis, an appropriate measure of economic income for several discrete time periods is projected into the future. This projection of prospective economic income is converted into a present value by the use of a present value discount rate. The present value discount rate is the investor's required rate of return over the expected term of the economic income projection period.

Arriving at the discount rate is a two-step process:

- Develop the discount rate applicable to the entire business, which includes a company-specific risk premium accounting for the company's unique risk differentials
- Isolate the discount rate applicable to the specific asset being valued, by identifying and quantifying the relative risks of investments in the Company's various assets and in similar assets measured in the open market.

The discount rate applicable to the intellectual property should reflect the rate of return an investor would require for an investment in the asset. For any individual asset, this rate must be determined in the context of the discount rate of the business overall. Conceptually, the discount rate for the business may be viewed as a weighted average of a series of discount rates applicable to the individual assets of the business from the least risky (e.g., cash, receivables) to the most risky (e.g., goodwill).

The capitalization rate, the rate used as the divisor in the Direct Capitalization Method, is derived from the discount rate and is determined by subtracting from the discount rate the projected average annual compound growth rate of an earnings stream. The reciprocal of the capitalization rate is the valuation multiple.

The discounted cash flow method (DCF) (Figure 8) allows an estimated future income flow to be converted to a present value by discounting future income estimates flow with an appropriately selected discount rate which is dependent on several parameters such as income stream either from product sales

or licensure of the patent, an estimate of the duration of the intellectual property's useful life, an understanding of the intellectual property specific risk factors. Economic factors such as inflation, liquidity, real interest and risk premium etc need to be accounted for in setting the parameters to arrive at the discount factor. Accounting parameters such as gross or net revenues, gross profit, net operating income, pretax income, net income (after tax), operating cash flow, net cash flow, incremental income, cost savings are to be taken into consideration in the derivation of the discount rate or capitalisation rate to arrive at the economic income.

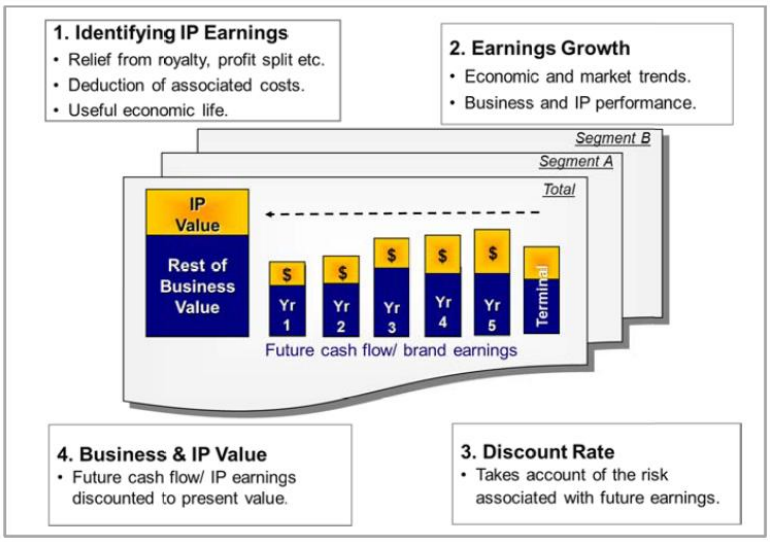


Figure 8: Discounted cash flow method

(Source: Intellectual Property Valuation and Royalty Determination by Tim Heberden (2011) http://brandfinance.com/images/upload/ip_valuation_royalty_rates.pdf)

In the capital asset pricing model (CAPM) or the build-up method that are generally used to estimate the discount rate are based on a basic summation concept which depends on the total return required on a long-term, risk-free investment, equity risk premium, and increments for risk differentials of the

particular business or investment.

These risk differentials result from risk factors that are specific to the business and related to its advantages and disadvantages over other competing entities in the market place. These factors should include, but are not limited to the industry, diversification of the licensing of the intellectual property, characteristics of the intellectual property, financial risks, diversification of the operations, lack of management depth, lack of access to capital markets, geographic diversification, risk of assets; and years in business.

An established intellectual property widely licensed may use an industry rate of return, while an intellectual property in an emerging technology area with high obsolescence may have a rate of return similar to venture capital.

Further, the calculations must take into account the isolated value to the income stream from the intellectual property under consideration from the aggregated income stream of the technologies under consideration. Such isolation would require:

- Incremental analysis — The estimation of the difference between (a) the amount of income the business would generate with the use of the subject intellectual property under consideration, and (b) the amount of income the same business unit would generate without the use of the intellectual property under consideration;
- Profit split analysis — The estimation of the total income that the business would generate from the use of the intellectual property rights under consideration where the total income estimate is allocated (in part) to the said intellectual property rights and (in part) to all of the other tangible and intangible assets that support the generation of the total income estimate; and/or
- Royalty income analysis — The estimation of the total amount of royalty income that the business could generate through the licensing of the said intellectual property rights.

The income approach methods are also commonly used with regard to infringement and similar damages analyses in courts. The income stream may be calculated as the income that the IPR owner lost (i.e., "lost profits") as a result of infringement or the income that the infringing party earned (i.e., "found profits") as a result of the infringement.

3.2.3 Cost approach

The cost approach is based on the assumption that a prudent buyer / investor would pay no more for an intellectual property than the cost to construct or develop an asset of equal desirability and utility / similar function which may be considered to be the value determined by aggregating the costs incurred in development of the asset (substitution). The cost-based approach seeks to measure future benefits of owning IP by quantifying the amount spent on developing an IP asset to its present form or the amount required to replace the future service capability of that asset. It ought to be appreciated that there is a non-liner relationship between the development cost of certain IP and its value as a lot of expense is incurred on R&D which includes a considerable amount of unsuccessful efforts that might be considered to be of negligible value. However such costs have also to be factored in while arriving at the replacement or substitution cost.

Factors that influence the costs are temporal factors such as supply and demand, externalities wherein gains or losses from external factors may accrue to intellectual properties, e.g. external conditions may cause a newly constructed intellectual property to be worth more or less than its original cost, functional Obsolescence leading to the depreciation in the value of an intellectual property due to its inability to perform the function or yield the utility for which it was originally designed, technological obsolescence resulting in a situation in which the value of an intellectual property gets reduced due to improvements in technology that make an intellectual property less than the ideal replacement for itself, economic obsolescence leading to the devaluation of the intellectual property due to conditions external to and not controlled by the current use or condition of the intellectual property.

Under the cost approach, a common formula for quantifying an intellectual property's replacement cost is:

Reproduction cost new = Replacement cost new - Curable functional and technological obsolescence

An intellectual property's deficiencies are considered curable when the prospective economic benefit of enhancing, or modifying the intellectual property, exceeds the current cost of the material, labour and time needed to change it.

Next, to estimate the intellectual property's value, the following formula may be used:

Value = Replacement cost new - Economic obsolescence - Incurable functional and technological obsolescence

An intellectual property's deficiencies are considered incurable when the current cost of enhancing or modifying the asset (in terms of materials, labour and time) exceeds the expected future economic benefits of improving it.

Each of the methods described above has their own weaknesses. The table 2 reproduced from the publication, "Valuation aand exploitation of Intellectual Property Rights (STI Working Paper 2006/5), Statistical Analysis of Science, Technology and Industry DSTI/DOC (2006)5, comprehensively summarised the comparative nuances of each of the methods described above.

Table 2: Comparison of the three main quantitative patent valuation approaches

	Cost approach	Income approach	Market approach
Advantages	• Objective and consistent • Reliability of historic cost data • If a recent acquisition cost of patent exists it is a reliable indicator of value	• Theoretically superior to other approaches as focused on future earnings or cash flow • Consistency can be achieved facilitating comparison across a patent portfolio • Widely accepted and concepts widely accepted and concepts widely understood	• Practical approach which makes use of prices actually paid for comparable assets • Variety of market-based approaches such as comparable companies, comparable transactions or a premium price-earnings-multiple approaches allow comparison
Disadvantages	• No correlation between expenditure on an asset and its value • Difficult to	• Requires subjective cash flow allocation • Translation of theory into practice requires assumptions which	• Given the uniqueness of patents, third party arm's length transactions

	distinguish between 'normal' operating expenses and patent investment expenditure • Subjective nature of estimate of costs of replacement and some patents may not be replaceable	are limiting • Relevant information is not always readily accessible from internal reporting systems	involving similar patents are infrequent • Transactions involving the shares of companies owning patents are more frequent but allocating value between the business and the patent is difficult
Typical use	• Only used in limited circumstances (e.g. when the replacement cost can be estimated with a reasonable degree of reliability and confidence). • Cost is, however, a relevant benchmark where a patent has recently been acquired	• Primary valuation methodology and the most widely used where information of an appropriate quality can be obtained. • The limiting nature of the assumptions needs to be understood and where possible scenario analysis should be performed	• Extremely important indicator of value, if information on recent transactions involving patents exists • In practice sufficient information is rarely disclosed and this methodology is used as a cross check on other more theoretical methodologies

In case of nanotechnology, most nano-enabled products are disruptive and so new, that present day market or sales data may not be available that can be used as the basis of future sales revenue. In cases where a nano enabled product replaces an existing product due to its superiority in functional performance, an appropriate factoring has to be incorporated in arriving at the discounting rate. Further, estimating the future risks associated with the nano-enabled product is also problematic as regulatory features with regard to nanotechnology are at an evolutionary stage at present.

3.2.4 Other valuation models

Web based technology valuation system

"A technology valuation model to support technology transfer negotiations" by Dong-Hyun Baek, Wonsik Sul, Kil-Pyo Hong and Hun Kim, *R&D Management*, Vol. 37, No. 2, 2007; http://www.researchgate.net/publication/228130296_A_Technology_Valuation_Model_to_Support_Technology_Transfer_Negotiations

Dong-Hyun Baek et al., in 2007 proposed a hybrid technology valuation model divided into three steps namely, "expected return analysis", "technology contribution analysis" and "technology valuation from buyer's perspective" represented in Figures 9 - 13.

The expected returns analysis (Step I) utilizes product market and cost structure analysis according to different technology types in order to calculate the amount of profit that can be created during a specific period. The amount of profit is then converted into its present value based on the discounted cash flow model.

Technology contribution analysis (Step II) calculates technology's degree of contribution (technology contribution coefficient) to expected returns by taking into account the technology's level of innovation and the characteristics of the industry it belongs. The technology contribution coefficient is then corrected to reflect technology's dominance, exclusivity, and limitations. The expected returns from Step I is multiplied by the technology contribution coefficient in Step II to produce returns contributed by technology, which is the objective value of a particular technology.

The technology valuation from the buyer's perspective (Step III) considers additional development costs, adjustment period and costs for commercialization, and dynamics of profit to assess the value of technology from the buyer's position. The decision on whether or not to purchase a particular technology depends on the comparison of this value to the returns contributed by technology calculated in Step II.

The publication by Dong-Hyun Baek et al describes each step in detail with the basis for the estimates of each of the parameters.

Technologies have been classified into three types based on their end effects namely , "new market creation technology" that contribute to profits though new products and services, "existing penetration technology" that contribute to profits through substitution of existing products and services and "cost structure improvement technology" that contribute to profits by improving cost efficiency.

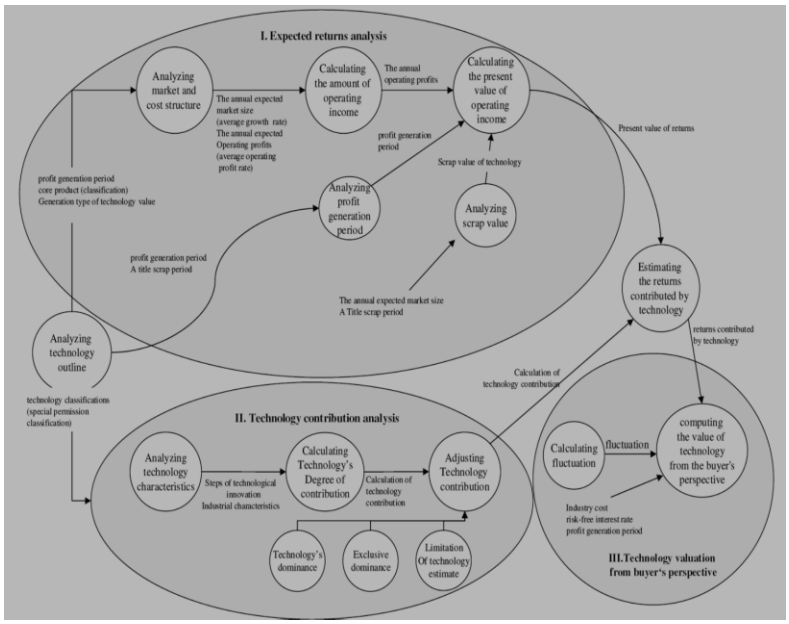


Figure 9: Technology valuation model

(Source: Dong-Hyun Baek, et al.)

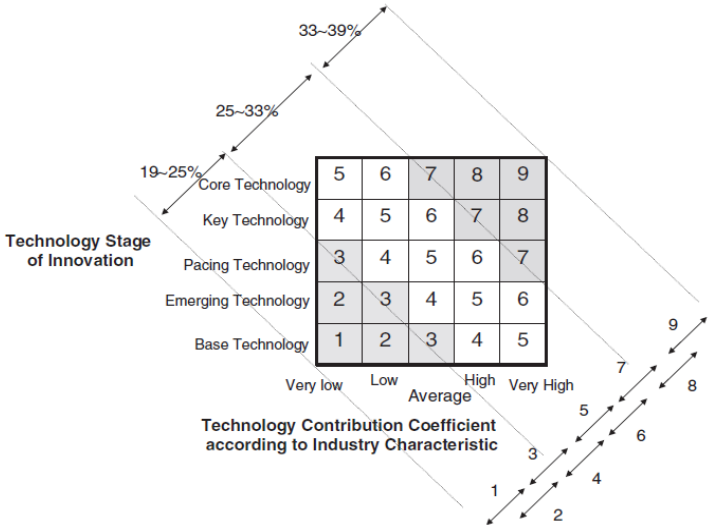


Figure 10: Matrix for technology's degree contribution

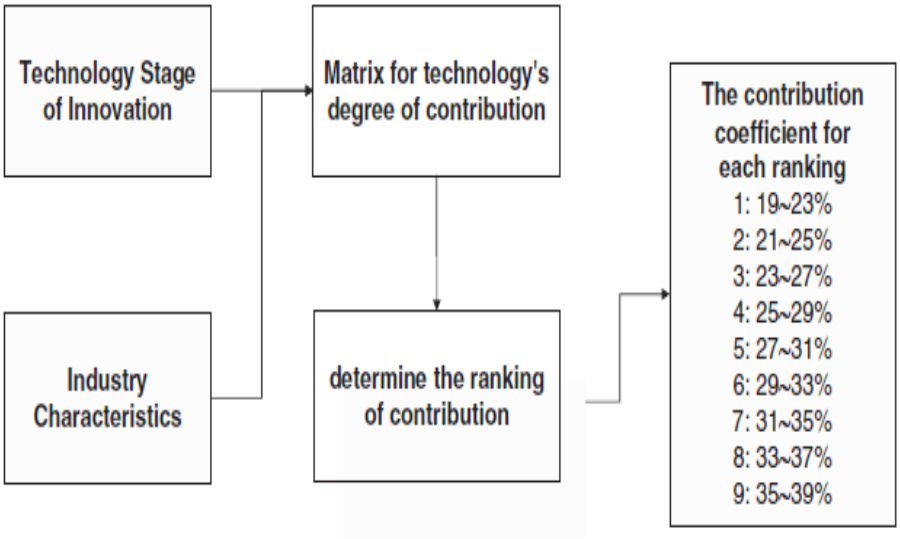


Figure 11: Calculation process for technology contribution coefficient

Level	Definition
(1)Basic	Low level of impact on competency. Relatively well-known and also commonly shared.
(2) Emerging	The potential influence on competitive power is uncertain.
(3) Pacing	The potential value has been proved, however, it has not been realized by end product or process.
(4) Key	Critical impact on the cost, quality, and performance of the product.
(5) Core	Critical impact on the cost, quality, and performance of the product. In addition, it is extendable to other industries as well.

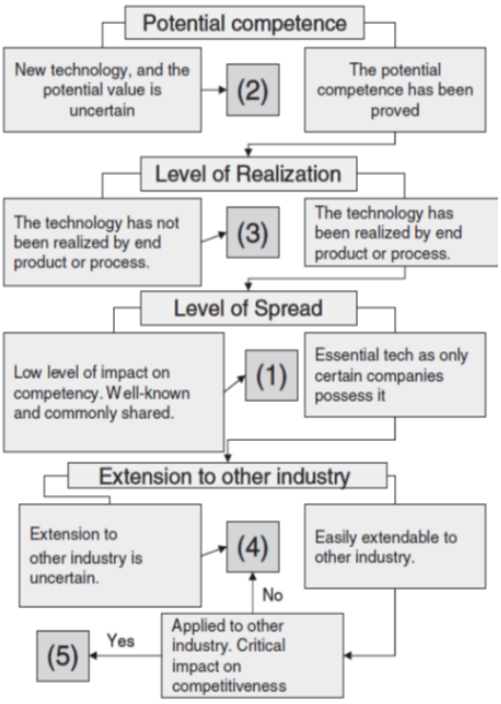


Figure 12: Logic to determine stage of innovation

$$V = N(d_1)S - N(d_2)Xe^{-rT}$$

$$d_1 = [\ln(S/X) + (r + 0.5\sigma^2)T] / \sigma\sqrt{T}$$

$$d_2 = d_1 - \sigma\sqrt{T}$$

V = the value of technology from buyer's position
S = the present value of expected returns from technology
X = the additional investment to commercialization
r = the risk-free rate
T = the time period for commercialization without losing rights to the technology
σ = the volatility of expected returns from technology
N(d) = the cumulative normal probability of unit normal variable d

Figure 13: Black–Scholes option pricing model modified by Dong-Hyun Baek et. al

This hybrid model has been applied to one of the technologies in Korea for the purposes of its valuation and the actual price at which the technology was traded was within the price range calculated using this technology valuation system.

A comparative methodology for estimating the economic value of innovation
A Report for DEFRA, UK, by Ben Walsh, Peter Willis, Alastair MacGregor, November2010 (http://www.oakdenehollins.co.uk/media/225/DEFR01_225_Methodology_full_Final.pdf)

Innovations in nanotechnology can have one of four effects on the current incumbent product and market place:

- The nano-enabled product does not extend the market of the incumbent;
- The nano-enabled product increases the size of the market compared to the incumbent;
- Enhanced functionality over existing products in a fixed market size; and
- Enhanced functionality over existing products with increased sales.

The developed methodology provides an approach to perform a comparative valuation between a nano-enabled product in terms of the relative benefit it produces *vis-à-vis* an incumbent product that is currently on the market which the nano-enabled product may replace.

The proposed method calculates the value over a set timeframe, exploring the benefits to the consumer and producer, as well as the wider benefits to society. It has been tested and validated through a series of case studies.

Equation (1) is used for the determination of the value added of a product:

$$\mathbf{V = PS + CS + E} \quad \text{.....(1)}$$

V is the Value Added; PS is the Producer Surplus; CS is the Consumer Surplus and E is the Externalities.

The Producer Surplus (PS) is the amount of money a producer of the nano-enabled products makes from its production and sale. PS can be determined from the equation (2):

$$\mathbf{PS = P - C} \quad \text{.....(2)}$$

P is the Sales Price of the product and C is the Unit Production Cost.

The Consumer Surplus (CS) is the value that the consumer takes from the product. This is equivalent to the value of the service the product provides less the purchase cost of the product. CS can be determined from equation (3):

$$\mathbf{CS = CV - P} \quad \text{.....(3)}$$

The Consumer Valuation (CV) is the value that the consumer places on the function of the product.

E denotes the externalities that are benefits and costs not directly experienced by either the producer or consumer of the product, but rather by an unrelated third party. These externalities are costs or benefits to the wider society and could be, e.g. environmental and social.

To compare a nano-enabled product with an incumbent non nano-enabled product, the value added of an incumbent technology needs to be subtracted from the value added of the nano-enabled product as ultimately the nano-enabled product replaces the incumbent. The (theoretic maximum) net value added of a product is:

$$\mathbf{NV = V_{Nano} - V_{incumbent}} \quad \text{.....(4)}$$

NV is the Net Value Added, Nano is the nano-enabled product, and Incumbent is the incumbent product.

These calculations must then be applied to each time period over which we expect the nano- enabled product would replace the incumbent.

Once the overall theoretic maximum net value added of the nano-enabled product has been determined, a few further steps are useful to reach a practical estimation of the benefits:

- Account for the phase-in of a product into the market over time (by modeling for diffusion); and
- Weight the valuation by the probability of successful launch of the nano-enabled product (by the choice of the discount factor).

It is possible that after the time of valuation the product will change from what was envisaged, or even that future advancements in technology will lead to the displacement or obsolescence of the nano- enabled product. These processes are difficult to predict, but are worth noting, as it may be necessary to revisit the valuations periodically.

Applying the principles discussed above, the steps of the methodology are:

1. Select the nano-enabled product
2. Define the functionality
3. Identify the incumbent product(s)
4. Select scenario
5. Market definition
6. Identify data requirements
7. Determine production costs
8. Determine sales prices
9. Establish market size
10. Determine externalities
11. Calculate surplus
12. Estimate economic valuation

The report details each of these steps and illustrates with examples from nanotechnologies on how to use the formalism.

Present Value After Evaluation ("PVAE")

"Reinterpreting Patent Valuation and Evaluation: The Tricky World of Nanotechnology" by Luca Escoffier (2011), Transatlantic Technology Law Forum, TTL Papers No. 8 (http://www.law.stanford.edu/sites/default/files/publication/205102/doc/slspublic/escoffier_wp8.pdf)
This proposed approach is an extension of the DFC method. The method attempts to reduce the arbitrariness in computation of the present value and therefore the output can only be used as a semi quantitative assessment prior to negotiations between the stakeholders for asset transacttions.

The method starts with the present value of a patent or technology obtained by the discounted cash flow method and then adds the following additional variables that are considered relevant to nanotechnology using a scale from 1 to 5 scale in which 1 is "poor" and 5 is "excellent":

- Patent relevance (it considers the relevance of the patent in the final product or process);
- Patent coverage (it considers the strength of the patent according to the claims and existing or potential litigation);
- Technology (it considers technology's future scenarios);
- Financing (it considers the attractiveness for investors);
- Regulation (it considers regulatory and legal barriers); and
- Market (it assesses the potential success of the product or process).

Patent Coverage and Patent Relevance are directly linked to the total present value of cash flows as opposed to the other variables that occupy a second layer of importance and provide an average output.

The PVAE model contains seven other assumptions namely: Growth rate (three variables); Discount rate; Royalty rate; Tax rate; Cost of goods sold (COG), overhead costs, etc.

As illustrations of the computation, the publication considers three scenarios:

i. All the variables are set on "excellent" (meaning that the technology is necessary to make the product or implement the process), that the claims of the patent have a wide and protectable breadth, that the technology is promising, and there are no regulatory and market barriers. Life expectancy of the technology is 15 years.
ii. All the variables are set at "3" thereby considering the technology to be of intermediate importance and that the said technology is not that crucial to the production of the product or the implementation of the process. It also implies that the claims of the patent have a medium breadth, that the technology is moderately promising, and that there might be some regulatory and market barriers. Life expectancy of the technology is 15 years.
iii. All the variables are set at "2" thereby considering the said technology definitely not crucial to the production of the product or the implementation of the process. It also means that the claims of the patent have a medium-low breadth, that the technology is not that promising, and that there might be some serious regulatory and market barriers. Life expectancy of the technology is 15 years.

The starting initial cash flow in cases i, ii and iii is considered to be of $100,000.

The assumptions in the three cases are as follows:

Growth rate (three variables): 1-5 years 7%, 6-10 years 10%, 11-15 years 5%; Discount rate 3%;

Royalty rate 8%; Tax rate 25%; and Cost of goods sold (COG) 30%.

The results are illustrated in the tables below:

Scenario i

PRESENT VALUE AFTER EVALUATION							
Patent relevance 1-5:	5						
Initial Cash Flow:	$100,000			Technology 1-5	Financing 1-5	Regulation 1-5	Market 1-5
Patent coverage 1-5:	5			5	5	5	5
Years:	1-5	6-10	11-15				
Growth Rate:	7%	10%	5%				
	Before Tax and CO	After Tax and COG					
Total of Cash Flows	$2,867,778	$1,505,583	Discount Rate	3%		Tax rate:	25%
Total PV of Cash Flows:	$2,192,010	$1,150,805	Royalty Rate:	8%		COG,etc.	30%
Total PV of Cash Flows Considering the Relevance of the Patent and Patent coverage:	$2,192,010	$1,150,805	Partial PVAE	$2,192,010	$2,192,010	$2,192,010	$2,192,010
Present Value of Royalties (after tax)	$107,226		PVAE Before Tax and COG:	$2,192,010	PVAE After Tax and COG:	$1,150,805	

Scenario ii

PRESENT VALUE AFTER EVALUATION							
Patent relevance 1-5:	3						
Initial Cash Flow:	$100,000			Technology 1-5	Financing 1-5	Regulation 1-5	Market 1-5
Patent coverage 1-5:	3			3	3	3	3
Years:	1-5	6-10	11-15				
Growth Rate:	7%	10%	5%				
	Before Tax and CO	After Tax and COG					
Total of Cash Flows	$2,867,778	$1,505,583	Discount Rate	3%		Tax rate:	25%
Total PV of Cash Flows:	$2,192,010	$1,150,805	Royalty Rate:	8%		COG,etc.	30%
Total PV of Cash Flows Considering the Relevance of the Patent and Patent coverage:	$789.123	$414.290	Partial PVAE	$473.474	$473.474	$473.474	$473.474
Present Value of Royalties (after tax)	$107,226		PVAE Before Tax and COG:	$473,474	PVAE After Tax and COG:	$248,574	

Scenario iii

PRESENT VALUE AFTER EVALUATION							
Patent relevance 1-5:	2						
Initial Cash Flow:	$100,000			Technology 1-5	Financing 1-5	Regulation 1-5	Market 1-5
Patent coverage 1-5:	2			2	2	2	2
Years:	1-5	6-10	11-15				
Growth Rate:	7%	10%	5%				
	Before Tax and CO	After Tax and COG					
Total of Cash Flows	$2,867,778	$1,505,583	Discount Rate	3%		Tax rate:	25%
Total PV of Cash Flows:	$2,192,010	$1,150,805	Royalty Rate:	8%		COG,etc.	30%
Total PV of Cash Flows Considering the Relevance of the Patent and Patent coverage:	$350.722	$184.129	Partial PVAE	$140.289	$140.289	$140.289	$140.289
Present Value of Royalties (after tax)	$107,226		PVAE Before Tax and COG:	$140,289	PVAE After Tax and COG:	$73,652	

Secnario	Total cash flow $	Total present value $	Total present value considering the relevance of the patent and patent coverage $	PVAE after tax, cost of goods sold and other expenses $	Royalties collected over time and their present value $
Scenario i	2.867.778	2.192.010	2.192.010	1.150.805	107.226
	The assignee would earn ten times as much than what was paid to the original patentee if the price of the transaction is equal to the present value of the prospected royalties.				

Scenario ii	2.867.778	2.192.010	789.123	248.574	107.226
	The present value of the prospected royalties is more than one third of the PVAE after tax, cost of goods sold and other expenses.				
Scenario iii	2.867.778	2.192.010	350.722	73.652	107.226
	The present value of the foreseen royalties is considerably higher than the PVAE after tax, cost of goods sold and other expenses.				

This proposed approach holds promise and is yet to be tested and validated by applying to real life cases. The publication stated that University of Trieste in Italy was considering the application of this approach to provide all potential assignees/licensees with a reliable method for the assessment of the value (post evaluation) of its posted available technologies.

4 Good practices in institutional policy frameworks for R&D and knowledge protection

Good Practices in institutions involve the formulation and execution of institutional innovation policies that integrate astute knowledge management processes and strategic use of intellectual property rights. The integrated knowledge-led activities comprehensively facilitate the creation, management and marketing of "value -added" intellectual assets to derive “first in the market advantage” in a framework of continual innovations. Nanotechnology Educational as we have already seen gets largely generated in academic institutions that are fountainheads of excellence and wellsprings of knowledge and therefore such institutions need clarity in in their knowledge creation and transfer activities.

Nanotechnology has experienced multitude modes of working such as government funded projects, contract research, sponsored collaborations, trans-border inter-institutional and intra-institutional cross-functional team working.

The synergy between academic-industry facilitates a process by which the industry gains access to world-class research resources and the best of human minds. On the other hand academic institutions discover an additional sense of purpose, gain exposure to demands of market realities, expand the

knowledge base to create new products and technologies and also explore new career options. Such symbiotic relationships pave the way to productive knowledge networks, enrichment of the educational systems with sustained knowledge renewal and creation of well-prepared human resources and nurturing of innovative culture. A prerequisite for a harmonious working between industry and academics is a formalized framework for “ownership” of the developed knowledge and systems for “fair benefit sharing” of commercial results between partners In such a working relationship the collaborating partners would need to freely share their respective knowledge, information and resources. To sustain innovation in such a working paradigm, intellectual property rights will have to get integrated with the value system in our academics and they will have to learn the art of maximizing value creation and realization of the human resources and intellectual assets/quasi assets.

All knowledge related activities such as accessing, creating, generating, trading and applying knowledge are intimately connected to intellectual property rights and their enforcement. All features of IPR are therefore inseparable from project management as they significantly influence the conception and strategic implementation of a project. One is then required to map the knowledge ownership girds to ensure that there no infringing overlaps and if there are any, then appropriate arrangements are worked to avoid litigations.

It is therefore imperative that focused cooperative efforts be initiated to speedily evolve and implement institutional IPR Policies between the government, the private sector, and academic institutions.

The aim of any Institutional IPR policy is to create an ecosystem that recognizes the importance of innovations and assists in translating them into products, processes and services to achieve the widest public good. Such a policy ought to set forth transparent guidelines and benchmarks for ownership, protection and commercialization of the developed Intellectual Property (IP) at the same time upholding the core moral values such as Integrity, Merit, Researchers' Freedom, and Excellence. Such a formalised platform would prepare the stake holders to meet growing demands of the emerging knowledge economy to effectively synergise transfer of technology, maximize value realization of their creative works both for the institution and themselves. Further it would help create an ambience for emergence of new ideas, research and flourish scholarship from which the leaders and innovators of tomorrow emerge.

Institutions that have good operational integrated innovation policies define scope and applicability while addressing issues concerning

- avenues and modes for interfacing with the external world through contracts and agreements; MOUs governing research contracts; modes of procuring and spending of grants
- the activities in the institution related to the creation and exploitation of intellectual assets; establishing and operating innovation gateways for real-time technology landscaping including IPR mapping and timely filing of appropriate IPR applications for protection of the intellectual creations
- mapping of completion and planning for strategic collaborations, acquisitions, mergers, joint ventures
- roles, responsibilities and rights of individuals within an institutional framework and that of individuals from other collaborating institutions
- roles and responsibilities of contractors, consultants, financers, and their like
- issues related to ownership and assignment of intellectual creations and their IPR
- structured disclosure of intellectual creations to the institution for purposes of institutional documentation and also for evaluation of possible IPRs and further for strategic publications in professional and general media
- technology and IPR due diligence to establish "freedom to operate" (FTO) of the developed technologies
- institutional modes for commercialisation, transfer of technology and / or IPR
- valuation of IPR

- revenue / benefit sharing
- resolution of possible conflict of interest
- approaches to avoid possible infringements, claiming damages, avoiding or atleast minimising liabilities
- structured Institutional IPR Audit
- jurisdictional considerations in contracts and agreements
- handling non-compliance of institutional policies

Institutions adopting such comprehensive practices have been successful aand several of the case studies in this chapter illustrate these realities.

5. Summary

Nanotechnology from the time the its concept germination has now evolved into its middle age with enormous promise to grow and offer path breaking applications in energy saving devices, medicine and operating techniques, robotics, food and agriculture, computation, genetic engineering, etc. Concurrent to the innovative developments, intellectual property rights will play a major deciding role in the way in which diverse working groups around the world will cooperatively compete to contribute and commercialise these innovations in the market place. Methods of valuation of such technologies and business enterprises together with strategic transaction of intellectual property rights will have to get integrated into the main stream of activities so as to ensure sustainability.

Further reading

1. Nanotechnology intellectual property rights….research, desing, and commercialisation, Prabuddha Ganguli and Siddharth jabade, CRC Press (Taaylor and Francis Group, USA), 2012, ISBN 978-1-4398-5528-7

2. Patenting Nanotechnology….Is There Really Plenty of room at the bottom? Jack B. Hicks, Gregory Grissett, and Bernard A. Brown,

3. (http://www.wcsr.com/resources/pdfs/nano030310.pdf)

4. Claiming Nanotechnology: Improving USPTO Efforts at Classification of Emerging Nano-Enabled Pharmaceutical Technologies, Jordan Paradise,
   w. J. Tech. & Intell. Prop. 169 (2012)
   (http://scholarlycommons.law.northwestern.edu/njtip/vol10/iss3/4)

5. Patent Protection in the field of Nanotechnology: The Position with respect to the European Patent Office, Sneha Venkataramani (http://www.legalserviceindia.com/articles/ptaav.htm)

6. Braod Concerns about nanotechnology Patents: Symptoms and diagnosis, Dannie Jost and Thomas Cottier, Working Paper 2012/13, 2012, NCCR Traade Regulation (http://www.nccr-

trade.org/fileadmin/user_upload/nccrrade.ch/wp3/3.3c/NCCR%20WP2012_13_NanoPatentsSymptomsDiagnostic_Jost_Cottier2012June.pdf)

7. Valuation And Exploitation of Intellectual Property STI Working Paper 2006/5

8. Statistical Analysis of Science, Technology and Industry; by Shigeki Kamiyama, Jerry Sheehan, Catalina Martinez; DSTI/DOC(2006)5; 30-Jun-2006 (http://www.oecd.org/sti/working-papers)

9. Intellectual Property Valuation Parts 1-4 ; June 2000, Smartpros Ltd; last accessed in December 2001

10. A working guide for determining the value of nanotechnology innovation….A Report for DEFRA, UK, by Ben Walsh, Peter Willis, Alastair MacGregor; November 2010 (http://www.oakdenehollins.co.uk/media/225/DEFR01_225_Working_guide_Final.pdf)

11. OECD/NNI International Symposium on Assessing the Economic Impact of Nanotechnology Background Paper 4 - Models, Tools and Metrics Available to Assess the Economic Impact of Nanotechnology; DSTI/STP/NANO(2012)13, March 16, 2012 by By Katherine Bojczcuk and Ben Walsh (http://www.nano.gov/sites/default/files/dsti_stp_nano201213.pdf)

12. Reinterpreting Patent Valuation and Evaluation: The Tricky World of Nanotechnology by Luca Escoffier (2011), Transatlantic Technology Law Forum, TTL Papers No. 8 (http://www.law.stanford.edu/sites/default/files/publication/205102/doc/slspublic/escoffier_wp8.pdf)
13. The valuation of nanotechnology firms: A Brunswikian approach by Carl-Clemens Köhler, April 2009 (http://pure.au.dk/portal-asb-student/files/5341/Master_Thesis_Carl-Clemens_Koehler.pdf)

14. Technology valuation model to support technology transfer negotiations by Dong-Hyun Baek, Wonsik Sul, Kil-Pyo Hong and Hun Kim, *R&D Management* , Vol 37, No. 2, 2007 (http://www.researchgate.net/publication/228130296_A_Technology_Valuation_Model_to_Support_Technology_Transfer_Negotiations)

Appendix 1: Sample Nanotechnology License

The following was taken from the PLI Intellectual Property Institute 2010 presentation on "Bankruptcy Issues In Copyright": Copyright 2010, J.T. Westermeier and Philip S. Warden. All Rights Reserved.

NANOTECHNOLOGY LICENSE AGREEMENT

This Nanotechnology License Agreement (the "Agreement") is effective as of _____, 20__ (the "Effective Date"), between_____, a _____ corporation, with offices at _____(_____("Licensor") , and _____, a _____ corporation, with offices at _____("Licensee").

WHEREAS, Licensee desires to obtain a license to certain Nanotechnology owned by Licensor; and

WHEREAS, Licensor desires to license certain Nanotechnology owned by Licensor.

NOW, THEREFORE, in consideration of the mutual promises of the parties, and of good and valuable consideration, the parties intending to be legally bound, agree to the following terms:

1. LICENSE GRANT; DELIVERABLES; SERVICES

1.1 License Grant. Licensor hereby grants to Licensee a [non-exclusive / exclusive], [non-transferable], [non-sublicenseable], [royalty-free / royalty bearing], [irrevocable], perpetual license to use, modify, [sublicense], create derivative works, and otherwise utilize the Licensed Program and Documentation as defined in Attachment 1 attached hereto. [The foregoing bracketed text reflects the possible variance of terms relating to the negotiated scope of the license. The issue of royalties is addressed in Section 3.] [Although sometime difficult to obtain, it is optimal for Licensee to obtain an "irrevocable license" to the Licensed Program, without allowing Licensor to terminate the Agreement. With an irrevocable license, the Licensor could obtain equitable relief and monetary damages, but could not terminate the Agreement except pursuant to the Bankruptcy Code. If the Licensed Program is particularly critical to Licensee, or large license fees are at issue, Licensee should seek to obtain an irrevocable license and limit Licensor's ability to terminate the Agreement or get a security interest in the licensed intellectual property.] [Licensor further grants to Licensee a [non-exclusive / exclusive],

[non-transferable], [non-sublicenseable], [royalty-free / royalty bearing], irrevocable, perpetual license to use, modify, [sublicense], create derivative works, and otherwise utilize the source code version of the Licensed Program, and all documentation of such source code, including without limitation programmers annotations, notes, schematics and flowcharts, all as such source code and documentation are released to Licensee by a designated third party.] [The foregoing bracketed text addresses the present granting of a right to source code to Licensee, with such source code to be released by designated third party (e.g., an escrow agent)]

1.2 Sublicensing. Licensee shall sublicense the Licensed Program solely pursuant to [the minimum terms and conditions set forth in Attachment 4] [Licensee's form Nanotechnology license agreement, materially in the form attached hereto as Attachment 4.] [In the event that Licensor grants Licensee the right to sublicense under Section 1.1, Licensor will require certain basic terms with respect to Licensee's sublicensing. Please note that sublicensing of Nanotechnology licensed from an entity in financial distress creates a material additional risk for Licensee. In the worst case, Licensee's right and ability to sublicense, and therefore its ability to meet its contractual obligations to its sublicensee, could be compromised, resulting in a possible breach by Licensee.

1.3 Delivery; Completion of Obligations. Licensor shall fully deliver to Licensee the Licensed Program and Documentation upon the Effective Date. [Note, if fully delivered, before any payment is made, risk of rejection as executory, is minimized.] Upon Licensor's delivery of the Licensed Program and Documentation, Licensor shall have no further obligations, material or otherwise, hereunder, and this Agreement shall not constitute an executory contract of Licensor. Licensor's delivery of any physical media or embodiments containing the Licensed Program and Documentation shall constitute an irrevocable transfer of ownership of such physical media and embodiments (but not including the Licensed Programs contained therein) and Licensee shall be the sole and exclusive owner of all right, title and interest in and to such physical media and embodiments, with Licensee having no right, title or interest, legal or equitable, to such physical media and embodiments. [Licensor needs to transfer all the Licensed Program and Documentation upon the Effective Date in order to mitigate risk. Inclusion of statements that Licensor's obligations have been completed and that the Agreement is non-executory are for clarification, as the Bankruptcy Court will on request of the Trustee conduct a fact based review of the Agreement overall, regardless of such language. Inclusion of the language regarding transfer of ownership of the physical embodiments helps prevent a possible situation whereby Licensor, upon its filing a petition for relief (bankruptcy), seeks to recover the physical embodiments of the Licensed Program and Documentation.]

2. OWNERSHIP

2.1 Ownership of Licensed Program. Licensee acknowledges and agrees a license to the Licensed Programs is granted under this Agreement and that the Licensed Program is and shall remain the sole property of Licensor. [In a situation where the licensee has great leverage, risk can be minimized by transferring title to the licensee so that the licensee becomes the actual owner. Such transfer of title would be closely scrutinized in a subsequent bankruptcy, including preference analysis, which focuses on the recovery of a greater percentage recovery by the preference recipient than is enjoyed by similarly situated unsecured creditors. Fraudulent conveyance analysis inquires into the imbalance between the consideration given and the consideration received.]

2.2 Ownership of Derivative Works. Licensee shall be the sole and exclusive owner to all right, title and interest in and to all modifications, enhancements, improvements to, and derivative works of, the Licensed Program and Documentation made by Licensee, including without limitation, all patent, copyright, trade secret and other intellectual property rights therein. [As the case law is unclear on the

issue of whether the licensor or licensee owns licensee's postpetition modifications and enhancements to Nanotechnology, the above language should be included. If licensor objects, the above clause could be revised to include a lead-in requirement that Licensor have undergone a defined "bankruptcy event" in order for such rights to be granted to Licensee.]

1. LICENSE FEES; PAYMENTS

3.1 License Fees. Licensee agrees to pay Licensor the license fees ("License Fees") set forth in Attachment 3. [This is a key aspect of the purpose of this form of Agreement. The license fee should consist solely of the fees attributable for the license to the Licensed Program, and should not include any fees attributable to services to be performed under the Services Agreement. Further, if Licensee's use of the Licensed Product is to include use of Licensor's trademarks, trade names, service marks or other designations of source or origin, then the license fees attributable to such trademark license need to be set forth separately from the Nanotechnology license fees. The notion is to avoid the result of Encino Business Management v. Prize Frize, Inc. (In re Prize Frize, Inc., 32 F.3d 426 (9th Cir. 1994)).]

3.2 Payment. Licensee shall pay Licensor the License Fees as set forth in Attachment 3. Licensor shall have the right to withhold amounts disputed in good faith without Licensor's assertion of a payment default or any late payment penalty. [Licensee should not front load license fees in order to mitigate the risk to licensee of rejection.]

3.3 Payment Requires Delivery. Notwithstanding anything to the contrary in this Section 3 (including without limitation the payment terms set forth in Attachment 3), Licensee shall not be obligated to commence any payment obligations hereunder unless Licensor has completely fulfilled its obligations under Section 1.3 upon the Effective Date. [In order for the Licensee to mitigate its risk, Licensee should not make any substantial payments until Licensor has delivered the License Program and Documentation pursuant to Section 1.3. It is recommended that Licensee's initial payment follow delivery the period of time that Licensee would need to validate that the Licensed Program and Document action were completely delivered and the Licensed Program is operational, taking into account the timeframes for any services required under the Services Agreement. Recall that upon rejection, the Debtor is relieved of its affirmative obligations under the license agreement. See Section 365(n)(1)(B) "… as such rights existed immediately before the case commences.…"]

2. TERM AND TERMINATION

4.1 Term. The term of this Agreement commences on the Effective Date and shall continue in perpetuity, unless terminated as set forth herein ("Term"). Each party agrees that time is of the essence hereunder. In the event of bankruptcy, licensor will determine whether to assume or reject within 30 days of the filing of a petition for relief.

4.2 Termination for Cause. Either party may terminate this Agreement for material breach by the other party that is not cured within _____ (__) days after the date of written notice of such

breach. [Licensor's right to terminate the Agreement should be removed if an "irrevocable" license was obtained in Section 1.]

4.3 Termination for Insolvency. Either party may terminate this Agreement for cause by delivering written notice to the other party upon the occurrence of any of the following events: (i) a receiver is appointed for the other party or its property; (ii) the other party makes a general assignment for the benefit of its creditors; (iii) the other party commences, or has commenced against it, proceedings under any bankruptcy, insolvency or debtor's relief law which proceedings are not dismissed within sixty (60) days; or (iv) the other party is liquidated or dissolved. [This section is included as a discussion point.] [See Bankruptcy Code section 365(e), the "ipso facto" provisions)).]

4.4 Rejection. Should licensor reject this license under section 365(n) of the Bankruptcy Code, licensee may treat the license as terminated, in which case licensee shall have a claim for damages against licensor equal to _____dollars ($_____). Alternatively, licensee may elect, under section 365(n) to continue as licensee under this Agreement, and shall only be responsible for the payment of the fees required in Attachment 3, and no other fees, charges or expenses. [This is to avoid the unhappy result of Prize Frize, supra.]

4.5 Effect of Termination. Upon termination of this Agreement for any reason, the rights granted to Licensee shall cease [provided that any sublicenses of the Licensed Program and Documentation shall continue in effect and uninterrupted and Licensee shall have the right to continue to license the Licensed Program and Documentation as set forth in Section 1 for the sole purpose of providing support to such sublicensees.] [This Section relates to sublicensees and should be included in the event that Licensee has the right to sublicense under Section 1. In the event that Licensee has obtained an irrevocable license under Section 1.1, this Section 4.5 should be revised accordingly.]

4.6 Survival. Sections [1], [1.2], 4.4, 5, 6 and 7 shall survive termination of this Agreement for any reason. [Sections 1 and 1.2 should be included if Licensee obtained an irrevocable license under Section 1.1.]

3. DISCLAIMER OF WARRANTIES

Each party acknowledges and agrees that neither party nor any of their parents, subsidiaries or affiliates makes any warranties whatsoever, express, implied or statutory, including without limitation any implied warranties of merchantability, fitness for a particular purpose, title, enforceability or non-infringement.

4. LIMITATION OF LIABILITY

In no event shall either party or their parent, subsidiaries or affiliates, or their respective officers, directors and employees, be liable to the other party or any third party for any special, consequential, indirect, incidental or punitive damages or lost profits, however caused and on any theory of liability (including negligence) arising in any way out of or in relation to this agreement, whether or not such party has been advised of the possibility of such damages. (*These limitations generally survive court challenge*.)

5. MISCELLANEOUS PROVISIONS

7.1 Trademarks. Neither party shall use the other party's trademarks, trade names, service marks, or other marks without the prior written consent of such party. [Recall that "Intellectual Property" as defined in the Bankruptcy Code, and which can be the subject of the Section 365(n) election, does not include trademarks.]

7.2 Entire Agreement. This Agreement constitutes the entire agreement between the parties solely with respect to the licensing of the Licensed Nanotechnology and Documentation (but in no event with respect to any development, consulting, support or other obligations of Licensor, regardless of whether such obligations relate to the Licensed Program and/or Documentation, as may be stated separately in a written agreement between Licensor and Licensee) and supersedes all prior written and oral and all contemporaneous oral agreements and understandings with respect to such subject matter. This Agreement shall prevail in the event of any conflicting terms or legends which may appear on any portion of the Licensed Program or Documentation.

7.3 Governing Law; Venue. This Agreement shall be construed in accordance with and all disputes hereunder shall be governed by the laws of the State of California, excluding its conflict of law rules and the United Nations Convention on Contracts for the International Sale of Goods. The Superior Court of San Francisco County and/or the United States District Court for the Northern District of California shall have exclusive jurisdiction and venues over all disputes between the parties. [Some may prefer arbitration.]

7.4 Headings. The descriptive headings herein are inserted for convenience of reference only and are not intended to be part of or to affect the meaning or interpretation of this Agreement.

7.5 Notices. All notices and other communications hereunder shall be in writing and shall be deemed to have been duly given when delivered in person, by telecopy with answer back, by express or overnight mail delivered by a nationally recognized air courier (delivery charges prepaid), by registered or certified mail (postage prepaid, return receipt requested) or by e mail with receipt confirmed by return e mail to the respective parties as follows:

if to Licensor:

_____

_____

_____

_____

Email: _____

if to Licensee:

_____

_____

_____

_____

Email: _____

or to such other address as the party to whom notice is given may have previously furnished to the other in writing in the manner set forth above. Any notice or communication delivered in person shall be deemed effective on delivery. Any notice or communication sent by e-mail, telecopy or by air courier shall be deemed effective on the first Business Day following the day on which such notice or communication was sent. Any notice or communication sent by registered or certified mail shall be deemed effective on the third Business Day following the day on which such notice or communication was mailed. As used in this Section, "Business Day" means any day other than a Saturday, a Sunday or a day on which banking institutions located in the State of California are authorized or obligated by law or executive order to close.

7.6 Assignability. Neither party may, directly or indirectly, in whole or in part, whether by operation of law or otherwise, assign or transfer this Agreement, without the other party's prior written consent; provided, however, that Licensee may assign this Agreement to a subsidiary or affiliate or pursuant to a merger or a sale of all or substantially all of the assets or stock of Licensee, without Licensor's consent. Any attempted assignment, transfer or delegation of this Agreement in breach of this Section shall be voidable at the sole option of the non-assigning party. Without limiting the foregoing, this Agreement will be binding upon and inure to the benefit of the parties and their permitted successors and assigns.

7.7 Severability. If any term or other provision of this Agreement is determined by a nonappealable decision of a court, administrative agency or arbitrator to be invalid, illegal or incapable of being enforced by any rule of law or public policy, all other conditions and provisions of this Agreement shall nevertheless remain in full force and effect so long as the economic or legal substance of the transactions contemplated hereby is not affected in any manner materially adverse to either party. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in an acceptable manner to the end that the transactions contemplated hereby are fulfilled to the full extent possible.

7.8 Waiver; Remedies Cumulative. No failure or delay on the part of either party hereto in the exercise of any right hereunder shall impair such right or be construed to be a waiver of, or acquiescence in, any breach of any representation, warranty or agreement herein, nor shall any single or partial exercise of any such right preclude other or further exercise thereof or of any other right. All rights and remedies existing under this Agreement are cumulative to, and not exclusive of, any rights or remedies otherwise available.

7.9 Exports. Licensee agrees to comply with all applicable United States laws and regulations which may govern the export of the Technology abroad, including the Export Administration Act of 1979, as amended, any successor legislation, and the Export Administration Regulations issued by the Department of Commerce.

7.10 Amendment. No change or amendment will be made to this Agreement except by an instrument in writing signed on behalf of each of the parties to such agreement.

7.11 Counterparts. This Agreement may be executed in two or more counterparts, all of which, taken together, shall be considered to be one and the same instrument.

WHEREFORE, the parties have caused this Agreement to be signed by their duly authorized representatives effective as of the date first set forth above.

By:	By:
Name:	Name:
Title:	Title:

MANUAL ON CRITICAL ISSUES IN NANOTECHNOLOGY R&D MANAGEMENT

AN ASIA-PACIFIC PERSPECTIVE

CHAPTER 3

Best Practices on Commercialisation of Nanotechnology R&D Results

Prepared for

Asian and Pacific Centre for Transfer of Technology of the United Nations – Economic and Social Commission for Asia and the Pacific (UNESCAP)

By

Prabuddha Ganguli

APCTT
Asian and Pacific Centre for Transfer of Technology

UNITED NATIONS ESCAP
Economic and Social Commission for Asia and the Pacific

This chapter was prepared by Dr. Prabuddha Ganguli, CEO, VISION-IPR, Mumbai, India and MHRD IPR Chair Professor, Tezpur University, Assam, India, under a consultancy assignment given by the Asian and Pacific Centre for Transfer of Technology (APCTT).

Manual on Critical Issues in Nanotechnology R&D Management: An Asia-Pacific Perspective

Asian and Pacific Centre for Transfer of Technology (APCTT) of the
United Nations Economic and Social Commission for Asia and the Pacific (UNESCAP)

Disclaimer

Reference to dollars ($) are to United States dollars unless otherwise stated.

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This manual has been issued without formal editing.

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Best Practices on Commercialisation of Nanotechnology R&D Results

1. Introduction

The last few decades has seen the development of nanotechnology as a field that has intersected diverse fields of science and technologies. In this rapidly growing sector, development of concepts i.e., the generative phase has coalesced into the application and trading phases, thereby demanding reengineered thinking and newer landscaping of innovation processes. The trends have been in effecting the dynamic creation and operation of enabling teamwork in a complex and pulsating knowledge space. Several models of innovation processes are available that serve as learning points for adoption such that the generation and expansion of knowledge is in tandem with competitive knowledge diffusion and transfer. Effective management of Intellectual Property Rights (IPR) now is becoming a key driver in innovation processes to gain strategic ownership of knowledge domains with speedy knowledge sharing, value creation and realization.

The challenge is to design and operate institutional innovation processes that would preserve intellectual excellence and at the same time amicably fit into a disciplined Intellectual Property Rights system. This chapter reviews approaches adopted by academic and commercial enterprises in institutional management of IPR including the impact on global research dynamics related to nanotechnology.

2. Nanomarkets……estimates to guesstimates

Since the concept of building materials atom by atom by Professor Richard Feynman in 1959 and the christening of the term "Nanotechnology" in 1974, this field has rapidly got enriched in terms of basic science. Its transition to workable technologies have begun to reach the market place as products and processes are already impinging our lives with major futuristic promises of an array of disruptive applications in materials, manufacturing and man-machine interface. There is a global market potential of US$ 2.15 trillion as projected by the National Science Foundation in the United States (Figure 1).

According to other studies, nanotechnology impacted US$254 billion worth of products in 2009. This impact is forecast to grow to perhaps US$2.5 trillion by 2015 [Ireland's Nanotechnology Commercialisation Framework 2010 – 2014, Forfas (Aug 2010), http://www.forfas.ie/media/forfas310810-nanotech_commercialisation_framework_2010-2014.pdf, page 6].

The largest nanotechnology segment in 2009 was nanomaterials. The market for all nanomaterials is estimated to increase from US$ 10 billion in 2009 to almost US$ 19.6 billion in 2015, representing an

annual growth rate of 14.7%. Sales of nanotools will also experience high growth of around 3.3% compound annual growth rate (CAGR) to reach $6.8 billion in 2015 (bcc research 2010, '*Nanotechnololgy: A Realistic Market Assessment*', http://www.bccresearch.com/report/NAN031D.html).

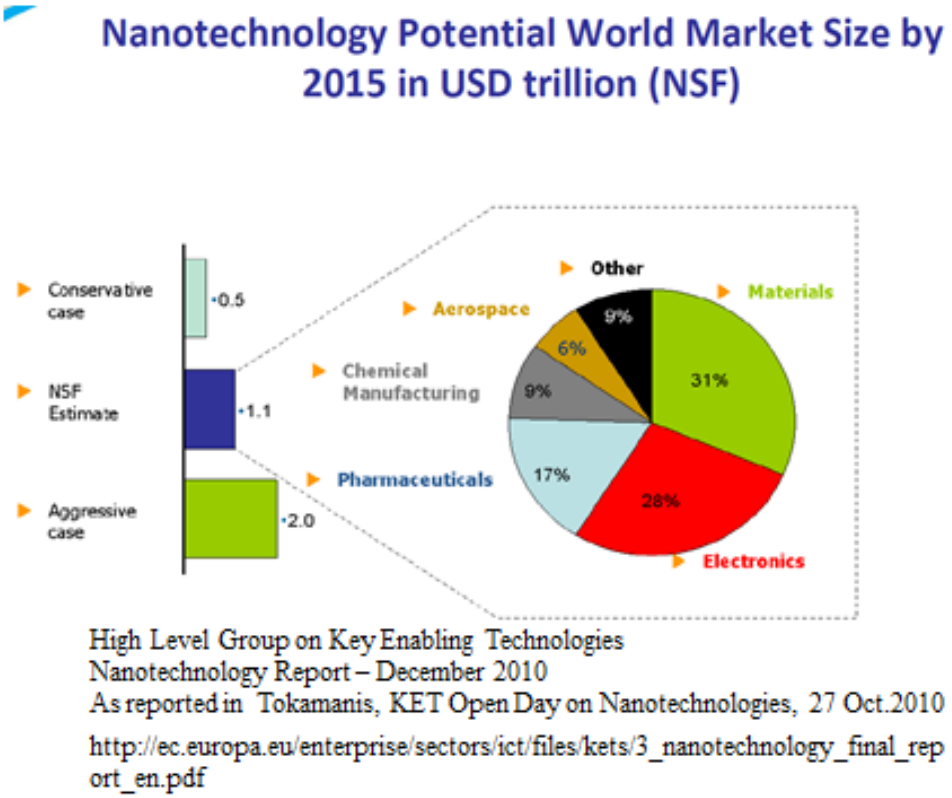
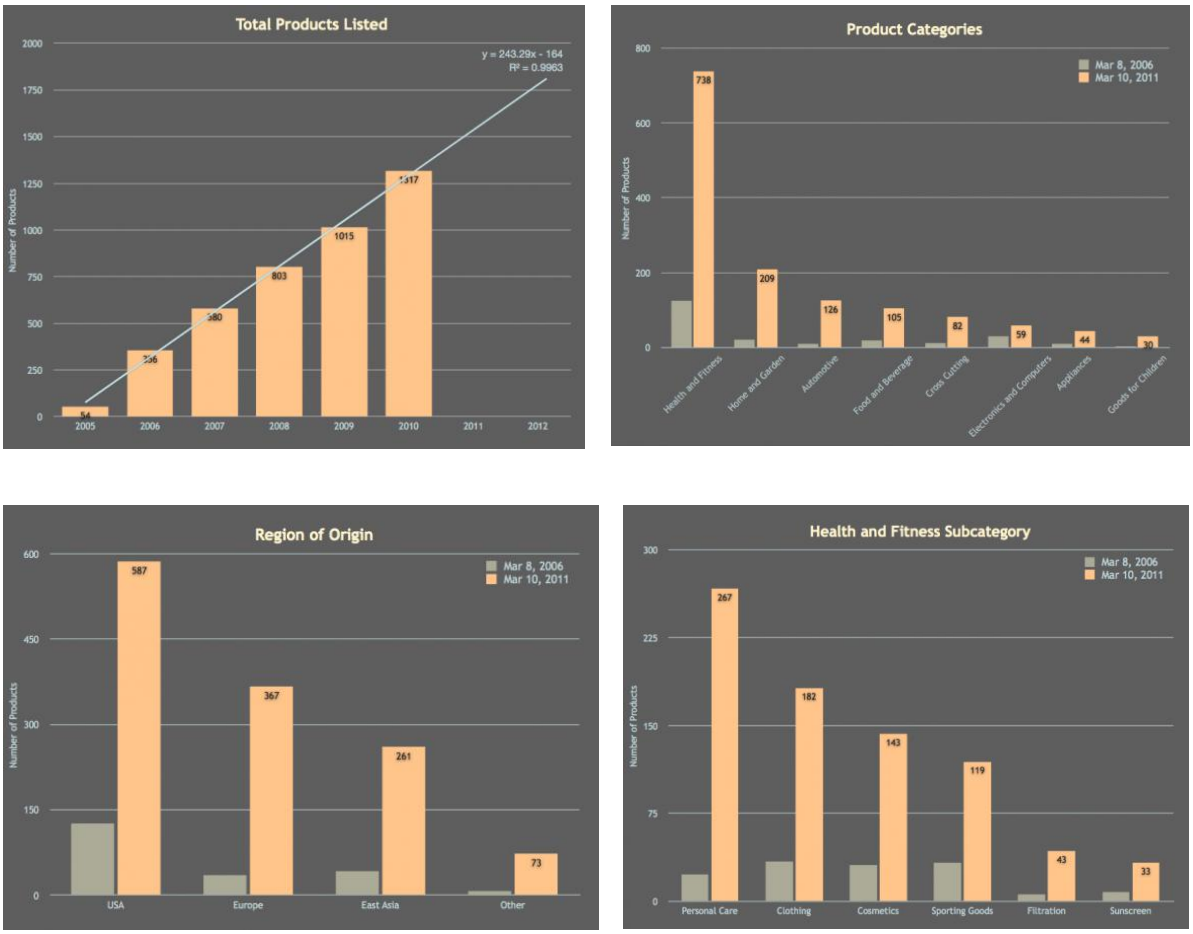


Figure 1: Estimate / Guestimate of nano market by 2015

The Project on Emerging Nanotechnologies (PEN), reports that 1317 nanotechnology enabled consumer products have found their way into the market place and the illustrations from the same report highlight some of the key market realities as of March 2011(Figures 2-5).



Figures 2-5: Nanoenabled consumer products in the global market
(Source: http://www.nanotechproject.org/inventories/consumer/analysis_draft/)

Starting with 54 nanotechnology enabled consumer products in 2005, the growth of the inventory has been 521%. USA leads in the global market of nano-enabled consumer products, followed by companies in Europe (UK, France, Germany, Finland, Switzerland, Italy, Sweden, Denmark, The Netherlands, East Asia (including China, Taiwan province of China, Republic of Korea and Japan), and elsewhere around the world (Australia, Canada, Mexico, Israel, New Zealand, Malaysia, Thailand, Singapore, The Philippines and Malaysia). The most common material mentioned in the product descriptions is now silver (313 products). Carbon, which includes fullerenes, is the second most referenced (91), followed by titanium (including titanium dioxide) (59), silica (43), zinc (including zinc oxide) (31), and gold (28).

Nanotechnology has reached its present position due to dynamic networking of diverse enterprises, and the overwhelming continued support of national governments (Figure 6). The Governments provide support through public funding of R&D and commercialisation including the creation and implementation of nanotechnology favouring national polices, extending funding to prototype and pilot manufacturing thereby reducing the risk for investments in nanotechnologies including the inbuilt inertia of commercial organisations to adopt new technologies involving new materials, products and processes

due to high initial cost of entry, corporations funding R&D and commercialisation, corporate venture funds and venture capital through equity investments. Funding through stocks and bonds has also made a beginning in nanotechnology, though its contribution has not yet reached significant dimensions.

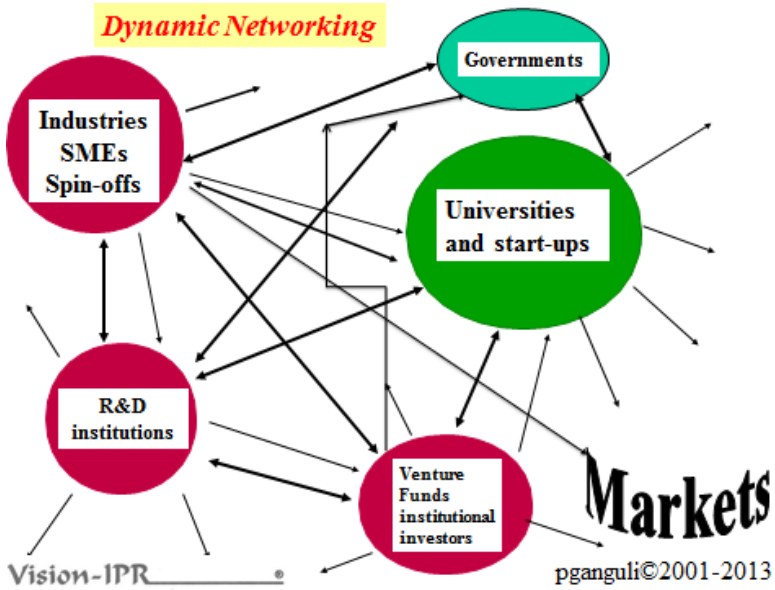


Figure 6: Enabling nano from R&D to Markets through stakeholders' networking

The stakeholders and beneficiaries in the global nanotechnology dynamic networks span from the universities, academic and national R&D institutions, industries including the manufacturers, suppliers, SMEs, technology integrators, university start-ups, corporate spin-offs, governments, institutional investors, venture capital funds and the consumers in the markets. The additional stakeholders are consortia (such as The Inno.CNT alliance), industry associations in various countries (e.g. in the US and Europe ---- the NanoBusiness Alliance and the Nanotechnology Industries Association). The interlinking of these participants in real time and working in unison and scaling up adaptations and/or integration along the nano value chain with minimum time-lag from concept to market, is the key to the creation of innovations and their successful translation to the markets as products and processes.

OECD Working Party on Nanotechnology Report DSTI/STP/NANO(2012)15 dated 16-Mar-2012 presented at OECD/NNI International Symposium on Assessing the Economic Impact of Nanotechnology as '*Background Paper 2: Finance and Investor Models in Nanotechnology*' quoting Lux Research reported :

- 2009 has been a turning point at which corporate investment (2009: US$ 8.4 bn, 2010: US$9 billion) equalled and then exceeded public investments (2009: US$ 8.4 billion, 2010: US$ 8.2 billion), the difference remains minor, and may not have persisted in 2011 due to the economic downturn having a greater effect on corporate investment.

- The amount of funding coming from venture capital is low (2009: 0.822 billion, 2010: US$ 0.646 billion) which is only 4% of total global funding.

- The majority of nanotechnology development occurs at established firms. The level of venture capital funding is a product of supply – the number of investors willing and able to fund nanotechnology ventures – and demand – the amount of nanofirms with sufficiently high growth potential

Table 1 has been reproduced from the OECD report (which quoted a Spinverse analysis of the data reported in European Nanotechnology Landscape Report, Observatory Nano, http://www.observatorynano.eu/project/catalogue/3EN/) shows the sources of funding for companies using nanotechnology in Europe.

Table 1: Sources of funding for companies using nanotechnology in Europe

Sector	Companies	% receiving external funding	% receiving public funding
Nanomedicine	16	13	88
Transportation and Aerospace	24	21	75
Electronics	16	44	88
Energy	11	55	82
Materials	26	15	88
Food and Food packaging	8	13	50
Others	30	7	67

It is interesting to note the high funding of companies especially in fields of nanomedicine, electronics, energy and materials.

3. Investment criteria of various funding agencies

Public funding is generally based on national policies to promote science, technology and innovative culture, to build human resources and infrastructure for the development of nanotechnology and also to derive benefits from international cross border collaborations, create demand and awareness for innovative products, establish regulatory frameworks for environment, health and safety as well as act to reduce the risk of investments especially by SMEs in new technologies by directly reducing costs, etc.

Corporate investments are generally guided by the need to build human resources and infrastructure for the developmental activities related to nanotechnology, enhance capability to absorb and adapt technologies from publicly funded institutional domains, ensure their industrial scale ups and building production facilities, and provide increased revenue from new or improved products in new or current markets, further existing markets, and/or to improve profitability by manufacturing reducing costs. Corporate investments are also done in an identified portfolio of technologies thereby mitigating the risks of investing too narrowly. In addition to the technology feasibility and market potential of a technology,

corporate decisions are also guided by strategic considerations related to the status of intellectual property rights (e.g. portfolio of patenting, value that may be realized by licensing out technologies to other firms, acquisition of patents, etc) and assured return on investment (ROI) through increased sales via enlargement of market share, entering a new market, and reduced costs.

Venture capital (VC), both active and passive generally get involved through independent venture capital funds and corporate venture funds via equity participation thereby receiving shares of ownership of the funded company, although other forms of investments such as convertible loans and senior debt are also used. Nanotechnology related active VCs bring in know-how and networks and invest mainly in familiar industries or technology fields, while passive VCs contribute money and general business acumen. VCs generally make calculated investments with the expectation of generating returns of ten or more times the original investment within a planned period. VCs judiciously combine several parameters such as profile of the company's management team, the market potential and business model, the development stage of the company and its technology, the state of technological and market readiness, and ability to achieve objectives and react positively to setbacks, how quickly the company can start demonstrating value and generating returns, the exit plan and the valuation of the company to guide them in their investment decision making. In addition to investments through funding, Corporate VCs also evaluate their options to feed in from their parent company, knowledge, knowhow, resources and other expertise into the promising venture to access potential disruptive technologies, or by funding and creating a portfolio of companies to drive demand for the parent firm's products.

Institutional investors including banks, insurance companies, pension funds and mutual funds have not been too involved in nanotechnology by way of investing in shares of publicly listed companies, corporate bonds, and venture capital funds, essentially due to the inconsistent and largely disappointing performance of publicly listed nanotechnology companies.

The inclusive nature of nanotechnology encompassing diverse aspects of material science and engineering has led to a continuous evolution and in several cases a burst of disruptive convergence of technologies leading to borderless applications of nano-enabled products and processes. The simultaneous challenge has also been in establishing reproducibility and cost effective up-scaling to manufacturing levels of the nano-enabled products and processes. The objective has been to bring about the sought after coalescence in the time gap between discovery and invention, and their coupled transformation into novel and useful applications.

The challenge has been and will continue to lie in crystallising the "plausible" into affordable "marketable tangibles" for profitable and sustained businesses. This is the acid test of practical commercialisation of R&D results.

The purpose of this chapter is to illustrate approaches taken by various workers in commercialisation of nanoscience and technology that involve production, translation and transfer of knowledge resulting in the transformation of research findings into innovations culminating into successful businesses.

4. Models of R&D in nanotechnology

The field of nanotechnology has also been the testing ground for a range of business models ranging from the classical modes of intense conceptualisation and knowledge generation and plausible applications development in centres of excellence within the academic environment and transfer of technology to commercial enterprises, to sprouting of start-ups within the academic domain and in several instances in organised science parks, creating and supporting spin-offs within commercial enterprises and then backward / forward integrating with them in due course, involving angels / venture capital for early stage support, SMEs taking up targeted technologies for commercialisation, large businesses adapting newer technologies within their businesses and/or discontinuing older technologies in favour of more effective newer replacing technologies and in recent times governments getting involved in public–private partnerships and consortia modes. A recent review titled '*The Future of Nanotechnologies*' by Vincent Mangematin and Steve Walsh, 1 - 9 Jan 2012 and references therein, presents an overview of the modes of technology development, transfer and commercialisation in the field of nanotechnology (http://halshs.archives-ouvertes.fr/docs/00/65/80/34/PDF/future_of_Nanotechnologies.pdf).

The main findings are of the OECD Study in 2010 titled '*The Impacts of Nanotechnology Companies: Policy Insights from Case Studies*' by OECD in 2010 (http://dx.doi.org/10.1787/9789264094635-en) are:

- Nanotechnology is an enabling technology (or set of technologies) and the company case studies show that this feature is a major reason for their entry into the field. Nanotechnology allows for both the improvement of existing and the development of completely new products and processes, and sometimes new services as well. Companies often experiment with multiple applications at the same time, many of which are still in the research phase. Several nanotechnology applications are also largely demand-driven as new functionalities of existing materials create new market opportunities even in some traditional industries such as textiles, energy, health care, water treatment, etc.
- Nanotechnology may best be described as a "science-based and demand-driven field". While all of the case study companies undertake in-house R&D, collaboration with universities and "star scientists" are also important sources of innovation and knowledge, especially for small companies. Larger companies in relatively mature nanotechnology sub-areas appear to focus more on applications which are driven by market demand and tend to collaborate with a broader range of organisations to leverage their in-house R&D.

  Nanotechnology has been a fertile ground for nurturing of academic entrepreneurship involving the "best in class scientists" with high-impact publications. This is a recognition that tacit knowledge and knowhow is of immense significance in the transfer of technology in nano related developments from labscale to industrial dimensions. Further it is interesting to note that most entrepreneurial activity in nanotechnology tends to cluster in regions with experience in related sciences, with top-level universities or research institutes, or with R&D laboratories of major companies.
- Nanotechnology mainly affects the R&D and production activities of the case study companies. Many of the smaller companies focus exclusively on nanotechnology, while the larger ones

typically blend nanotechnology with a range of other technologies. In the larger companies it is thus difficult to single out the share of nanotechnology in total labour costs, R&D expenditure, production costs, capital spending and sales.

- The larger companies in the sample have typically been involved in nanotechnology for many years and seem well placed to assimilate nanotechnology due to their established critical mass in R&D and production, their ability to acquire and operate expensive instrumentation and to access and use external knowledge. The relative strength of larger companies in the early phases of nanotechnology developments runs counter to what the traditional model of company dynamics and technology lifecycles would predict where smaller, younger companies are generally considered more innovative.
- The case studies illustrate that nanotechnology is a complex field owing to its dependency on various scientific disciplines, research/engineering approaches and advanced instrumentation. Further, many nanotechnology sub-areas are in an early, immature, phase of development. These features of nanotechnology can often create barriers to entry especially for smaller companies which have limited human and other resources. They also contribute to the poor process scalability of nanoscale engineering during the transition from R&D to pilot and industrial scale production.
- Difficulties arise for recruiting human resources, especially for R&D and production activities. The need for employees, or so-called gatekeepers, who combine specialist and general knowledge (knowledge integration) and can manage interdisciplinary teams is also a challenge.

  One of the concerns in various companies that have got involved in nanotechnology and/or nano-enabled products and processes is the need for new competences that may even lead to the disruption of the existing competence base of companies. It would be important to learn the art of managing uncertainties in discontinuous radical technologies, human capital, and other resources in a dymanic mode.
- Challenges to funding R&D and related activities are often mentioned, especially by business start-ups. The poor process scalability of R&D, which raises costs and prolongs new product development times, can make nanotechnology less attractive to investors. Uncertain regulatory environments and public perceptions of nanotechnology's environmental, health and safety (EHS) risks can also influence R&D funding.
- The novelty of nanotechnology, the established interests of stakeholders, and difficulties that companies can have in communicating the value proposition of applications to potential customers (e.g. other companies), makes their entry and positioning in value chains harder. The challenge is even greater for smaller companies that experiment with multiple applications and have to monitor many different industries and business environments.
- Intellectual property rights (IPR) may become an issue as commercialisation progresses and nanotechnology matures as there is already a very wide range of patent claims, and the possible formation of patent thickets (interrelated and overlapping patents), which could contribute to barriers to entry for companies.

- The potential for overreaction to both actual and perceived Environment Health and Safety (EHS) uncertainties and risks, combined with regulatory uncertainties, complicates the business environment for companies. Global harmonisation of future EHS regulations is considered important.

4.1 Traditional models of R&D and technology commercialization

In the days gone by, R&D activities in nanotechnology were carried out in two sequential phases, namely upstream (basic) general in academic institutions and downstream (applied) in industry (Figures 7 and 8).

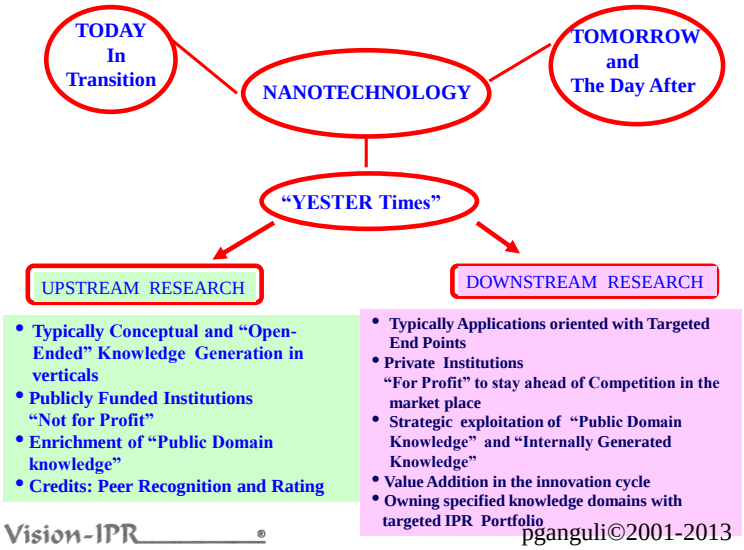


Figure 7: Traditional R&D modes

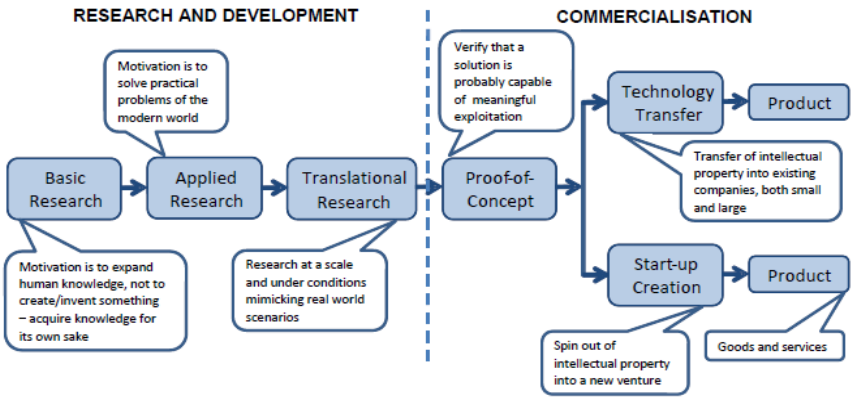


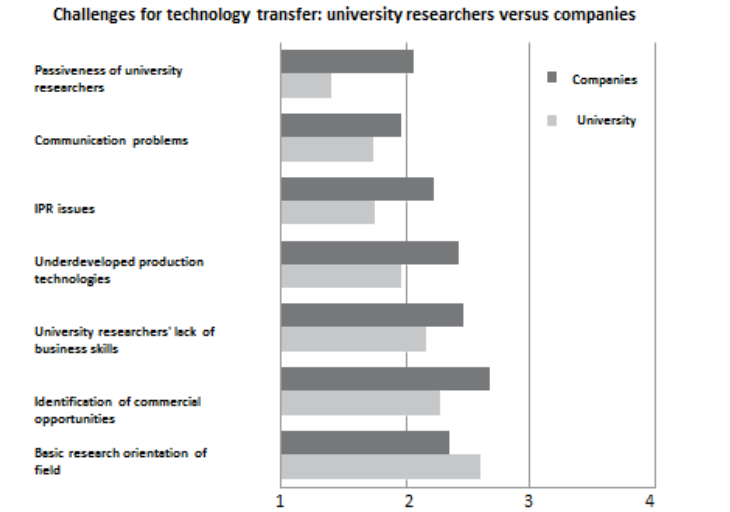
Figure 8: The traditional nanotechnology commercialisation value chain

(Source: http://www.forfas.ie/media/forfas310810-nanotech_commercialisation_framework_2010-2014.pdf, p.39)

Knowledge transfer from academics to industry has traditionally occurred through consultancy arrangements in which industrial problems were addressed by academics through contracts in which industry posed its probles to the academics for solutions. The consulting academic institution (more appropriately the scientist / technologist) was expected to respond these problems with solutions which were then taken up by the industry for implementation. In some cases, research contracts were offered to academics by industry to develop specific or even platform technologies which were then adopted by industry as per its need. Any intellectual property that resulted from such contracts generally became the property of the contracting industry and in return the academicians benefited from the consultancy fees, research grants, resources bought under the consulting contract, grants for their masters and PhD degrees, post-doctoral fellowships, etc.

In some traditional modes, academics especially involving the engineering disciplines conceived of industrial problems mostly independent of their stake holders and offered solutions to such problems through their R&D. In such cases most technology transfer processes remained partially fulfilled and did not find industrial acceptability as the technical problems were either not realistically conceived, and/or the solutions including their scale ups were not cost effectively implementable in existing manufacturing systems. Such working modes that were adopted in the early days of nanotechnology too met with very low success.

A study by Palmberg in 2008 on Finish Universities brought forth some of the perceptive differences between the university researchers and the industry workers (Figure 9).



Palmberg, C. (2008), "The Transfer and Commercialisation of Nanotechnology: A Comparative Analysis of University and Company Researchers", Journal of Technology Transfer, vol. 33, no. 6.

Figure 9: Responses to diverse issues by companies and universities in Finland

Walsh, et al. (2002) in their paper '*Differentiating Markets Strategies for Disruptive Technologies by Walsh*', *IEEE Trans. Engineer Manage*., 49: 341- 351, proposed a model for technology commercialisation as shown in Figure 10 (http://ieeexplore.ieee.org/xpl/login.jsp?tp=&arnumber=1176863&url=http%3A%2F%2Fieeexplore.ieee.org%2Fiel5%2F17%2F26421%2F01176863.pdf%3Farnumber%3D1176863).

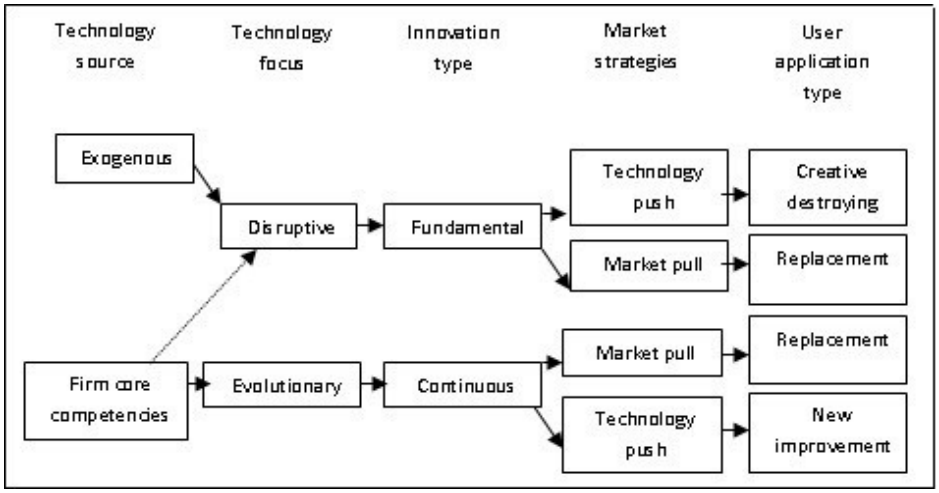


Figure 10: Disruptive technologies and commercialization (Walsh et. al.)

Based on their survey of 72 micro-electro-mechanical-systems (MEMS) manufacturing firms they show that established firms rarely commercialize disruptive technologies and then prefer to use market-pull strategies to accomplish this. New firms select primarily disruptive technologies and choose either market-pull or technology-push strategies for commercialization. Further their study suggests that the time to market for new firms have two advantages in commercialization of disruptive technologies namely flexibility in marketing strategy and much shorter times to market which is generally one-fourth that for established firms. Their model is represented below:

In a publication titled '*Commercialization of Nanotechnology in Developing Countries'* by Roya Naseri and Reza Davoodi in the 3rd International Conference on Information and Financial Engineering IPEDR, Vol.12 (2011), the authors discuss the Walsh model as applicable in developing countries and conclude that in developing countries (http://www.ipedr.com/vol12/70-c162.pdf):

- Most activities for commercialization of nanotechnology projects are performed by start-ups;
- Due to lack effective laws and regulations for supporting right of intellectual properties and absence of an appropriate framework for patent registration in developing countries, granting the ownership of intellectual properties is not an appropriate way of founding new companies;
- Independent entrepreneurship is not a common method for complexity and considerable costs for nanotechnology development and patent registration;
- Challenges in commercialization of nanotechnology can be classified into the following four groups namely, Infrastructural issues, Managerial issues, Sociocultural issues and Economic issues;
- Commercialization of fundamental technologies in developing countries is much riskier than evolutionary technologies; and

- Most of the nanotech firms in these countries are start-ups that adopt technology push strategies for commercialization of their nano products.

A study titled '*The Global Technology Revolution 2020, In-Depth Analyses ……..Bio/Nano/Materials/Information Trends, Drivers, Barriers, and Social Implications*' pubished by RAND Corporation in 2006, reports the technology acquisition and implementation capabilities of various countries including the drivers and barriers to such processes (http://www.rand.org/content/dam/rand/pubs/technicalreports/2006/RAND_TR303.pdf). In countries such as USA, Canada, Western Europe, Republic of Korea, Japan, Australia and Israel, technology acquisition (TA) is strongly driven by a high level of S&T capacity with the presence of many drivers but few barriers. Countries such as China, India, Poland and Russia have been reported as countries for which implementation of technology acquisition is strongly driven by a high level of S&T capacity and the presence of many drivers but for which many barriers are simultaneously present. Countries such as Brazil, Chile, Mexico, Turkey, South Africa, Indonesia, Colombia represents countries for which implementation of technology acquisition is not supported by a high level of S&T capacity and for which the number of both drivers and barriers is small. Further, countries such as Cameroon, Chad, Dominican Republic, Egypt, Fiji, Georgia, Islamic Republic of Iran, Jordan, Kenya, Nepal, Pakistan represents countries for which implementation of TAs is not supported by a high level of S&T capacity and for which the number of barriers exceeds the number of drivers. Commercialization of nanotechnology in these countries will be accordingly impacted.

Nanotechnology is now on a non-linear development trajectory with some of the traditional fields of material science, metallurgy, chemistry and physics of condensed matter, polymer science, electrical engineering, instrumentation, and biology now interfacing with plasmonics, metamaterials, spintronics, graphene, synthetic biology, neuromorphic engineering, quantum information systems, etc. Such hybridisation is leading to new convergence technologies with concurrent applications in fields hitherto unthought-of and unforeseen creating a pan-industry framework that not only include the adoption of materials, devices, systems and components but also demands their interoperability. Technologies resulting from such convergence are those with nano as a prefix, e.g. nanomaterials, nanochemistry or nanoelectronics, nanobiotechnologies, nano-energy, nano-engines, and new diagnostic tools from a merger of nanoelectronics and biotechnologies.

All these require speedier advance in knowledge related to nanoscience, with almost simultaneous targeted synthesis of technologies for an array of applications ideally moving into commercialisation with minimal time-lag.

Traditional modes of R&D and technology transfer do not meet such aggressive needs especially as ownership of knowledge and transaction of "owned knowledge" begins to play a dominant role in present day and future knowledge dynamics in nanotechnology. The key limitations of the traditional modes to service the special needs of nanotechnology stem from the segregated modes of working of the academic community and the commercial enterprises, both in physical locations and in acceptable time scales of operation, diversity in culture between them, preparedness of commercial enterprises to absorb new

scientific developments into their system, ability of the academic community to accelerate comprehensive knowledge transfer and provide timely and adequate cover through strategic intellectual property rights portfolio to the inventions as also providing to confidence that developments made are non-infringing with regard to prior patents and design registrations, fuzziness in knowledge ownerships, etc.

4.2 Recent models of nanotechnology R&D and commercialization

As the level of understanding in nanoscience matured and promising applications as mentioned above started emerging especially using government grants in publicly funded institutions such as national research centres and universities, venture capital organisations, angel investors, and industry in general began indulging in nano-related activities by "proximating" with such centres of excellence in academic institutions via linkages and collaborations, partial funding of R&D and setting up channels for facilitated knowledge transfer and development (Figure 11). On the other hand several academic institutions initiated processes for the sprouting of first generation entrepreneurs evolving into "start-ups" and large companies nucleating "spin-offs" and further developing them as "nanobators" (nano-incubators) till they see the light of the day in commercial terms in the market place. With this mixed bag of technology centric "nanovities" (nanoactivities), the upstream and downstream mixed in diverse proportions resulting in what may be termed as a transiting "turbulent mode" for a relatively "rapid" transformation of the results of R&D to commercialization.

Figure 11: R&D modes of the recent past

The recent modes in R&D in nanotechnology for faster commercialization are initiatives from industry in which there is significant shift in evolving methods for Co-Production of Upstream Knowledge and Concurrent Transfer between industry and centres of excellence in publicly funded / industrial R&D

centres, thereby blurring of boundaries and collapsing of timelines for knowledge bridging and integration.

There is also a gradual shift to establishing pre-competitive collaborative R&D operating as consortia, bringing together tributary streams of knowledge and skills to speedily supply the critical resources and expertise to build or fill the targeted gaps in the nano-knowledge domain. The partners in the consortia have agreements in which the conditions for the use of the generated pre-competitive knowledge in their respective commercialisation activities (Figure 12). Such consortia can work successfully only with cooperation among its members along the value chain. The challenge before consortia therefore lies in framing a pragmatic approach, including the publication of best practice including intellectual property rights (IPR) requirements that take into consideration foreground and background knowledge.

There is also a set of working models in which science and technology developers either working independent of each other or networking in clusters work closely with "commercialisation distributaries" through appropriate cost and benefit sharing arrangements.

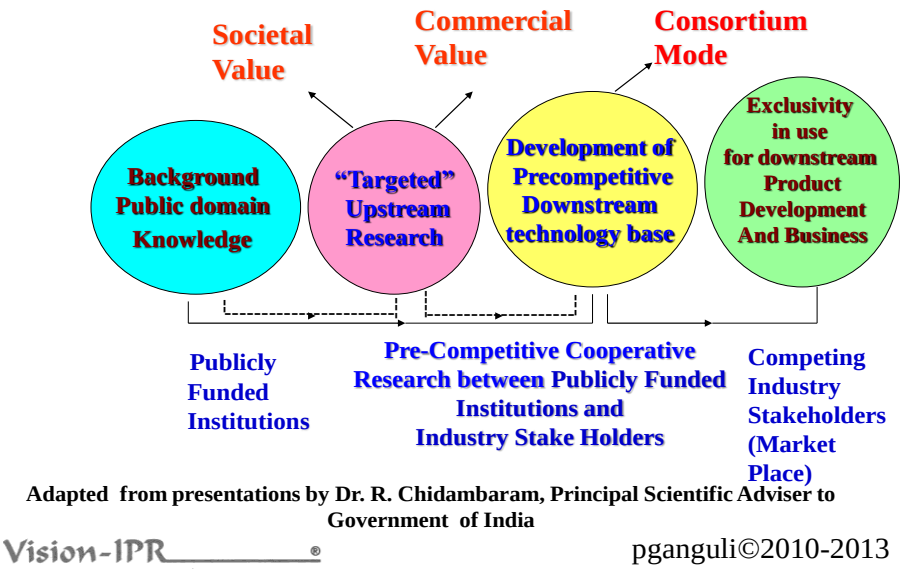


Figure 12: Collective modes for precompetitive collaborations

A distinct contrasting feature in nanoscience and technology as compared to the developments in other knowledge led areas is the concurrent co-production of upstream and downstream knowledge is what I term as "Tailored Cavitation" mode (Figure 13). This term is borrowed from the field of "Cavitation" wherein a flowing liquid obstructed by a mechanical/physical barrier leads to the formation of "bubbles" (i.e. cavities) which lock and concentrate quanta of diffused energy depending on the nature of the liquid, characteristics of the bubble / cavity, such as size and contents which adiabatically implode downstream of the above said obstruction in the liquid flow to locally release the energy in a single event (termed as

transient cavitation) or multiple events (termed as stable or oscillatory cavitation). Thus if such cavitation is tailored, the formation of the bubbles (energy packets) can be controlled for release in quanta at desired location and in desired form in the flowing liquid for its targeted utilization (physical, chemical or biological conversions requiring energy supply).

The knowledge streams in nanoscience and technology which are in a diffused form now needs to be "cavitated" in a tailored manner so that the learning from the diverse contributing fields (tributaries) confluence to create a main knowledge stream that is "quantized" in a targeted manner with clear demarcation of their "ownerships" (Intellectual Property Rights, IPR) for effective release at desired points and in desired form of the main knowledge stream to ensure the effective utilization of the generated knowledge at the desired "application gates" with "appropriate acknowledgement and benefit sharing" including commercialization through distributaries that derive their feed from the main knowledge streams. It is imperative for the knowledge distributaries to create complementarities by smoothening interfaces that may act as barriers to learning, promote inter institutional collaboration with the creation of shared cultural spaces, norms and practices.

Most start-up or small company innovators have major limitations of resource and hence partnership linkages with academic institutions and researchers provide a very effective path to extended R&D activities. Such partnerships typically lead to the creation of appropriate and timely intellectual property, licensing, and technology transfer simultaneously helping to merge cultures of academic researchers and small businesses alike, both in providing new perspectives for each into the innovation cycle, as well as accelerating the time and path to commercialization.

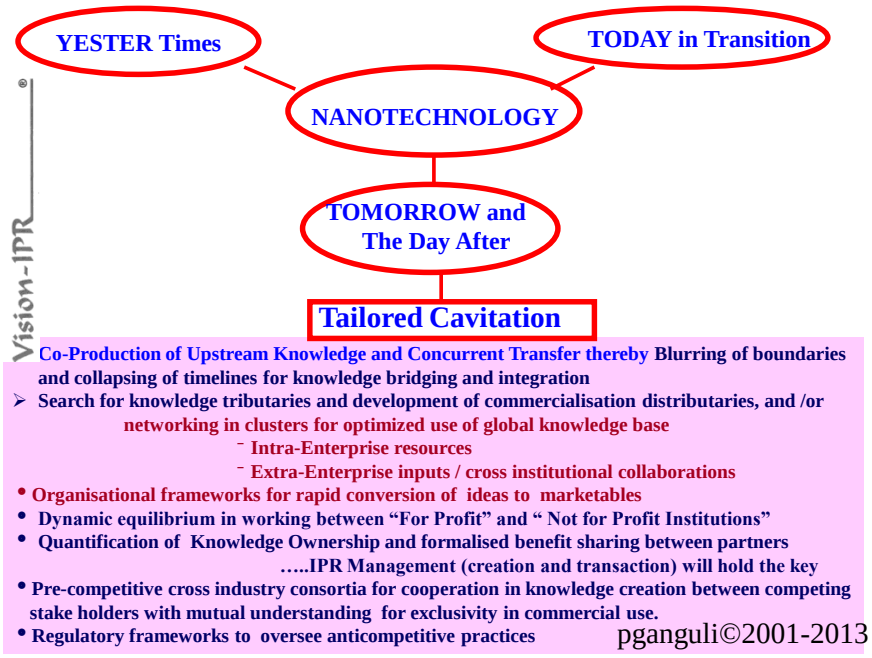


Figure 13: Present day and near future R&D modes

Such an example of a productive partnership is between Rolith Corporation and Professor Jay Guo's Research Group at the University of Michigan (USA) which has resulted in the licensing of a method to pattern nanoscale features in a surface over very large areas using a continuous optical lithography, using masks formed from a cylindrical polymer, the technique being termed as Rolling Mask Lithography (RML). The approach is inherently scalable with the process being limited only by the width of the cylindrical mask, and optimization of the photoresist and light source. RML is a "platform" technology, which can be applied to a wide variety of applications and markets. This nanopatterning, with its extraordinary flexibility and scalability, could open vast possibilities for advance products in commercial electronics, energy generation and storage, biotechnology, defense and others that include AR surfaces, self-cleaning, anti-fog, anti-icing, anti-drag, anti-bacterial surfaces, transparent electrodes for displays, solar cells and LEDs, dye less color filters, absorption enhancement layers for solar cells, extraction enhancement layers for LEDs, 3D solar cells, and wire-grid polarizers. Such a platform technology provides an excellent example of nanomanufacturing technologies transitioning from academic research groups providing a platform to effective scaling the process for numerous high impact applications and markets.

Drivers and barriers to technology transfer, acquisition and implementation have to be balanced to ensure speedy transition of an idea to the market place. An institution's ability to acquire such technologies through their R&D efforts, through technology transfer, through R&D collaboration, or through purchasing / importing commercial off-the-shelf systems would only reflect the S&T capacity of that institution, particularly its ability to conduct R&D activities or import know-how. For successful commercialization, the institution ought to have the capacity to successfully implement the acquired technologies. The institution should be able to match a technology application to a targeted problem, translate the technology application from the development phase into the market at affordable cost to the consumer, and the market must be able to sustain that use over time. The entire process needs the support for financing the access to the technology application, infrastructure to support its use, skilled workers to maintain it with continual technology improvements developed by technology generating workers, feeding into the market. Finally, individual users and the society as a whole must be able to benefit from the use of the technology application and be willing to support its implementation.

All such modes require reengineering of organizational frameworks for agile Intellectual Property Rights (IPR) Management that would facilitate the facile creation and transaction of IP.

Another area that is an emerging challenge in nanotechnology commercialisation is the compliance with evolving stringent regulatory platforms addressing environmental and health concerns, and in the market place overseeing possible anticompetitive practices.

5 Integration of IPR Management in R&D

IPR has become an integral component in any competitive pursuit, especially in technology centric fields such as nanotechnology. It is therefore imperative that IPR be concurrently managed with R&D and not be considered as a post "R&D" activity.

Technology transfer processes in nanotechnology including sustenance of product pipelines, foresees a very special role of inventors due to high content of "know how" which does not form a part of patent disclosures. Access to the tacit knowledge of inventors and their technical expertise is crucial to the successful translation of R&D findings into innovations. Documentation of the tacit knowledge is therefore of immense significance in the integration of IPR Management in the R&D process.

Similarly innovation administrators with new sets of technical competencies and skills are beginning to play knowledge-bridging pivotal roles in the development of collaboration architectures to minimise organisational inertia in the process of technology transfer.

The rapidly growing "prior art" both in terms of publications in journals & diverse media, and densification of patents with overlapping claimed knowledge domains (growing patent thickets), poses challenges to the R&D scientists and businesses to craft patent non-infringing paths and also creating innovations that are novel and non-obvious with respect to the existing prior art (existing in open freely usable domain and in patents / design registered domains). Early identification and analysis of relevant prior art is of immense significance and therefore "nanolytics" (nano-analytics) including timely generation of "Freedom to operate (FTO)" reports ought to form essential modules of nano R&D, technology transfer documentation and business strategy.

Structured technology transfer documentation with clear status of prior art vis-à-vis the technology that has been developed and being transferred including its "freedom to operate" in specific jurisdictions is of immense value as such transparency would facilitate timely disclosure of the developed knowledge, identification of closely related patents, spot potential collaborators, assist in legitimate IP transactions (such as acquisition / licensing), minimize litigations related to patent infringement, thereby paving the way for speedier, synergized and cost effective transformation of developed knowledge into innovations and profitable businesses. Only then would affordable genuine products and processes be made available to people in the market place.

There is an urgent need for the formulation, endorsement and implementation of R&D and innovation policy at the institutional level for purposeful preparedness directing good practices for R&D and innovation with synchronised management of IPR.

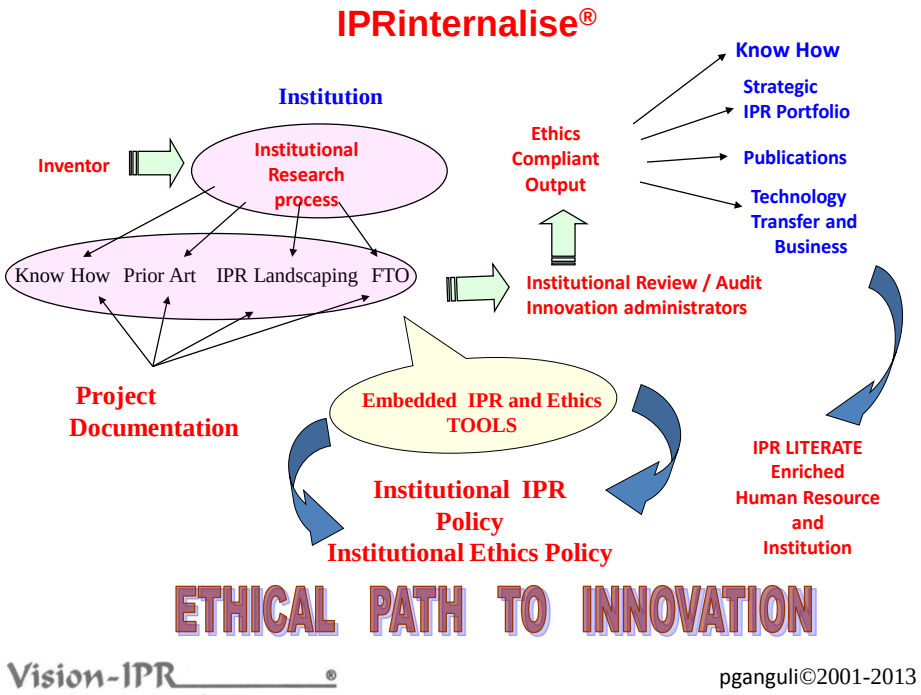


Figure 14: Model IPR internalise®

The author's model termed as "IPRinternalise®" that seamlessly integrates IPR in the innovation process in a structured manner that involves the inventors and innovation administrations in appropriate proportions drawn into the innovation stream by a natural tide of the innovation process, originating from one's immediate requirements to play their respective and combined roles in the creative, technology evolution, technology transfer and business development phases (Figure 14). "IPRinternalise®" starts at the problem definition phase where a researcher is explores and ethically exploits the prior art to contextually build on and provide creative solutions to the identified and assessed problem, get the explicit and tacit knowledge documented and have his solutions appropriately IPR protected and building of a strategic IPR portfolio by the innovation administrators for further processing to commercialisation. "IPRinternalise®" also provides a "stress and burden free" but "relevant and need based" gateway for early stage assessment of inventions, have them checked for possible infringement of others' IPR, introduce mid-course corrections to then design the inventions to ensure that the solutions with the built-in IPR ethics satisfy all conditions for its "freedom to operate" in diverse jurisdictions thereby facilitating smooth technology transfer and commercialisation.

6 Business development and planning and implementation of R&D commercialization / technology transfer projects

The N2M booklet CSA-SA 233476 NANO2MARKET, titled '*Towards Good Practices for IPR and Technology Transfer in Nanotechnology Developments*' under the 7th framework programme in Europe

(accessible at http://www.nanofutures.info/sites/default/files/N2M_Booklet.pdf) presents the Iterative Nano2Market-Approach observing that individual IPR and Technology Transfer are often heavily influenced by the size of the market the respective technology is planned to be commercialised within, as well as the level to which the technology would disrupt that market (Figure 15).

Accordingly specific technology maps are required to be generated to provide (a) a generic market vision of the technology, (b) a list of key-players of the technology, (c) a description of company segmentation, and (d) an introduction to the regulations governing the technology.

As illustrated in the report, Nano2Market Technology Maps were generated based on a search strategy, composed of accurate combinations of key-words, enabling the collation of information related to a specific nanotechnology application. Innovative data-mining techniques were subsequently applied to combine the technology map with an analysis of sector-dependent IP cultures, with a view to identifying underlying clustering and other market conditions influencing intellectual property and technology transfer.

The analysis resulted in an illustration of the evolution in patents and scientific publications, as well as an overview and brief introduction to the top companies in the respective technology capability in patents and publications, on both (a) the global level, and (b) the European level.

The N2M Report further observed that even for a specific sector, it is difficult to assert that only one optimal strategy for technology transfer is appropriate. Aspects such as the regulatory framework, standardization, cost vs. benefit, converging with bio/IT technologies and its feasibility, etc., can vary greatly from one application to the next, and have to be carefully reviewed and covered. One single breakthrough scientific advance can lead to a manifold of products, each of them to be sold to different markets and consumers, with different barriers to overcome.

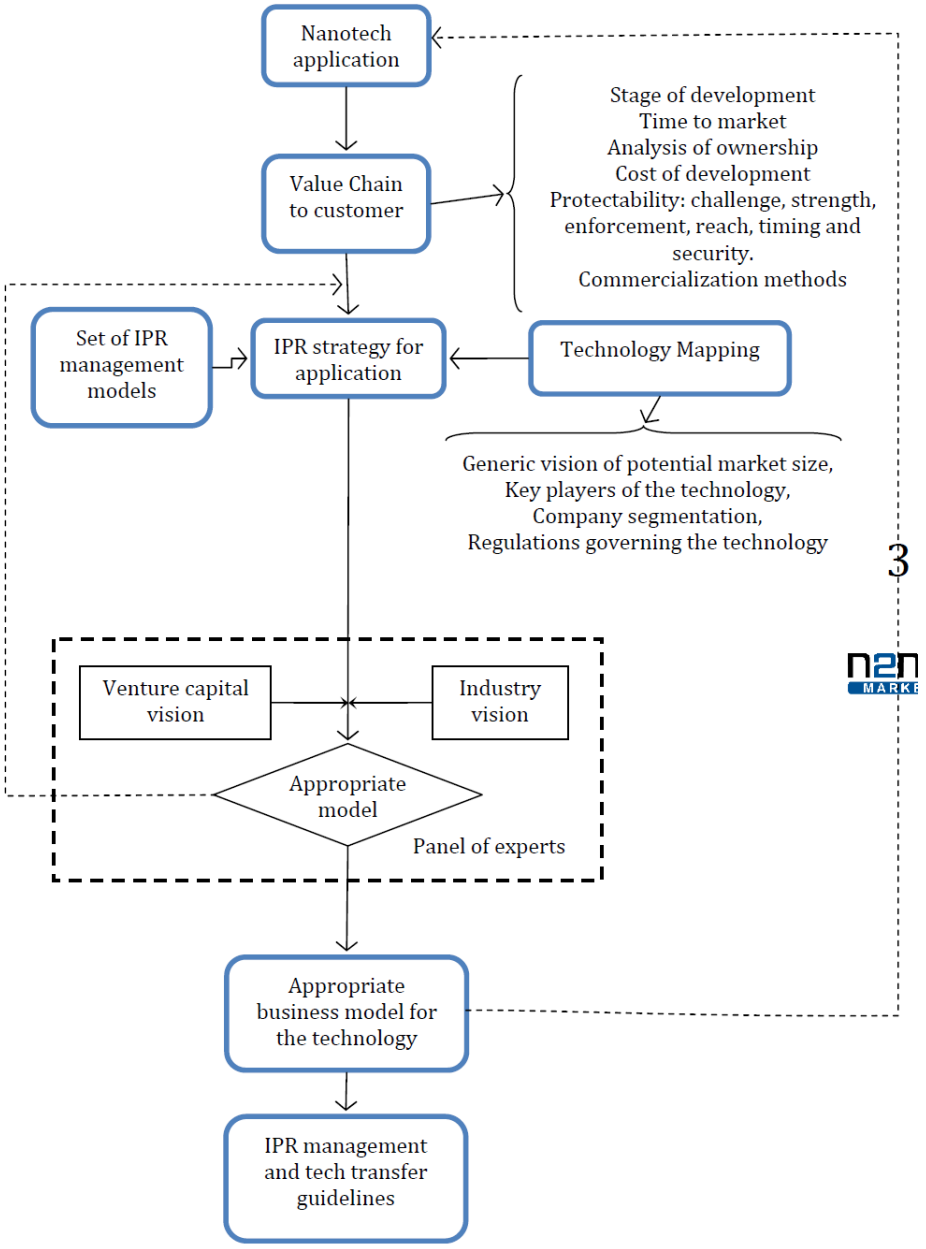


Figure 15: The iterative Nano2Market approach

(Source: http://www.nanofutures.info/sites/default/files/N2M_Booklet.pdf)

In terms of patenting and licensing, the report further observed that each sector has its own nuances and that there is no standard patenting / licensing mode cutting across all the sectors. Hence the complexity of patenting / licensing is sector specific and all associated characteristic to that sector must be taken into consideration in drafting patents and striking licensing deals and accordingly structuring an appropriate business model. The case studies presented later in this chapter clearly illustrates these aspects.

The N2M Report shows that there is an ascending order in the value chain involving nanotools, nanomaterials, nano-intermeddiates and nano-enabled products. The pateentting / licensing complexity also follows the same order as in the value chain (Figure 16).

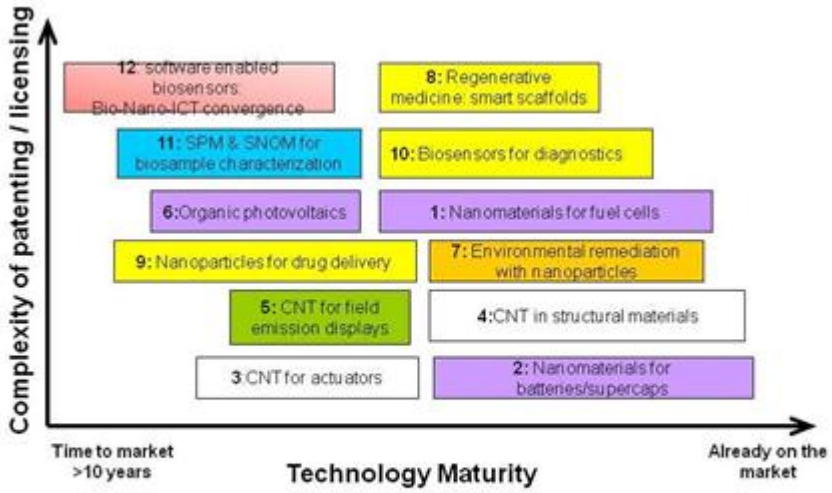


Fig. 16 Complexity in Patenting / licensing vs. Technology Maturity

Source: CSA-SA 233476 NANO2MARKET

The report further presented the investors' perspective (Figure 17) on the equity lifecycle that has an influence on technology transfer and the business model to be adopted

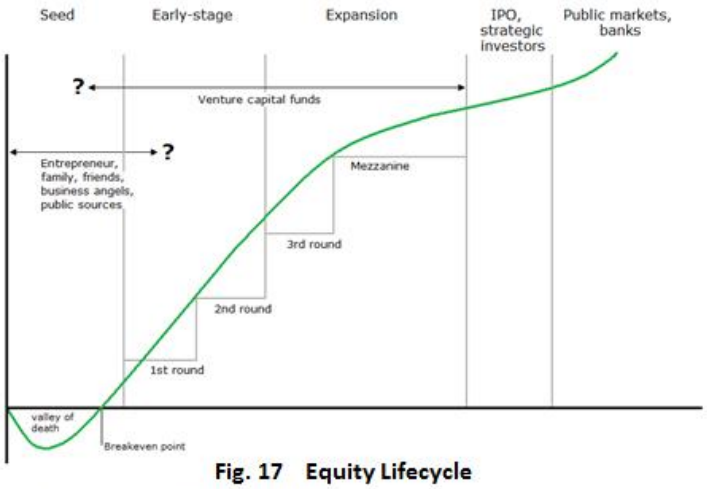


Fig. 17 Equity Lifecycle

Source: CSA-SA 233476 NANO2MARKET

All these factors are of significance and have to be taken into consideration before working on the N2M Iterative Approach presented in Figure 15. The case studies presented in this chapter also illustrate these features.

7 Role of technology transfer / licensing offices of Universities and R&D institutes

Technology Transfer Offices (TTOs) in Universities and R&D Institutions are the main gateways to technology transfer across the institutional walls (Figure 18). The role of TTOs is multifarious that ranges from managing the innovation cycle in the institution from concept to periodic progress review, ensuring appropriate documentation, confidentiality, evaluating commercial potential, conducting periodic due diligence, filing of appropriate intellectual property applications for the creation and management of strategic IPR portfolios, establishing Freedom to Operate Reports on institutional innovations, developing commercialization strategies, marketing, negotiating IP transactions such as assignments and licenses, facilitating the formation of start-up companies, encouraging entrepreneurs, validating new practices to minimise market, technology, financial, managerial and legal barriers, maintain beneficial partnerships with public and private sectors in research and technology, actively pursue commercialization opportunities for nanotechnology-based inventions and promote controlled diffusion of institutional knowledge with a pragmatic revenue model say in nanotechnology to the commercial world.

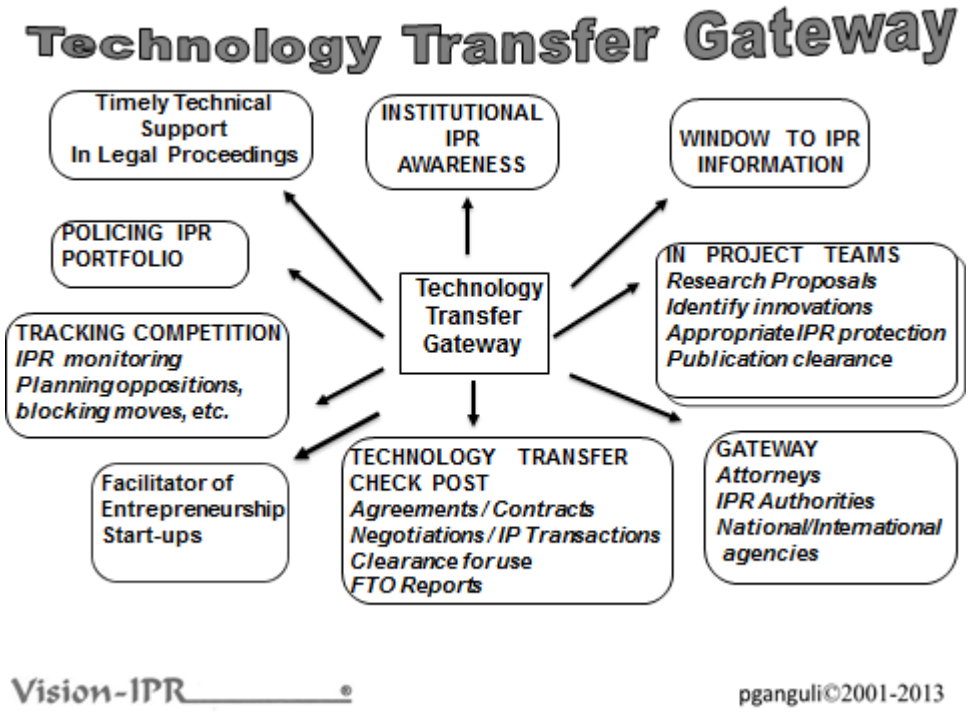


Figure 18: Technology Transfer Gateway

8 Due diligence for technology transfer

Technologies may be developed to provide solutions to existing problems and to fulfil the unmet needs. On the other hand one may have developed new understanding in nanotechnology or developed new materials with new properties or have found new properties of known materials for which innovative applications in diverse fields are explored and found.

The diverse motives to acquire technologies range from expansion of markets with territorial coverage & exportability, getting access to strategic and targeted resources, establishing a manufacturing platform for the region and minimizing the learning curve in adapting technologies, complying with specific requirements of certain governments that require operating companies to transfer technologies and know-how for the development of the region and to ensure accessibility and affordability of IPR protected products meeting global standards within their jurisdictions thereby meeting domestic content requirements, preempting competition, avoiding tariffs, etc.

Technology transfer is considered a special case of knowledge transfer because in many cases what is transferred is not the technology itself, but the knowledge that can result in the technology. It ought to be appreciated that technology transfer requires continual interaction between the transferor and the transferee through multi step processes leading to a range of activities that should ideally strengthen their inter-relationships for mutual benefits.

In all such cases technologies may be transferred between interested parties which not only involve the dynamic translation of knowledge by way of knowhow and / or right to use the intellectual property rights (e.g. patents) of the technology/knowledge owner through negotiated agreements. During such technology transfer processes, one conducts due diligence on the developed technology, legal aspects such as intellectual property rights ownerships and freedom to operate in markets of interest (diverse jurisdictions), marketability of the technology, regulatory issues, etc. The collaborative partners may differ in their working culture, role and competence during different phases of the technology transfer process, and management of this multifaceted often conflicting interface is the real challenge.

One needs to prepare well in advance for any technology transfer exercise. Several searching questions need to be addressed prior to detailed negotiations between the parties. Some basic questions are: What is the background and history of the party interested in transferring the technology and why? What is the background and history of the party interested in acquiring the technology and why?

8.1 Broad aspects of due diligence

Any technology transfer process is preceded by a due diligence on various aspects linked to the technology being transferred. The main broad categories of the due diligence may be classified as:

- Scientific / technical strength and weakness
- IP ownership and rights
- Validity and infringement of the associated IPR

8.2 Checklist for scientific /technology related due diligence

- What is the field of invention? What is the problem being addressed? How comprehensive is the solution to the problem? Is it a platform technology that can be adapted to provide solutions to other related problems?
- What is the relevant background information available in the literature and in the open domain including the market place?
- Has a feasibility report and market opportunities on the technologies developed been prepared by the party intending to transfer the technology / technologies? If no such report is available it would be advisable to get such a report prepared by a competent party / technology broker.
- What are the competing technologies and what is the gap between existing technologies in prior art and the developed technologies? What is the probable life cycle of the technology to be transferred?
- Does the party intending to transfer the technology have sufficient know-how and know-why to make the technology work? What is the nature and structure of documentation available with the party intending to transfer the technology? Have they made a proper listing of the appropriate documentation, computer packages including source codes, oral communications, e mails, minutes of meetings, project reports, certified laboratory note books recording the work done both in terms of successful and unsuccessful experiments, drawings including clarity on the ownership to the copyright to such drawings, prior art search including data bases searched, analysis, search strategy adopted, etc to aid in the transfer of technology?
- What is the level of expertise with the party intending to transfer of technology in the field of the technology developed? Can they do a hand-holding exercise during and after the technology transfer exercise? Can they provide support in setting up plants, establishing production processes, quality control procedures, etc?
- Can the party intending to transfer the technology have resources to undertake Contract Research and Development?
- Does the party intending to acquire the technology have the technical capability in terms of equipment and skilled human resource to absorb the technology and convert it into a commercial reality?
- Does the party intending to acquire the technology have a feasible business plan to market the technology?
- Does the party intending to acquire the technology have adequate financial resource to complete the technology transfer and diffuse it into the business plan of the company?
- Does the party intending to acquire the technology have the capability of developing the technology in terms of applications, etc after the acquisition?
- Does the party intending to acquire the technology have the intention to continue the linkages after acquiring the technology?

8.3 Checklist for IPR related (patents, trademarks, industrial design registrations, copyrights, trade secrets, domain names) due diligence

- What is/are the sources of funding used for the development of the technology or technologies? Are there any terms and conditions of the funding agency / agencies on the ownership of the IPR / rights to use the technologies? If so, what are they?
- If the party intending to transfer the technology is an institution, then does it have an Institutional IPR policy? If so, what are the boundary conditions set in the Institutional IPR Policy on matters related to confidentiality, publications, permitted disclosures, pirating, reverse-engineering, creation of start-ups, spin-offs, knowledge purchase or lease mechanisms, transfer of technology and IPR?
- What is the chain of title associated with the IPR?
- Has an evaluation been done on the patentability of various facets of the technologies developed? Would any aspect of the said technologies fall within the ambit of exceptions to patentability in selected jurisdiction [an example of such an exception to patentability would be Section 3(d) together with its explanation of the Indian Patents Act 1970 (as amended in 2005]?
- Have all aspects of the developed technology been covered by appropriate IPR applications before public disclosure?
- Would one have to file additional IPR applications?
- Have all the documentation related to correspondences and office actions with the patent offices been examined for completeness of all office actions including pending office actions? Are all priorities claimed in the patent applications valid?
- Has an assessment been done on how well have the trade secrets and confidentiality been protected?
- Have appropriate assignments been taken from the inventors / collaborators? Further does the party intending to transfer the technology have the rights to those technologies by way of assignments, and are they the legitimate owners of the IPRs/ IPR applications? Do the collaborating institutions have joint rights to the said IPR? If so, are there any agreements controlling the rights to negotiate, assign, benefit sharing between the collaborating parties? Does anyone have the first right to refusal? Does anyone else have an option over the IP?
- Are there other contracts with carried forward interests, options for rights, or for shares? Are there any breaches of existing contracts? What are the terms and conditions of such contracts? Are there any performance obligations and/ or are there any termination rights that may have accrued?
- Have the employee contracts been examined for the confidentiality clauses, assignment and transmission of rights, warranties, non-compete clauses, etc?
- Are there any preconditions on the rights to further develop the technology? If so, who would own the IPR on such further developments?
- Are appropriate materials transfer agreements in place with rights to use the materials for further work, investigations, etc?
- What are the search reports and opinion on patentability of the various PCT applications?

- What is the strength of the claims of the granted patents and would they survive if validity is challenged?
- Have the patent claims been appropriately constructed to enforce them against alleged infringers?
- Is any party already infringing the claims of the granted patents and/or of the claims of the patent applications? If so, what actions have been taken or contemplated?
- Have all the renewal fees to the IPR offices in the appropriate jurisdictions been paid? Has the term of each IPR in the IPR portfolio been assessed and recorded? Have any of the IPRs lapsed in any of the jurisdictions?
- Have any of the IPRs been mortgaged? If so what are the details? Are there any lock-in clauses?
- Has "Freedom to Operate (FTO)" in jurisdiction of interest been assessed? Do other parties have the right to operate within the given field of technology?
- Are there any regulatory issues that may come on the way of exploiting the IPR/IPR applications? If so, what actions have been taken or need to be taken?
- Have any related aspects of the technology been in-licensed by the party intending to transfer the technology? Have those licensing agreements been examined for all the terms and conditions including rights to sue and claim damages for infringements? Are these licenses related to the core area and / or peripheral area of the technology being transferred? Are the licenses exclusive or non-exclusive?
- Have any of the aspects of the technologies developed been out-licensed by the party intending to transfer the technology? If so, have the agreements been examined? Are these related to the core area and / or peripheral area of the technology? Are the licenses exclusive or non-exclusive?
- Have any of the aspects of the technologies developed been cross-licensed by the party intending to transfer the technology? If so, have the agreements been examined? Are these related to the core area and / or peripheral area of the technology? Are the licenses exclusive or non-exclusive?
- Have any of the IPRs / IPR applications been assigned to other parties? If so have those agreements been examined? What has been assigned? Who has the rights to the knowhow related to the assigned applications or granted patents? Who would have the rights to the knowhow related to the assigned applications to file further patent applications? Is the assignment of the patents linked to physical assets of the patent holder?
- Are the licenses and assignments free of conflicts?
- Are there any ongoing litigations and / or proceedings with regard to any of the IPRs in the IPR portfolio? If so, what is the status?
- What is the market value of the IPR Portfolio?
- Are there any liabilities associated with the IPR Portfolio?
- Do any of the transactions associated with the IPR portfolio (e.g. grantback provisions, tie-in provisions, front-end lump-sum fees, royalties, technical assistance fees, payment in equity, payment for supplies, value of grantbacks, etc.) fall within the ambit of the provisions of competition law / anti-trust law in jurisdictions of interest?
- Are there any tax liabilities / benefits associated with the transfer of technologies / IPR in the jurisdiction of interest including issues related to cross-border transactions?
- Who would bear what costs?

9 Case studies on technology transfer and commercialization

9.1 **'Influence of partner diversity on collaborative public R&D project outcomes: A study of application and commercialization of nanotechnologies in the Netherlands'** by Ariane von Raesfeld, Peter Geurts, Mark Jansen, Johannes Boshuizen, Regina Luttge (2012), *Technovation*, Vol 32, pp. 227–233

The authors have reported their study on university–industry collaboration related to nanotechnology and the impact of the technological diversity and value chain complementarity in multiple partner collaborative public nanotechnology research projects. They their findings are:

- A non-significant effect of technological diversity on application development.
- Value chain complementarity has a positive effect on both application development and commercial performance of the collaboration projects. These findings also hold for public nanotechnology R&D projects.
- A U-shaped effect of technological diversity on commercial performance of the projects. In the nanotechnology projects, the effect of technological diversity first shows a decrease followed by an increase of application development and commercial performance.
- The participants' commitment has an overall positive impact on the outcomes of nanotechnology research projects.

9.2 **'Which model of technology transfer for nanotechnology? A comparison with biotech and microelectronics'** by Corine Genet, Khalid Errabi, and Caroline Gauthier (2012), *Technovation*, Vol 32, pp. 205–215

The authors investigated the model of technology transfer in nanotechnology, focusing on the position of smaller and larger firms in that model. They created a database of nanotechnology firms and conducted a network analysis of R&D collaborations between the partners in the sector. Their findings suggest that nanotech SMEs do not play a key role in bridging the gap between public research institutes and large companies but rather perform as providers of specialized services/technologies. In contrast, their results indicate that large firms play a key central role in knowledge co-production processes in nanotechnology.

9.3 '**Market challenges facing academic research incommercializing nano-enabled implantable devices for in-vivo biomedical analysis'** by E. Juanola-Feliu, J.Colomer-Farrarons, P.Miribel-Catala, J.Samitier, J.Valls-Pasola (2012), Technovation, Vol 32, pp. 193–204

This article reports on the research and development of a cutting-edge biomedical device for continuous in-vivo glucose monitoring. This entirely public-funded process of technological innovation has been conducted at the University of Barcelona within a context of converging technologies involving the fields of medicine, physics, chemistry, biology, telecommunications, electronics and energy. The authors examine the value chain and the market challenges faced by in-vivo implantable biomedical devices based on nanotechnologies.

Using a case-study approach, the authors have examined the high-tech activities involved in the development of this nano-enabled device and describes the technology and innovation management process within the value chain conducted in of a public-funded R&D&I environment involving a University typified by the convergence of technologies and disciplines –Hospital–Industry–Administration–Citizens framework.

The Department of Electronics at the University of Barcelona, in collaboration with the Institute for Bioengineering of Catalonia (IBEC), the Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN) and the Biomedical Research Network in Diabetes and Metabolic Diseases (CIBER-DEM), promoted an alliance with the aim of developing a cutting edge multidisciplinary research and commercial team covering the entire range from applied research to clinical diagnostic. In this way, research centers, hospitals, firms, health policies and citizens shared the same goal: launching onto the market safe, reliable and affordable biomedical devices for the diagnostic and therapy of diabetes, improving the quality of life of those who have to control their blood sugar level by on-line monitoring and keeping the requested glucose level constant (by using a Radio Frequency activated clock-alarm or with exact doses administered directly from an insulin reservoir).

The overview provides the value chain of research and technology transfer processes and highlights the importance of a common framework in which multidisciplinary teams and organizations can work together directed by determined scientific leadership. In this specific case, the Department of Electronics at the University of Barcelona has had overall charge of the research and commercialization activities. The resulting biomedical device is nano-enabled in a dual sense: when miniaturizing the system (fluidics, electronic, energy autonomy) and when new functional structures are included (nanobiosensors developed by the IBEC). The CIBER-DEM joins the value chain when clinical research and commercialization are considered.

The process described offers an efficient method for performing experiments at large test and clinical facilities, within an innovative framework that takes advantage of new scientific tools and discoveries. Biomedical devices represent a strategic gamble for the future of Spain's scientific and technological policy areas as they seek accelerated economic growth within the knowledge-based society. In this way, the country's regions can strengthen the network links between their R&D agents – science and technology parks, institutes and research centres, hospitals, technology platforms and incubators – as they explore and confront the new scientific and market challenges.

9.4 Nanotechnology entering into the Danish glass window market

A paper presented at the DRUID 2011 on 'Innovation, Strategy, and Structure - Organizations, Institutions, Systems and Regions' at Copenhagen Business School, Denmark, June 15-17, 2011 titled '*Silent innovation - Corporate Strategizing in early Nanotech Evolution*' by Maj Munch Andersen, Technical University of Management, Denmark analysed how firms organize innovation in the early embryonic stages of a technology and how the market as a selective device undergoes qualitative change as part of economic evolution. The traditional Danish window chain is used as a case study.

A model of nanotechnology evolution has been proposed which suggests that nanotechnology commercialization is significantly driven by small and medium-sized firms based on their internal know-how, with larger firms as important suppliers of knowledge. These smaller firms are adept at addressing social needs which appear to be key factors in the nano-commercialization process. A qualitative study was undertaken to understand how nanotechnologies entered into the window supply chain in the Danish market.

This case study typically represents the urge of technology development, transfer and commercialization based on "market pull" to satisfy an unfulfilled need or what may be considered as a "continuous demand for enhanced performance by way of innovative coatings to meet an unmet meet" through nanotechnology strategies and innovation activities of core actors in the Danish window chain market.

The Danish window chain comprises those firms active in Denmark in the market for windows, as well as their suppliers and customers. Interestingly, the Danish window chain comprises of "start-ups", "multinational companies", and small to medium sized enterprises, with the producers of glass and windows generally headquartered in Denmark. These firms network with relevant (nano-active) suppliers and with customers in wholesale and retail trades fully commercializing nano-enabled products. They are also involved in a variety of development projects and emerging new nanotechnology applications with the multinational glass companies taking lead in developing advanced nanocoatings.

Pilkington for example spends around £33 million a year on R&D, organized within their two business lines of building products and automotive products. Additionally, Pilkington cooperates with the R&D labs of the parent Japanese NSG Group. Pilkington marketed the first selfcleaning glass in 2001. This has garnered international recognition as one of the first commercially-available nano-consumer products. Within a year, PPG Industries, Cardinal Glass Industries and Saint Gobain also launched their self-cleaning glass products. Self-cleaning glass is now widely available in glass wholesalers' product portfolios, although it still awaits a major breakthrough in market demand.

Another entrant in nano-enabled glass is Sunarc, a small Danish up-start company, specializing in the production of nano-structured anti-reflective surfaces on large glass sheets was stablished in 2000. The capabilities underlying Sunarc's production are mainly tacit and rest with core employees. The critical elements lie in the fine adjustment of the production process, which is essential to achieve a uniform high product quality. The company has chosen not to patent its technology. Others have tried to copy what they are doing, including the larger glass companies. However, although laboratory-scale production is easy, scaling-up to commercial levels is difficult, and Sunarc is still the leading full-scale global producer with this technology.

VELUX is the dominant company within the VKR Group, with a well-known international brand and specializations in roof windows and skylights. Nanotechnology has long been of interest to VELUX because it plays an important role among a number of their suppliers and in the components of their products. VELUX has its own R&D department, which is divided into two sections, one for the frame and one for glass. Both sections are involved in nanotechnology R&D.

Dovista, also part of VKR, is the holding group of the main two Danish producers of vertical windows, Velfac and Rationel. Dovista undertakes R&D for these two affiliates. In the past, Dovista was not focused on nanotechnology and did not undertake targeted searches into nanotechnology innovations. However, interest is now growing. In 2009, Dovista began their first nanotechnology R&D project, with a Danish university, aimed at reducing condensation problems of windows (which, as noted, is a major issue in increasingly energy efficient buildings). There is also cooperation between VELUX & and Dovista: they draw heavily on each other's R&D and engage in common product developments and marketing.

According to VELUX, their main sources of knowhow are not research institutes but their varied major international suppliers who VELUX sees as being at the forefront of technological development, including for nanotechnology.

The VKR Group has recently become engaged in nano-enabled product development for wood impregnation.12 VKR has long been looking for more environmentally-friendly wood preservation methods. In 2006, VKR bought Superwood, a Danish start-up company, which offers a nanotechnology-based and environmentally-friendly wood impregnation method using supercritical carbon dioxide (CO). The method is based on a 2001 patent. Superwood was started in 2002 as a buy out from FL Schmidth – a Danish-based global supplier to the cement and minerals industries. Superwood struggled with scaling up, and went bankrupt in 2003.

Following VKR's purchase of the company in 2006, VELUX, Dovista and Superwood are jointly engaged in further development of Superwood's technology, targeted specifically to window products.

A further nanotechnology entrant in the window chain is Photocat A/S17, a Danish startup company. Photocat produces nano-structured materials and coatings with photocatalytic properties, e.g. self-cleaning functions. Photocat has a product directed at the glass market, ShineOn® Pro, which is an aftermarket treatment to make window glass self-cleaning. The company is a spin-out from SCF Technologies A/S, a dedicated Danish nanotechnology company that from 2003 also specialized in supercritical technology, similar to Superwood. SCF initially experimented with a range of applications for supercritical technology. SCF focused relatively quickly on bio-oil from organic waste, which is now the core focus of the company. In the advanced materials area, SCF focused on self-cleaning glass. For this product SCF initially relied on imported nano-materials from China, but after encountering technical challenges the company began work to design its own nanoparticlesof the patented ShineOn® product in 2005.

Additionally, working with a Swedish floor company, Välinge Innovation, in 2007, a new patented composite flooring material was developed (ActiFloor). Photocatalytic nanoparticles are integrated in the floor material matrix, the first of its kind. These floors are depolluting, improving the indoor climate (formaldehyde release is eliminated from the floor itself, while the floor also removes formaldehyde from other sources). With SCF seeking to focus on products other than self-cleaning materials, Photocat was spun-out in 2009, with plans to start industrial production of the floors in 2010. Meanwhile, ShineOn has been licensed by Photocat to wholesale companies in the UK and US, with moderate success. The users are professional glaziers and renovation companies. In Denmark marketing activities have been limited and no license partner has been found.

Key learnings from the Danish experience

The Danish experience over the last three decades indicates that medium-size players in the Danish window industry (both in size and chain position) play a key role as integrators of a variety of nanotechnologies. Internal R&D combined with input from their large suppliers form the basis of their internal nano-capabilities. The recent observed strategic shift among mid-chain window producers from window to green building providers strengthens their roles as system integrators, indicating that they may become even more important carriers of nanotechnology commercialization in the future.

Nanotechnology has already affected the organization and operation of the window sector. Large companies play a central role, through the provision of nano-based coatings (by the large glass companies) and chemicals and metal materials. A small number of these large integrated organizations placed upstream have substantial nanotechnology capabilities which function as a source for firms further downstream. They are complemented by nano-dedicated start-up companies who, in the Danish window case, have developed several promising new nano niche products.

While there seems to be a distributed set of nano-capabilities in the window chain, this case study also highlights the widespread disinterest and lack of awareness among many of the smaller and medium-sized companies who dominate the construction sector. Even companies that are innovative in other domains (such as Fiberline) are not very engaged with nanotechnology.

The Danish market may be categorized into various types of enterprises based on their involvement in the nanotechnology sector, namely:

Category 1: the makers of instruments, equipment, facilities and software for nanotechnology production;

Category 2: producers of generic nano-materials; and

Category 3: producers of nano-services, e.g. specialized consultants who advise on aspects related to nanotechnology.

Firms in these three categories enable other firms to develop and apply nanotechnology.

The next set of firms is downstream, moving towards nanotechnology used.

Category 4 comprises *dedicated nanotechnology firms* (such as Superwood, Sunarc and Photocat) where nanotechnology makes up a fundamental part of the firms capabilities and innovative activities and it is applied to develop innovative (nano) products.

Category 5 consists of *nanospecialized firms* where nanotechnology forms a serious but not central part of their capabilities. The multinational glass producers are leading nanotechnology developers within the construction area, but they also possess other important capabilities and lines of business.

Category 6 comprises *nano-active firms*, where nano R&D play a modest but not very central role for their innovative activities and capability development. An example is VELUX, whose nanotechnology innovation is mainly centered on applying and integrating nanotechnology developed by others.

Category 7 consists of *nano-explorative firms*, with no development activities in nanotechnology but with interest and some level of research into nanotechnology opportunities (as for Pro-Tec and Velfac/Dovista).

Category 8 encompasses *nano-tacit users* with no R&D in nanotechnology themselves but applying nano-enabled products (e.g. many construction companies and architects). They may be more or less knowledgeable about the nano-content of their products.

Category 9 contains what can be termed *nano-shadow* companies. Nanoscience forms part of their underlying technology base and is applied in niche products by others in the sector. However, companies in this category have limited or nil efforts themselves in developing or applying nanotechnology. These companies are typically relatively high tech and are potentially nano-dedicated companies. An example of such a firm is Fiberline.

Technology transfer takes place at various points in the value chain between the collaborating and business partners who are mainly integrators through business deals, contracts and diverse types of agreements.

9.5 Nantero

Adapted from the book titled "Nanotechnology Intellectual Property Rights….Research, Design, and Commercialization by Prabuddha Ganguli and Siddharth Jabade, CRC Press (Taylor and Francis Group) USA, 2012; ISBN 978-1-4398-5528-7

Nantero is a nanoelectronics company based in Massachusetts, with around 400 patents relating to carbon nanotubes and "next-generation semiconductor devices" for mass memory storage, such as NRAM. Nantero also specializes in logic switches, sensors, carbon nanotube antennas, and liquid solutions. Further experimentation and explorations in nanotechnology is still a major priority of the company, as well, and it is supported through the company's strong relationships with corporations, the United States government and academic institutions. Nantero has always explored for true partners who will give as much as they get. Nantero is the licensor of technologies, and its intellectual property portfolio allows the company to choose under which terms and conditions its IP will be shared with its licensees. Nantero has already built up an impressive portfolio of 200 US patents filed of which 120 have already been granted and many more around the world, including valuable manufacturing know-how that could be licensed to others who want use their technologies for diverse applications.

In 2001, Greg Schmergel a Harvard M.B.A. and former management consultant and Thomas Rueckes a researcher at Harvad University along with Brent M. Segal, another former Harvard chemistry doctoral student, formed Nantero, a name whose genesis again combined the small ("nano") and the large ("tero," a corruption of "tera," or trillions, as in trillions of bits). The immediate mandate for Nantero was to move beyond an advanced graduate project to create a device that could be manufactured in a working semiconductor facility. The company set up shop in a Woburn, Mass., industrial park populated largely by biotechnology firms.

When Nantero started, no good options existed for forming a nanotube on the surface of a wafer (the round silicon disk from which chips are carved) without interfering with adjoining electrical circuitry. Deposition of nanotubes onto the wafer using a gas vapor required temperatures so high that the circuitry already in place would be ruined. Nantero devised a proprietary solvent suitable other than the banned excessively toxic chlorobenzene for spin coating. The thin film of nanotubes left after the solvent is removed can be subjected to lithography and etching that leaves the surface of the wafer with evenly spaced groupings of nanotubes that resembles a helter-skelter unwoven fabric. An electric field applied to one of the fabric elements bends it downward until it contacts an electrode, a position that represents a digital 1. ASML, a major semiconductor tool manufacturer, helped to refine this process with Nantero.

Nantero in 2003 in collaboration with LSI Logic, a leading maker of customized chips for the telecommunications, storage and consumer electronics industries, initiated a project to bring the process for making what Nantero calls nanotube random-access memory (NRAM) into its factory in Gresham, Oregon and within nine months, the collaborators had a working prototype. The project was quickly put on an early-development track, and brought it into first commercial production memories by 2006 using the process in a standard CMOS facility. LSI and Nantero then worked together to increase "yield," the ability to scale up to make millions of nanotube memories with near-perfect repeatability.

Nantero also set up collaboration with BAE Systems, to work on defence and aerospace applications for the radiation-resistant NRAMs. It also set up a partnership with the American global aerospace, defence security and advanced technology company, Lockheed Martin. In 2008, this partnership culminated in Lockheed Martin purchasing Nantero's government business unit and creating Lockheed NanoSystems. The federal government also plays a large role in nanoelectronics, and companies can benefit from government involvement, as Nantero did with an opportunity to test their memory chip's durability by sending it up on the space shuttle Atlantis in partnership with National Aeronautics and Space Administration (NASA).

When looking for manufacturers with which to partner, Nantero considers sophistication, experience and credibility of the potential partner such that the potential could provide Nantero the greatest possible market penetration. Nantero also looks to areas where they can manufacture while also limiting possible competition and infringement. Once a product is manufactured, the partner identifies the location of the user market and begins to commercialize the product. Above all else, Nantero focuses on making sure that their inventions are fully employable in a current and modern infrastructure.

A large research and development team, and the steps Nantero takes before it approaches manufacturers and marketers, helps Nantero leverage its company's IP. Nantero is at the forefront of their field of industry, and plans stay this way.

Lessons on technology transfer

Nantero develops the core technology and then partners with high tech companies who are actively involved in applying the core technology with active participation between the technical teams of the partners to convert the developed technology into successful commercial opportunities. Technology

transfer therefore takes place through licensing of the patents, sharing of knowhow and targeted working to achieve set objectives by the partners.

In nanotechnology development, large firms hybridize their existing knowledge base with the newly emerging technologies, and strategically invest in pre-adaptation so as to speed up the development of new technologies and to be ready as markets emerge. Large firms play a prominent role in the process of coproduction and transfer of knowledge in nanotechnology by acting as a node of high centrality directly linking the industry's co-patenting network with research in small organisations / institutions.

9.6 Invitrogen (presently Life Technologies Corporation)

Adapted from the book titled "Nanotechnology Intellectual Property Rights….Research, Design, and Commercialization by Prabuddha Ganguli and Siddharth Jabade, CRC Press (Taylor and Francis Group) USA, 2012; ISBN 978-1-4398-5528-7

Invitrogen is a typical example of a company which was initiated as a start-up in 1987 with an impressive growth to a robust, successful and profitable sustainable enterprise in the field of "bio-molecular labeling" offering the world's largest line of products for gene expression. The company's pragmatic business model ensured targeted technology development, technology transfer, commercialisation, procurement of funds from diverse sources, planned mergers and acquisitions, timely exit from unprofitable activities, enforcing its intellectual property rights when necessary, and effective networking with stakeholders and clients. The company was seeded as a biotech enterprise essentially to develop and supply kits but over time expanded it to provide some of the most sophisticated products based on novel specially coated fluorescent nanocrystals and metal alloys for applications in multicolor labeling, sorting and imaging of cells, lateral flow immunoassays, and fluorescent inks for automated assays of complex biological samples

Invitrogen was founded in 1987 by three scientist/entrepreneurs to make and sell kits to help molecular biology scientists make cDNA libraries. Libraries, or collections, of cDNA are important for identifying new genes. As a startup with limited resources, but with some experience in the venture capital industry, Invitrogen focused on short-term product development ideas that could rapidly generate revenues with a minimum development cost. Some of these products failed, but the investment in the failures was low enough so as not to have a significant financial impact on the company.

During 1992 and early 1993, the company went through a challenging phase as there were mounting back orders caused by products failing quality control. High scrap rates drove production costs up and slowed sales growth to single digits for the first time in the company's history. The founders of the company - typically scientists/entrepreneurs, had no manufacturing experience. However, with concentrated efforts the company completely reorganized the manufacturing process by adopting a focused six-month Manufacturing Excellence program. By the end of 1993, the manufacturing issues were sorted.

In 1997, based on a market survey, the company explored the expansion of its custom cloning service business, based on its proprietary "topoisomerase (TOPO) mediated cloning" specifically targeting the pharmaceutical companies as a value added proposition to significantly reduce drug development

timelines and expenses. The positive response was so overwhelming that Invitrogen pulled the project back to rethink the objective.

Realizing that the company was getting into an area outside of their core competencies of kits and services, the company brought in experts in pharmaceutical drug development to help develop a business plan that could be used to sell the service to large pharmaceutical companies based on its value. To further test the value of the service, they performed some initial work for Merck and Co.

This is a good example of knowledge development, acquisition and transfer during the business development phase.

In June 1998 of a new division, Invitrogenomics was created as the functional genomics services division of Invitrogen to provide high-throughput cloning and gene expression services to genomics companies and large pharmaceutical and agricultural chemical companies.

From 1998 onwards, Invitrogen adopted an aggressive mode of technology acquisition and consolidation through periodic mergers and acquisitions including venturing into the nanotechnology area to ensure speedy business response in a growing market (Table 2). These moves provided Invitrogen timely technology, market base coupled with strategic and invincible IP protection to ward off competition.

Some of the key milestones of Invitrogen are listed below:

Table 2: Invitrogen's noteworthy milestones

Dates	Transactions by Invitrogen
August 1999	Merger with San-Diego based NOVEX a developer of products used for gene and protein analysis, in a $52 million deal
December 1999	Research Genetics Inc, Huntsville, Ala, for $139.2 million in stock
June 2000	$15.1 million acquisition of Ethrog Biotechnologies Ltd. Of Israel which had developed and patented a system for the electrophoretic separation of macromolecules. This was followed by a cash and stock merger valued at $1.9 billion
July 2000	Dexter Corp, a chemical maker, and Life Technologies Inc, which makes biological material for genetic research, for $1.9 billion in cash and stock Dexter has 75 percent stake in Life Technologies
September 2000	completes its takeover of chemical maker Dexter
March 2001	Invitrogen agrees to sell division housed on 240,000-square-foot site to Human Genome Sciences Inc for $55 million
October 2002	$42 million agreement to acquire Informax, which developed software that helped to design, manage, and interpret research kits for gene identification and cloning
July 2003	Acquires Molecular Probes Inc for about $325 million to add drug-discovery products

December 2003	Acquires BioReliance Corp for $430 million to expand its production ability for biotechnology customers
February 2005	Agrees to acquire closely held Dynal Biotech for $381.6 million to gain technology for cell research to speed development of products
July 2005	US$ 130 acquisition of BioSource International with expertise in functional proteomics. This deal augmented Invitrogen's growing collection of protein and primary antibody products gained through its earlier acquisitions of Zymed Laboratories and Caltag Laboratories
October 2005	Announced the acquisitions of Quantum Dot Corporation and the BioPixels(R) business unit of BioCrystal, Ltd. and the early closing of the Biosource International, Inc
June 2008	Agrees to $6.7 billion in cash and stock to buy Applied Biosystems company that provided most of the equipment for Human Ge Project and created a supplier of machines and materials for u academic, pharma industry, R&D laboratories, with about $3.5 annual sales The overall company is called Life Technologies.
October 28, 2008	Buys VisiGen for $20 million to Bolster Its Third-Gen Platform the expertise and IP of the budding developer of a real-time, s molecule sequencing-by-synthesis technology to become the leader i new genomics era
Mid 2010	Acquisition of computer chip DNA sequencing company Ion To Systems

The acquisition of Quantum Dot Corporation and BioPixel® by Invitrogen Corporation (IVGN) was done in October 2005. Invitrogen Corporation (IVGN), with its Molecular Probes was then a leading life science company providing innovative labeling and detection technologies to support disease research. Quantum Dot Corporation offered novel solutions for biomolecular labeling and detection that employ Quantum Dot (Qdot(R)) semi-conductor nanocrystals. The company also held the broadest intellectual property portfolio in the life science industry for semi-conductor nanocrystals with more than 160 patents and applications, and had built a significant customer base that was using this latest labeling and detection technology. BioPixels(R) provided novel specially coated fluorescent nanocrystals and metal alloys for applications in multicolor labeling, sorting and imaging of cells, lateral flow immunoassays, and fluorescent inks and represented a promising technology for the development of automated assays of complex biological samples. The combination the three companies allowed the creation of smaller, brighter, lower toxicity particles that do not blink.

At around the same time Invitrogen also announced an agreement with Georgia Tech Research Corporation to exclusively license novel "nanocluster" technology. Taken together, the combination of these acquisitions and licenses provided Invitrogen with a significant intellectual property position and robust platform for cutting edge product development. Further the added capability enabled Invitrogen to create new innovative products based on advanced inorganic materials science for molecular detection that enable life science researchers to better visualize and understand cellular processes, molecular

interactions in proteomics, genomics, gene expression, and imaging and other factors essential to diagnosing and treating disease. Terms of the acquisitions and license were not disclosed.

In 2008, Invitrogen virtually doubled its size with the purchase of biotech instrumentation company Applied Biosystems, maker of DNA sequencing and PCR machines and reagents. The company then renamed the overall organization as Life Technologies. The Invitrogen brand and most of the brands acquired still exist on product packaging, although the overall company is called Life Technologies.

In summer 2010, the company acquired the computer chip DNA sequencing company Ion Torrent Systems. In June 2010, Evident Technologies Inc. admitted infringing three patents and agreed to an injunction as part of a settlement in a case brought by Invitrogen Corporation (now known as Life Technologies Corp) over quantum dot semiconductors. The parties stipulated that Evident had infringed and induced infringement of the patent-in-suit, and that the patents' claims were valid in all... Judge Leonard Davis of the U.S. District Court for the Eastern District of Texas signed off on a consent order and permanent injunction in the case. This is an example of strategic enforcement of one's patent portfolio in business.

Through this history of acquisitions and continued product research and development, Invitrogen / Life Technologies now have over 50,000 products.

Lessons on technology transfer

This case-study provides the following lessons:

- Essential to develop a pragmatic business model with effective networking with stakeholders and client;
- Ensure targeted technology development;
- Strategise technology transfer and commercialisation;
- Organsie procurement of funds from diverse sources;
- Explore technology acquisition and consolidation through mergers and acquisitions;
- Make provisions for timely exit from unprofitable activities; and
- Enforcing its intellectual property rights when necessary.

9.7 'Transfer of nanotechnologies from R&D institutions to SMEs in India'

Two case studies from the Advanced Centre for Powder Metallurgy and New Materials (ARCI), Hyderabad, India', Article by H. Purushotham, Asia-Pacific Tech Monitor, Vol. 29, No. 4, pp. 22-33, Oct-Dec 2012, http://www.techmonitor.net/tm/images/4/49/12oct_dec_sf3.pdf

9.7.1 Nano silver suspensions for anti-bacterial textiles

M/s. Resil Chemicals Pvt. Ltd. (Resil), Bangalore, a company that supplies chemical finishes to the textile industry sensed the business opportunity in the use of nanosilver suspensions to manufacture odor-free antibacterial textiles that find applications in hospitals, innerwear, sportswear, socks, active wear,

baby care products, etc. The company collaborated with ARCI to develop a highly stable nano silver suspension for such antibacterial textile applications.

ARCI developed the technology for the lab scale preparation of nano silver suspensions having particle size of 20–50 nm by a chemical route. These suspensions were tested by Resil for anti-bacterial activities and appropriateness for applications in textiles. ARCI scaled up the process to a 15 liters batch size. The process parameters were optimized to obtain consistent quality and physico-chemical properties of the nano suspension, including stability after dilution, packaging and transport. These suspensions demonstrated wash-durable anti-bacterial activity up to 100 washes, at concentrations of 1wt% nano silver suspension in the treatment bath. The nano suspension produced at the ARCI pilot plant was tested by Resil, which demonstrated reproducible results and met all the industry requirements.

ARCI has transferred this technology to M/s Resil Chemicals, on an exclusive license. The pilot plant facility of ARCI was used to demonstrate the process to the company personnel who then prepared one tonne of nano silver suspension in the same facility. The technology development and transfer has been completed by ARCI over a period of two years. Resil has successfully commercialized this technology by establishing an in-house facility to manufacture nano silver suspensions in batches sizes of about 60,000 kgs. The product is marketed by N9 World Technologies (a marketing arm of Resil) under the brand name of "N9 Pure Silver". Since then the company has been supplying these finishes in India and abroad to several textile/garment manufacturers.

9.7.2 Nanosilver incorporated ceramic candle filters for water disinfection

ARCI developed a technology, incorporating nano silver into ceramic water filter candles to provide safe drinking water in rural areas, where the main sources of water (ponds and canals) are contaminated and existing water purification systems are expensive and unaffordable.

Considering the social need and huge market opportunity, ARCI developed a simple and inexpensive method to synthesize nano silver coated ceramic candle filters. The pores of the candle filters were coated with nano silver.

These nano silver coated candle filters were extensively tested for their anti-bacterial activity at two accredited laboratories and a hospital which demonstrated reduction of bacterial concentration from 10^5 cfu/ml to 0 cfu/ml after filtration. ARCI conducted a life cycle analysis of the candle filters to evaluate silver leaching into the filtered water as a function of usage time and long-term anti-bacterial activity. The amount of silver leaching out of freshly prepared candle filters was carefully monitored and the values for five successive filtrations were noted. The results were found to be well within the WHO limits of 0.1 mg/L. for silver in ionic form in drinking water and US EPA limits for colloidal silver intake by humans.

Extensive field trials of these nano silver incorporated candle filters were conducted in 40 villages in collaboration with a Non-Governmental Organization (NGO). The filtered water was tested daily by H_2S vial test to ascertain the absence of bacteria after filtration. The data obtained using canal and pond water from one village over a seven month period revealed the total absence of bacteria in the filtered water

even after storage of 72 hours. Similar data was obtained for tap and tank water.

The candle filters used in the field trials were tested for silver leaching by Inductively Coupled Plasma Optical Emission Spectrometer (ICPOES) analysis. The tests showed that silver leaching out of the used filter met the WHO limits even after one year of usage. Accelerated tests, carried out on fresh candle filters by immersing them in boiled water for 30 minutes, showed release of less than 0.08 ppm of silver (below the WHO prescribed limit) into the water.

As the in-house developed technology has major societal implications, ARCI took a policy decision to transfer the technology on a non-exclusive license basis to entrepreneurs / industry. Technology Development Board (TDB) of the Government of India also decided to extend financial assistance to the companies for commercializing the technology.

The technology was successfully transferred to M/s SBP Aquatech Pvt. Ltd., Hyderabad. The company had set up a plant in Hyderabad with production capacity of 1000 filters per day and the product was marketed under the brand name of PURITECH®.

Although the technology was successfully transferred and the product was commercially launched in the market, the company could not sustain its growth in the market due to several financial, management and marketing problems.

ARCI is continuing to explore opportunities with other entrepreneurs to transfer this technology who would possibly have appropriate financial backup and marketing skills to enable wider accessibility of the innovative product is the country.

Lessons on technology transfer

- Publicly funded institutions can meaningfully collaborate with private sector on to develop technologies for unmet needs identified by entrepreneurs / companies.
- Technologies developed for needs identified by the Publicly funded institutions may be transferred to entrepreneurs/ private sector, but care needs to be exercised in the selection of the partners who would commercialise the technology based on their financial back up, technology skills, adaptability, marketing acumen, etc.
- Socially relevant technologies developed by publicly funded institutions need to be transferred on a non-exclusive basis to ensure wide and affordable availability of the developed technology to the society at large.

9.8 Bilcare Research, Pune India

Developing technology in house, coupling with knowledge tributaries and commercialization through knowledge distributaries, Bilcare Research is an innovation-led company which started as a solution provider for packaging of sensitive pharmaceutical products with its own R&D and production centre in Pune, India. Over the years it has expanded into diverse operations including intense R&D to provide anti-counterfeit solutions based on nano-tags and associated technologies. It has also created a strategic portfolio of patents around its technologies.

The research model adopted is one of in-house research on identified targeted problems, selectively draw upon external knowledge tributaries (selected commercial vendors working in partnership or even contract to provide targeted solutions, devices developments, etc) for knowledge in-flow, create IP protected solutions to the targeted problems, and strategically combine with a range of knowledge distributaries to commercialise the IP protected technologies in the global market (Figure 19).

Close working with the vendors and other collaborators ensure that technology transfer is complete at the early stage of development to create technology convergence around Nanotag which becomes a knowledge centre for the authentication, registration and compliance technologies with the unique "nano tags" as products, miniaturised devices, relevant software , etc. This in-house knowledge centre which is IP protected then interacts with diverse knowledge distributaries to provide distinct and integrated solutions for diverse identification, authentication, track-n-trace and anti-counterfeit solutions.

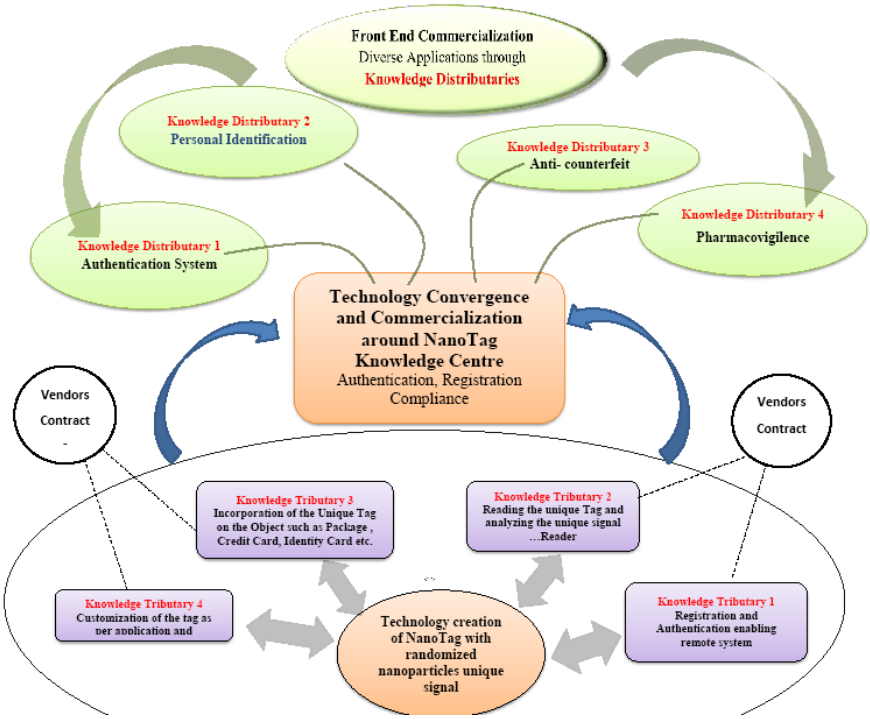


Figure 19: Business model of Bilcare Research, Pune, India on technology development and transfer (Figure adapted from Prabuddha Ganguli and Siddharth Jabade, "Nanotechnology Intellectual Property Rights, Research, Design, and Commercialization", CRC Press USA, July 2012)

An example of this focused working, in January 2008, Bilcare Singapore Pte Ltd a wholly owned subsidiary of Bilcare Limited bought 100% of Singular ID a SME in Singapore engaged in research, development and creation of micro and nanotechnology based novel products and the provider of integrated high technology enterprise brand security system, for a consideration of Singapore $ 19.58 million. Singular ID had in-licensed two patent applications PCT/SG2004/000216 (titled "A method of identifying an object and a tag carrying identification information") and PCT/SG2005/000012 (titled "Identification tag, object adapted to be identified, and related methods, devices and systems"), from the

Agency for Science Technology and Research (A*STAR), Singapore. Singular ID was quickly integrated into Bilcare Technologies ....a division of Bilcare Research which works closely with its knowledge distributaries (clients) to tailor its technology to meet specific customer requirements. This is a good example of a university created knowledge that was IP protected found application and became the basis for a development which could not have been done in the university system. It is interesting to note that the present form of the technology that is actually in use in the market place is very different from the technology licensed from A*STAR.

Bilcare Technologies has now successfully developed novel proprietary nonclonable™ nano and micro structured materials based tags (randomly distributed micro and nano particles and cannot be reproduced or duplicated), and proprietary Bilcare specialty handheld/portable readers/scanners and proprietary associated software to authenticate the tags in real time in a fool proof integrated ICT system for security systems including anticounterfeit applications in brand protection and management. This unique technology has been protected by a portfolio of issued patents and patent applications in various countries. This technology significantly enhances security levels with an impregnable personal access control and identity management system that can be adapted for wide ranging applications spanning security, anticounterfeiting, etc. The heart of this system is the tamper-evident nonClonableID™ nanotag capable of seamless and secure integration with any ICT system wherein the proprietary reading device scans the fingerprint and instantly communicates the encrypted information with a secure server through mobility platforms such as GPRS, 3G or Broadband to generate an instant complete authentication report on a mobile or computer using robust web enterprise secured applications and data management at the back-end.

Commercialisation of this technology based on nano materials has involved close collaborative efforts of Bilcare with knowledge tributaries such as developers of the special reading devices and knowledge distributaries such as technology integrators to incorporate communication systems into the reading devices and / or integrating the reading device with mobile telephony systems including developers of secured enterprise management systems. Another set of knowledge tributaries have been those having expertise in the incorporation of the nonClonableID™ nanotags into diverse substrates in a robust manner to withstand harsh operating ecosystems and platforms where the nonClonableID™ nanotag retains its unique signature and tamper evident characteristics.

An early large scale commercial application of Bilcare Technology's nonClonableID™ nanotag was when they were incorporated in the high secure Identity cards adopted by the Delhi Police in India for real time authentication of the individual policeman and centralise the duty planning rooster for planning and monitoring. Other commercial applications of this technology are being explored with governments for authentication and secured election systems, anti-counterfeit packaging including e-pedigree and secure track-and-trace increased visibility across the supply chain, patient compliance, clinicom solutions including tackling issues of diversion and theft in the supply chain in pharmaceutical industry, agrochemical industry and high value components & luxury goods.

Lessons on technology transfer

- Such a business model based on next generation technologies integrates the desired flexibility and cooperative network in real time with partners (knowledge tributaries and knowledge

distributaries) having diverse expertise to deliver targeted products, processes, and business solutions in the market place.

- Co-development of devices, software, ICT solutions for commercial implementation.
- Ensures phasewise holistic technology transfer with minimum knowledge transfer gaps.
- Continually hybridises strategic management of innovations with IPR protection, IP transactions, confidentiality, benefit sharing arrangement for profitable cash flows for the operating partners, regulatory compliance, including risks and liabilities.
- Ensures phase wise freedom to operate of the developed technologies and solutions thereby avoiding time and cost consuming legal battles in the market place.

9.9 Vista Therapeutics Inc.

Vista Therapeutics founded in 2007 by Spencer Farr and Charles Lieber, Professor of Chemistry at Harvard University got involved in the development of nanowires that would provide a means for continuous and real-time monitoring of multiple biomarkers in blood and urine using biosensors. Applications using functionalised nanowires to monitor and detect on a continuous and dynamic basis antibody-antigen interactions, enzyme substrate interactions and gene expression were also conceived.

Vista signed License Agreements with both Harvard University and Nanosys (a company that was a Harvad University spin out by Prof Charles Lieber in 2001) covering several patents and patent applications related to the use of nanowires for biosensors.

Under the terms of the agreements, Vista secured the exclusive, worldwide rights for the use of nanowires for detection of biomarkers associated with organ or tissue damage, and any form of treatment or therapeutics-associated adverse response(s). In consideration, Harvard and Nanosys received an equity position in Vista, as well as upfront license and downstream royalty payments. This arrangement allowed Vista to commercialise through manufacture and sale of nanowires that are formatted to provide real-time, continuous measurement of blood and urinary biomarkers of organ and tissue injury (Figure 20).

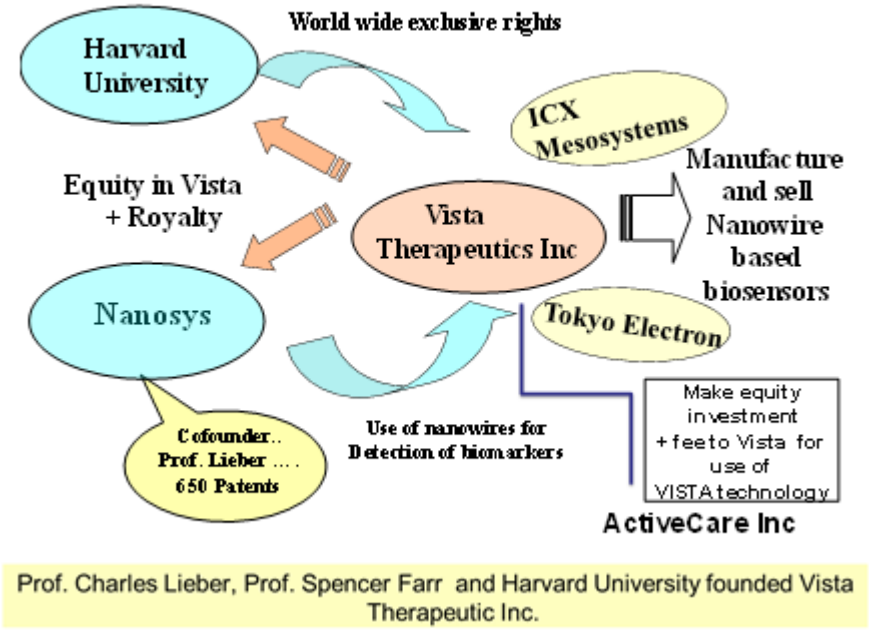


Figure 20: Business model of Vista Therapeutic Inc.

The company has strategic partnerships with MesoSystems/ICX and California-based TEL Venture Inc which is a subsidiary of Tokyo Electron Limited, the world's second-largest semiconductor equipment maker will help manufacture and distribute the device.

ICx MesoSystems, an ICx company, is a leader in developing and commercializing innovative and practical solutions for bio-threat surveillance and incident response. Founded in 1997, ICx MesoSystems commitment to providing fast, effective, and affordable solutions has led to multiple product successes, including BioCapture®, the most widely used air sampler for bioterrorism response. The linkage of Vista Therapeutics Inc with ICx MesoSystems provides Vista the ready platform for the use of its devices in real working situations.

Vista Therapeutics Inc. received a $1 million investment in from TEL Venture Inc. to build out the technology, which Vista licensed from Harvard University. Vista has already developed a NanoBioSensor to provide real-time snapshots of protein changes in patients, allowing medical personnel to continuously assess an individual's condition and measure responses to medication in trauma situations. As Tokyo Electron Ltd will manufacture the device, its investments in Vista Therapeutics will rise significantly.

Vista has created a model in which their team of world-class experts in medicine, biotechnology, nanotechnology, engineering, chemistry, and informatics develop cutting–edge technologies in their laboratory, continually collaborate in essential fields with Harvard University, and actively linkup with pharmaceutical companies, doctors, and medical researchers for the development and deployment of its

Nano Biosensors. Interestingly such products do not need FDA approval and therefore the time to market reduces significantly. The technologies are protected with strategic patent portfolio.

The management of IPR is of immense significance to Vista Therapeutics as most of the assets are intellectual assets which can be effectively traded as part of business and technology transfer deals.

In June 2010 Active Care Inc and Vista created a strategic relationship to integrate Vista's nanowire technology in Active Care's products and services. The terms of the strategic agreement between Vista and Active Care is to make an equity investment in Vista Therapeutics and to pay a fee for the development of products utilizing Vista's Nano Biosensor technology. As part of the strategic agreement, Active Care will have exclusive use of the Vista Therapeutic's technology in the elderly market (excluding hospitals, for which Active Care will have the right to acquire an exclusive sublicense) [http://activecare.com/]

Lessons on technology transfer

- In breakthrough and disruptive technology related developments, the continual involvement of Star Scientists in the development of the products and supporting their manufacture is an imperative.
- Licensing agreements with the parent Institution has to be facilitating rather than restrictive. In this case Harvad University had well defined and yet a fairly facilitating licensing agreement with Nanosys aand then with Vista Therapeutics which helped them to progress their business plans without much hindrance.
- Early linkage with manufacturing companies is also an imperative. In this case Tokyo Electron which is the world's second-largest semiconductor equipment maker struck an early deal to manufacture and market the product.
- Early linkage with institutions that will provide the platform for large scale testing and use of the manufactured products is also an imperative.
- Creation and management of IP portfolio is of immense significance.

10 Summary

A range of business models have been applied in the field of nanotechnology. In the earlier days of nanotechnology, classical models have been used in which the science and concepts took roots in government funded academic institutions before applications were developed followed by independent groups creating markets, searching for commercialization and seeking transfer of technology from academic institutions. Nanotechnology however provided the opportunities for sprouting of start-ups within academic institutions in which evolution of concepts and applications under the same roof shortened the time scale for technology development and creation of possible markets for these developments. The early funding by venture capital and angel funding to such startups became significant. The involvement of large commercial enterprises was in the form of support to small enterprises, startups and spin-offs and in many cases backward / forward integrating / adapting the developed technologies with the existing businesses within the large enterprise and/or creating new

businesses. Public–private partnerships and consortia modes of operations in nanotechnology businesses also provide examples in which the time from concepts to commercialization has been significantly compressed due to the creation of facile conduits for transfer of technology. In recent times the funding of nanotechnology by the private sector has shown a sharp rise. Such developments have brought issues related to intellectual property rights to the centre stage. Technology transfer and commercialization in nanotechnology therefore provide challenges to institutions as they not only have to serve as centres of excellence, but also learn to work in complex international knowledge networks, manage transfer of technology with strategic handling of intellectual property rights in a holistic framework of knowledge management. The present chapter illustrates all these features with several institutional examples.

Suggested readings

1. OECD (2010), The Impacts of Nanotechnology on Companies: Policy Insights from Case Studies, OECD Publishing, http://www.inovacao.unicamp.br/report/inte-ImpactsofNanotechnology101213.pdf

2. Global Perspectives on Technology Transfer and Commercialization, edited by John Sibley Butler, David V. Gibson (2011), http://books.google.co.in/books?id=VcArVlSysesC&pg=PA255&lpg=PA255&dq=nanotechnology+technology+transfer&source=bl&ots=V1h5a16N-Y&sig=qdM8IitqtkwBE4h3_UNdjrXKxKo&hl=en&sa=X&ei=FXqSUbGyL9CxrAfPjoCADQ&ved=0CFoQ6AEwBzgU#v=onepage&q=nanotechnology%20technology%20transfer&f=false

3. Silent innovation: corporate strategizing in early nanotechnology evolution; Andersen MM. (2011), *The Journal of Technology Transfer, Vol.* 36(6): 680-696 http://orbit.dtu.dk/fedora/objects/orbit:66121/datastreams/file_5871984/content

4. Rejuvenating Clusters with Sleeping Anchors: the Case of Nanoclusters; Baglieri D, Cinici MC, Mangematin V (2012), *Technovation*, Vol. 32(2) http://hal.archives-ouvertes.fr/docs/00/53/61/95/PDF/Rejuvenating_clusters.pdf

5. Convergence and Multidisciplinarity in Nanotechnology: Laboratories as Technological Hubs; Battard N. (2012), *Technovation*, Vol. 32(2) http://arrow.dit.ie/buschmarart/101/

6. Which Model of Technology Transfer for Nanotechnology? A Comparison with Biotech and Microelectronics, Genet CE, Khalid; Gauthier, Caroline (2012), *Technovation*, Vol. 32(2) http://halshs.archives-ouvertes.fr/docs/00/74/91/52/PDF/Model_of_technology_transfer.pdf

7. Process-Based vs. Product-Based Innovation: Value Creation by Nanotech Ventures, Maine EL, Sarah; Garnsey, Elizabeth (2012), *Technovation*, Vol. 32(2) http://www.academia.edu/2457835/Process-based_vs._product-based_innovation_Value_creation_by_nanotech_ventures

8. The Global Technology Revolution 2020, In-Depth Analyses Bio / Nano/ Materials/ Information Trends, Drivers, Barriers, and Social Implications, Richard Silberglitt, Philip S. Antón, David R. Howell, Anny Wong with Natalie Gassman, Brian A. Jackson, Eric Landree, Shari Lawrence Pfleeger, Elaine M. Newton, and Felicia Wu, RAND Corporation (2006) http://www.rand.org/content/dam/rand/pubs/technical_reports/2006/RAND_TR303.pdf

MANUAL ON CRITICAL ISSUES IN NANOTECHNOLOGY R&D MANAGEMENT

AN ASIA-PACIFIC PERSPECTIVE

CHAPTER 4

Development and Commercialization of Nanotechnology-based Value Added Products

Case studies from Asia and the Pacific

Prepared for

Asian and Pacific Centre for Transfer of Technology of the United Nations – Economic and Social Commission for Asia and the Pacific (UNESCAP)

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Manual on Critical Issues in Nanotechnology R&D Management: An Asia-Pacific Perspective

Asian and Pacific Centre for Transfer of Technology (APCTT) of the
United Nations Economic and Social Commission for Asia and the Pacific (UNESCAP)

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1. Preamble

Today the world has realized Feynman's dream……..

> ***"I want to build a billion tiny factories, models of each other, which are manufacturing simultaneously. . .The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom. It is not an attempt to violate any laws; it is something, in principle, that can be done; but in practice, it has not been done because we are too big"***
>
> —Richard Feynman

……*and* nanotechnology became a revolutionary field which has made huge impact on several areas of material sciences and has applications in every field of science. But the true realization of his dream has led to an explosive improvement in our understanding of nanoscience and has produced new possibilities for the investigation and application in various fields of science.

The prediction that a very large market for nanotechnology enabled products is in the offing, has made the world realize that with the help of this new technology many new jobs may be created. Thus, it will have potential economic impacts. No wonder, governments are developing strategies to promote the R&D and commercialization of nanotechnology.

Over the past three decades scientists, economists, policy planners, Government authorities, and industrialists are trying to understand and apply nanotechnology for the betterment of mankind.

The realization that bringing the fruits of nanotechnology to masses is possible only through the extensive research in this field; both public and private sectors are investing in this sector. No other technology in the past had received such huge investment in such a short time as nanotechnology has.

The second challenge is converting the outcome of research to production through industries. Like all the other products, most of the manufacturing competitors are located in the Asia-Pacific countries. Hence, the status of industries in nanotechnology in the Asia-Pacific countries demands an assessment.

Industries have also realized that advancement in the production of nanotechnology-based products is totally dependent upon R&D; therefore, in-house R&D of companies have also become very active. The R&D efforts have given them the understanding that nanotechnology can not only upgrade the

traditional industries by adding value to the product or by enabling new functionalities of production, but it can also converge with other technologies and create novel innovative products.

This chapter presents some case studies, which summarize the efforts of Asia-Pacific countries in the research & development and commercialization of nanotechnology-based value added products.

2. Problem description

With increase in world population, demand for all requirements are continually increasing, whether it is land to live, land for agriculture, land for industries, more consumable products, more food, consumable water, healthy environment, health-care products and industries that produce without creating pollution and toxic outputs…. the list is endless. This has created a demand for researching new approach and generation of efficient environmentally friendly products. Nanotechnology has entered into the arena to help in solving such problems.

Lux Market Research Group (2004) estimated that the sales of products incorporating nanotechnology would rise from less than 0.1% of global manufacturing output in 2004 to 15% in 2014, totalling $2.6 trillion.

The global market for Quantum Dots (nano particles having <10 nm size) that has great commercial application in life sciences is projected to reach more than $700 million by 2013. The biggest growth sector will be in optics for QD-based lasers and other optical components in telecommunications. The other growth sector is in electronics for QD-based flash memory and optoelectronics in lighting and displays (electronics).

Agro-sector is in dire need of increased production. Advancement in controlling fertilizer, pesticide and herbicide inputs, crop improvement and solving plant pathological problems are also the need of the hour.

Health-care of mankind fighting with dreaded diseases like cancer and HIV is another area that is looking at novel innovative and less toxic therapy as well a diagnostic kits that can ensure early disease detection.

Research carried out so far has given strong indications that nanotechnology can contribute in solving these problems and requirements.

However, like all other technologies there may be the darker side of this technology pertaining to environment, long term effects on health, etc that needs a closure scrutiny and accordingly the strategies are to be formed.

3. World-wide scenario of nanotechnology

Right from the beginning, development of mankind has been through developing technology. Thousands of years ago the hunters and gatherers developed stone and wood armaments and then they developed cultivation technology. With the advancement the technology shifting towards the development of wheels and pulley, finally many machines, electricity and electronics came into

existence thus accelerating the very pace of growth and development. With the invention of atomic force microscopy (AFM), Scanning electron microscopy (SEM), transmission electron microscopy (TEM) and the vision of Feynman that "*There is plenty of the room at the bottom"*, a new branch of science and technology – NANOTECHNOLOGY evolved in mid-20th century.

Nanotechnology has now become a part of the rich tapestry of scientific knowledge. Although enormous advances in our understanding of nanoscience have occurred, their strategic applications still constitute a major growth area in nanotechnology. Last three decades has seen nanotechnology as an emerging technology that has attracted world-wide attention. Not only scientists are paying attention to it but governments of various developed countries like USA, European countries and Asian countries like China, Japan, and the Republic of Korea are also developing strategies and investing funds to promote research and industrialization of nanotechnology. Its emergence has been spurred by key inventions in instrumentation and sizeable R&D funding, the funding of new research centres and new agencies. Investment by private sector in both R&D and production is steadily increasing. The capabilities of industries are based on the access to R&D sources or their own in-house research.

Since one of the big markets, USA has adopted the policy of non-manufacturing, the scope for Asian countries with cheap labour and large scientific and technical man-power has increased.

Establishment of organizations like Nanotechnology Industries Association (NIA**)** by multinational companies active in Nanotechnology including Unilever, BASF, Smith&Nephew, Qinetiq with ~50 Registered Members (February 2010) based in Australia, Belgium, Finland, France, Germany, Portugal, Spain, UK and US are operating across Europe and liaising with US, Australia, Japan, Asia Pacific**,** etc. NIA is a sector-independent, responsible voice for the industrial nanotechnologies supply chains. It promotes the ongoing innovation and commercialization of nanotechnologies and promotes their safe and reliable advancement.

4. A brief introduction to nanotechnology

Nanotechnology refers to the applied part of nanoscience involving synthesis and use of nano-sized particles in the range of 1 to 100 nm. Nanoparticles are multi-atomic nanostructures straddling between atomic and bulk scale. All atoms functionally obey quantum mechanical principles; whereas bulk scale matters follow the principles of classical physics. Since nanoparticles are multi-atomic nano-structures they exhibit a blend of quantum behaviour and specific properties of nano-sized material, e.g. they exhibit dominantly statistical mechanical principles in which the energy is well quantized and discrete. This consequently leads to the dominion of surface energies due to the excited electrons of the surface atoms of nanomaterials. This has also intrigued material scientists to comprehend the unique nano-scale phenomena such as quantum confinement and quantum tunnelling which exhibits special characteristics to nanomaterials. The orchestration of small size, ability to confine resonant photons within its small size, complex organizational patterns, potential for very high packing densities, strong lateral interactions and high ratios of surface area to volume makes nanoscale materials a powerful armamentarium for a plethora of applications, e.g. single-electron

transistors (SETs) and light emitters, catalysis, optoelectronics, optics, photothermal therapy, reprography, non-linear optical devices and photo electrochemical applications, etc.

The elements of nano-scale products are sub-miniature compounds that are incorporated into ordinary materials during or after the original manufacturing process. Nanotechnologies hold the promise of breathing new life into these industries, primarily through the development of radically new products. The process of "molecular manufacturing," that is, precisely building a material molecule by molecule, means near-perfect assembly. Molecular manufacturing also stands to greatly reduce the environmental impact of manufacturing. Waste can be practically eliminated; many current manufacturing techniques involve copious use of harsh chemical reagents which are often dumped into the environment in developing countries with lax regulations. Instead, the manufacturing precision afforded by Nanotechnology means that not a single atom has to go to waste. Any unwanted atoms can be neatly repackaged for recycling or be returned to their source.

According to the National Nanotechnology Initiative (NNI), USA, nanotechnology-based manufacturing processes are believed to lead up to 99% reduction of the energy and materials used today. However, initially heavy investment is needed for training manpower to develop and apply new technology, and capital investment in new manufacturing techniques and machinery. In addition to these costs, the largest expense is likely to be the investments in research and development needed to move from the current nanotechnologies to production.

5. Nano-products in the market

Nanotechnology Nanotechnology is an emerging scientific field creating materials, devices, and systems at the molecular level. By being able to work at this ultra-small scale, nanotechnology is being used to deliver innovations in industries including clean energy, environment, health and personal care, electronics, transport, construction, telecommunications, manufacturing and mining. One Indian entrepreneur said it best when he proclaimed:

"For entering into Nanotech products my industry needs senior managers and researchers with the frontier mentality found at Apple or Intel or Biotech start-ups."

Many products endowed with extraordinary properties are made possible via nanotechnology. Possible end products that are envisaged and already in the market include: *Textiles* – having stain and wrinkle resistant garments and super strong fabrics that can be used for multiple purposes (e.g., astronaut suits, bulletproof vests, outdoor pavilion tents, etc.); *Automotive requirements; Medicine, Therapeutics and Diagnostics; Environmental and Hygiene.*

Some of the nano-products that are being envisaged as future possibility are:

- Agriculture and Food - Producing and preserving food through nanotechnology
- Nanotechnology in water management for safe and sufficient water
- Nanotechnology to make the environment sustainable
- Solar energy on one's roof top through nanotechnology
- Effective and precise medical services, medicine and health care with nanotechnology

- Nanotechnology for easy to make, smart to trade, smarter to wear textiles
- Nanotechnology in automobile, electrical and aerospace
- Nanotechnology in electronics
- Nano materials in construction, i.e. beyond bricks and mortar
- Nanotechnology to change the chemistry and produce advanced materials

Initially the most commercially used nano-particle has been nano silver that is endowed with the anti-bacterial property. Another nano-particle that has found wide application in industries is carbon nano tubes often used as composites with polymers, in electronics, automotives and sporting goods, etc. However many other nanoparticles and nanocomposites based products are in the market.

6. Countries selected for case study of R&D institutes and industries involved in nanotechnology

With the hype of nanotechnology during the last decade of 20th century, Governments from all the developing countries started investing in R&D of various aspects of nanotechnology. Emphasis was on developing technologies that would be applicable for the masses as well as in the economic development of the country.

Success of R&D efforts of any technology depends on its:

- Commercialization,
- Patents generated,
- Publications, and
- Collaborations.

At present world over, four types of research centres are functioning:

1. Government funded research institutes,
2. In-house research divisions of the industries,
3. Private research institutions, and
4. Collaborative Private and Government funded research institutions.

For the present case study, emphasis has been on the efforts and output of Government funded research institutes and commercialization of their innovative research efforts.

However, it must be mentioned that many of the well established companies, through their in-house R&D efforts, have either updated their products through the use of nanotechnology or developed new products and processes involving nanotechnology..

In this report at least two case studies of companies and/or R&D institutions involved in nanotechnology based products, from each of the selected countries have been reported. The case studies are drawn from 11 countries and cover a range of R&D institutes, company sizes, nanotechnology sub-areas and fields of applications. The countries selected for the case studies vary greatly in their implementation of nanotechnology. There are some Asia-Pacific countries that are at par with most developed nations like USA and Germany, e.g. Japan and the Republic of Korea;

whereas there are fast growing countries like China and Malaysia that are catching up with both R&D as well as industrialization of nanotechnology. There are countries that have contributed immensely research-wise but are comparatively slower at industrialization, e.g. India, and there are also countries in the nascent stage of entering into this field.

Nanotechnology is a rich branch of science which has inputs from all the disciplines of science such as physics, chemistry, electronics, biology and engineering. Hence, nanotechnology covers a broad range of applications and products. It is difficult to single out challenges which are truly specific to one type of nanotechnology output. Moreover, the findings may not necessarily apply to all sub-areas and application fields.

For the case studies, efforts made in the following countries are touched upon: *China, India, Indonesia, Japan, Republic of Korea, Islamic Republic of Iran, Malaysia, Pakistan, Philippines, Sri Lanka and Thailand*.

7. Limitations in the study

This report suffers from the limited access to reliable and comparable data. Due to the complex nature of nanotechnology, official statistics often link it to various different categories (e.g. risk regulation efforts involve not one but many sectors where it cannot be identified correctly or the definition is at least questionable).

Large scale survey dedicated to market prospects and the company data about nanotechnology faced limitations due to ignored response from the industries.

Data available on the respective website provided valuable information, but lack of comparability with data retrieved from other surveys. It has been attempted to draw a most complete picture with the data available and to draw conclusions on their basis. It was neither possible and nor the intention of the author to generate data.

Often surfing on web site for nano-products resulted in products having 'Nano' suffix, due to hype and attraction that the word 'Nano' has caused these days; but it has nothing to do with nanotechnology.

8. Country-wise case studies

8.1. CHINA

Government initiatives:

The People's Republic of China entered into the realm of nanotechnology in mid-eighties through the efforts of Chinese Academy of Sciences (CAS) and National Natural Science Foundation of China (NSFC). The Government of China has very systematically implemented their plan to develop domestically crafted science and technology based output for export and domestic consumption.

By 1990, the Ministry of Science and Technology (MOST) realized the importance of nanotechnology and initiated *"National Climbing-Project*" on nanomaterials research. In 1999, *973 Program on "Nanomaterials and Nanostructures*" by MOST was funded. Later in collaboration with NNI of the United States, they expanded their efforts and funding into various areas of nanotechnology having commercial potential. The most effective programme in China's scientific research and development is the '*863 Program' for "Promoting the development of key novel materials (including nano-materials) and advanced manufacturing technologies for raising industry competitiveness" [*2]. [Under this 863 plan, US$ 27 million were funded to over 1000 nanotech projects [3].

Main funding bodies of China are MOST, CAS, National Natural Science Foundation of China (NSFC), NCDR (National Commission of Development and Reform) and MOE (Ministry of Education). CAS and NSFC created many nanotechnology research centres in China. Apart from research funding keeping market demand in consideration, China also addressed priorities for the commercialization and development of (i) nano-materials, (ii) bio-nanotechnology and nano-medical technology, and (iii) nano-electronics and nano-chips. Moreover, some private industries of China also funded nanotechnology research, for example, the Tsinghua-Foxcom Nanotechnology Research Centre, Beijing was donated by the President of one of the largest private industry Foxcom Corporation of Taiwan province of China.

These initiatives have not only provided trained scientists in nanotechnology but also instigated Chinese scientists to train abroad and return to China. Moreover, such star scientists have played a pivotal role in international collaborations for the advancement of nanotechnology in China. It could be that low labour and infrastructure costs might have also helped.

The three above mentioned programmes were meticulously planned and monitored:

"*863 National High Tech Research and Development Program" initiated in 1986,* supported in meeting the growing technological and innovation gap between China and the West; for promoting the development of key novel nano-materials and advanced manufacturing technologies for raising industry competitiveness.

"National Climbing-Project" *initiated in 1990, and implemented in 2001* was mainly to train and bring young scientists in to basic research. National Climbing Project covers 7 branches of basic

research (Astronomy, Biology, Chemistry, Geography, Mathematics, Mechanics and Physics) and 8 branches of applied basic research (Basic Agronomy, Basic Medical Sciences, Energy, Engineering Science, Information & Computer, Material, Resource & Environment and Space Science).

"973 – The National Basic Research Program of China was implemented in 1997 - to organize and mobilize China's scientific talents in conducting innovative research in (i) nanotechnology (ii) Proteome, (iii) Quantum control, and (iv) Reproduction. Two notable projects under the 973 Program that helped in the progress of nanotechnology research and commercialization were: (i) Standardization of measurement techniques, and (ii) Synthesis of nanometer-sized materials (*Science and Technology Indicators, Organization for Economic Cooperation and Development (OECD), 2009).*

Case-study of a health-care company in collaboration with CAS - Suzhou Nantong Bionanotechnology Co. Ltd. (NanoMed)

About the Company:

Suzhou Natong BioNanotechnology Co. Ltd, in Shanghai **was founded in 2007.** It is a clinical-stage medical product company focusing on developing and commercializing non-invasive drug delivery technologies. For its commercial venture, it was funded by Softbank's SB China Venture Capital (SBCVC) in January 2010. **This company** has licensed two patents from the Xinjiang Technical Institute of Physics and Chemistry of CAS and has applied for 12 more patents for its intra-dermal FMA-TM technology, six of which have been granted, including one in the US and five in China. It has a strong research base and has launched a regional research division in the US also.

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Problem/Issue:

The most jeopardizing situation of a transformed biological cell is its impenetrability of chemotherapeutic agent due to its high diffusion rate and enhanced reticuloendothelial system (RES) clearance. This physiological change poses a hostile consequence of low retention of the drugs inside a solid tumour (Jain, 1999). This necessitates the development of tumour specific targeted drug delivery cargoes to ferry drugs, exploiting the leaky tumour-micro-vasculature. Targeting drugs to their sites of action is a challenge in pharmaceutical research. Most current cancer therapies are non-specific, with surgery, radiation and chemical ablation having the potential to cause damage to the surrounding tissue.

Solution:

Nanomedicine plays a gigantic role in the delivery of payloads to the target using specifically addressed nano-cargoes. Such nano-cargoes, due to size and surface properties can circumvent the problem of systemic toxicity of drugs. Moreover, they get anchored to certain tissues, thus decreasing the efficiency of diffusion and uniform tissue distribution. Targeting the nano-vehicle using the specific ligand facilitates balance between tissue penetration and cellular uptake leading to optimal therapeutic efficacy.

To address the above problem, researchers from CAS under the guidance of Dr. Xu (2004 to 2007) carried out extensive research along with researchers in the Technical Institute of Physics and Chemistry of CAS to develop a novel drug delivery system using nanoscale MEMS fabrication technology. In 2007, Dr Xu was awarded "The Science and Technology Pioneer Award", from

Suzhou Industrial Park (SIP) for developing and commercializing his innovative intra-dermal drug delivery technology.

Moreover, Dr. Xu's one of the concerns was to have a painless injection system of the drugs. As they believed that compared with the high risk (up to 90%) of developing new drugs, the risk of developing new drug delivery system using FMA-TM technology is almost zero.

The group successfully developed and commercialized this innovative intra-dermal drug delivery technology, also known as Functional Micro Array (FMA-TM) technology. The drug-delivery device uses a set of needles smaller than human hairs for painless injections. This is a non-invasive drug delivery technology, which has four distinct advantages compared to the conventional needle injection; it is painless, less toxic for potent drugs, has improved drug efficacy and reduced treatment time. This Micro Array FMA-TM Patch has found several potential clinical applications in the areas including delivering drugs for skin diseases, diabetes, tumours and pain relief. The products that are made using this technology are:

- **Liteclear-TM** In collaboration with Beijing PLA General Hospital using FMA technology,

Liteclear-TM was developed to treat Acne. Liteclear-TM was launched in the market in March 2010 with funding from Softbank's SB China Venture Capital and it received such good response that the company expected to break even in 2011, as total sales across all of China was expected to be around $1.5 million.

Liteclear-TM reduces acne lesion size, diminished redness and pain in as little as 12 hours, eases inflammation in one week, compared to several weeks using conventional acne treatment technologies/products.

The critical challenge for drug delivery into skin is penetration into the stratum corneum, the outermost layer of human skin. NanoMed's FMA-TM Patch fabricated based on the MEMS technology is equipped with nanoscale needle tips and is capable of delivering painless injection in 10 seconds.

- **LidoFast** – This was the second product developed for pain relief. It is a FDA approved low concentration anaesthetic drug, IND filed in the United States.

- **InsuRite**: This is the the third product based on Functional Micro Array technology. It provides basal delivery of insulin for patients depending on daily insulin injection.

No wonder NanoMed is regarded as the fast growing BioNanotech start-up Company in China. Now they are looking for collaboration with pharmaceutical companies all over the world to innovate their drug delivery system.

Concluding remarks:

Dr. Xu is a returnee to China after 20 years of education and training overseas. He could envision the unique advantages for building a successful Bionano company in China, as he realized that in China he is able to lower the operation costs and have access to a wealth of clinical resources compared with

that in North America and other developed countries. These efforts converted him into an entrepreneur; running a high-tech start-up in China. The shortage of financial and legal professionals has been quite a challenge for a scientist like Dr Xu, but by the end of January 2010, NanoMed signed a funding agreement with Softbank's SB China Venture Capital (SBCVC). This funding was seen as an important milestone for the company.

There are strict and stringent restrictions on monitoring and evaluation of the dose, therapeutic index or ratio of formulations and specific drug delivery system during clinical trials on human. Nanomaterials are developed for their unique (surface) properties in comparison to bulk materials. Since surface is the contact layer with the body tissue, and a crucial determinant of particle response, these unique properties need to be investigated from a toxicological standpoint. When nanoparticles are used for their unique reactive characteristics it may be expected that these same characteristics also have an impact on the toxicity of such particles. Although current tests and procedures in drug and device evaluation may be appropriate to detect many risks associated with the use of these nanoparticles, it cannot be assumed that these assays will detect all potential risks. So, additional assays may be needed. Since the work has been done in collaboration with a hospital, it is expected that such care must have been taken. Moreover, Poly(lactic-co-glycolic acid) (PLGA) being a polymer composed of lactic acid and glycolic acid, both are metabolic products of the living system; it is a well-accepted biocompatible and biodegradable material to be used in drug formulation or delivery and is not expected to be a toxic material.

Case-study of a nano-carbon related company in collaboration with Chinese Academy of Sciences (CAS) - Chengdu Organic Chemicals Co. Ltd & CAS (Timesnano)

About the Company:

Timesnano is the research and development centre for carbon materials. This centre belongs to Chengdu Organic Chemicals Co., Ltd, Chinese Academy of Sciences (CAS) and since 1996 it has been involved in CNT synthesis and application research. The Chengdu Organic Chemicals Co Ltd (CAS) was supported by the National High Technology Research and Development program of China, under Program 863 (the Basic Research Program of China). Their research has resulted in 80 publications and 33 patents.

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Problems/Issues:

With the discovery of carbon nano tubes by Iijima in 1991, all over the world there was onset of research activity in this novel class of materials [1, 2] because of their unique physical properties which span a wide range from structural to electronic. Possibility of its use for many applications came to the fore, e.g. pharmaceuticals, agriculture, medicinal, transport, fast moving consumer goods products, etc. This demanded mass production of different types of high purity nano carbon.

Solutions:

Realizing the need for mass production of nano carbon and demand of research to develop application of different types of nano carbon (carbon nano tubes, carbon nano fibres, carbon nano beads or spheres and other unique morphology of nano carbon), CAS focussed its attention in many of their labs, with government funding for programmes like '863' in 2002**.**

One of the success stories of 863 Program is providing various nano carbon production technology to Chengdu Organic Chemicals Co. Ltd for commercial production of carbon nano tubes (CNTs) since 2003. CAS is the largest research institute in China and comprises of at least 80 national institutes.

Chengdu Organic Chemicals Co. Ltd. through Timenano is manufacturing many kinds of CNTs and related products. Timesnano is exclusive CNTs provider in the Chinese Academy of Sciences (.They have invented moving-bed catalysis technology for continuous production of high purity, low cost and consistent quality CNTs. Now, they provide hundred kinds of CNTs and CNT related products. Their products in the market are listed below:

- Single-walled carbon nano tubes at 100Kg/annum with purity>90% and 30T/a. Since it greatly improves the cycle performance, thermal safety and C-rate performance of Li-ion battery, lead acid layer battery and electrical double layer capacitor by forming robust electrical conductive network in the electrodes, it has a great demand in the market.
- Multi-walled carbon nano tubes with OD 20-30nm and purity >95% - Because of its high conductivity, transparency and adhesion to substrate, CNT thin film is being used in flexible touch screen, transparent antistatic packaging material and solar cell.
- Double-walled carbon nano tubes with OD 2-4nm having >60% purity
- CNT Dispersant
- CNT and polymer composite. It has high tensile strength and low density; therefore CNT with reinforcement is in demand for making light weight and high strength metal based composited and polymer based composites which have huge demand in the aerospace field, wind driven generators and automobile industries.
- CNT-conductive filter
- CNT functionalized with different functional groups (hydroxyl, carboxyl, etc)
- Graphene. They are concentrating on beyong Graphene, i.e. Graphane and Graphyne, which differs in chemical structure from graphene. This may give them interesting mechanical and electrical properties thus could provide an edge over graphene in certain applications.
- Graphene oxide
- Graphite Nanoplates

- Nano-cellulose is their new product. This gel like material obtained from plants has 5 – 20 nm lateral dimensions. It is light weight, stiffer than Kevlar®, electrically conductive, non-toxic, the crystalline form is transparent, gas impermeable, very high tensile strength - 8 times that of steel, and highly absorbent when used as a basis for aero gels or foams. Nano-cellulose can be used in pharmaceuticals, food and medical industries.

Concluding remarks:

With various applications of carbon nano materials (CNM) in the market, it is needed by researchers and industries involved in CNM based applications. Invention of moving-bed catalysis technology for continuous production of CNTs with high purity, low cost and consistent quality has been one of the best contributions to mass production of carbon nano materials.

8.2. INDIA

Government initiatives:

The Government of India launched in October 2001, Nano Science and Technology Initiative (NSTI) for investment in variety of educational, HRD and R&D programs. Investment planned for first five years (2002 – 2007) was Rs. 60 Crore; for which active role of the Department of Science and Technology (DST), the Defence Research and Development Organisation (DRDO), the University Grants Commission (UGC), the Council of Scientific and Industrial Research (CSIR) and the Department of Biotechnology (DBT) for significant commercial results was envisaged. The emphasis of NSTI was on fundamental research program, focusing primarily on equipment for research. Other identified areas are nano drug delivery systems, energy, solar-cell, environmental and safety aspects of nanotechnology, and fundamental research program – focusing primarily on equipments research.

To further promote the activities of NSTI, Mission on nanoscience and technology (Nano Mission) was launched in May 2007. DST is the nodal agency for implementing the Nano Mission, with an allocation of Rs. 1000 Crore for the next five years. Apart from promoting research and research facilities, the Nano Mission is involved in establishing Centres of Excellence in nanotechnology, to promote industry-institution linked projects through increased public private partnership and promoting entrepreneurship through the establishment of business incubators. So far Nano Mission has established 14 Centre of Excellence in nanotechnology all over India.

Moreover, the Indian Government is keen on solving nanotechnology related moral, ethical and other issues through drawing a regulatory framework taking into consideration - liability for environmental hazards, environ-health impacts, transparency and public involvement, right to information and legal obligation. For risk regulatory governance, coordination of Ministry of Science and Technology, Ministry of Environment and Forest, Ministry of Chemicals and Fertilizers, Ministry of Labour and Employment, Ministry of Health and Family Welfare, Ministry of Consumer Affairs, Non-Government Organizations like the Federation of Indian Chambers of Commerce and Industry (FICCI) and *the Energy and Resources Institute* (TERI) is being sought.

So far as commercialization of nanotechnology is concerned, India has tremendous possibilities for any technological intervention. But India has been slow to adopt technologies and even slower to experiment them. This has happened primarily because the risk taking ability of individuals, organizations and the governments and the level of confidence in the innovations has been low in India.

However, realizing the immense potential of nanotechnology, in the last two decades, India has gained not only confidence to try out new technologies but also to experiment and innovate. This is primarily because the entrepreneurial base as well as purchasing power has increased and India is ready to adopt and adapt to nanotechnology, as government support and funding is also offered extensively with initiation of organizations for nanotechnology studies. Umpteen numbers of universities and colleges even from remote areas have been given grants to work on projects in almost all the disciplines of nanotechnology ranging from chip design, nano medicine, nanomaterials, use of nano materials for drug delivery, diagnostic kits, improved water filters and sensors, solar-cells and for reducing pollution from vehicles. Moreover, many international collaborations for nanotechnology with countries like UK, USA, France, Spain, Italy, Germany, Sweden, Japan and the Republic of Korea has been supported by DST and DBT. There are many consultancy companies that have cropped up in India, e.g. SAiNSCE that are providing information related to nanotechnology.

In India, many nanotech products are not translating into market products due to weak links between Indian scientific institutes and industry and the domestic industry's reluctance to manufacture large quantities of nanomaterials proven to have commercial application. Nanoscientists take more pride in declaring themselves as fundamental scientists than applied scientists. India needs to work on converting lab scale success into commercially viable, globally competitive relevant products. However, the sparks of entrepreneurship is now visible in business community and venture capitalists.

Case--study of a health-care company based on technology provided by ARCI, Hyderabad – SBP Aquatech Pvt Ltd.

About ARCI: The International Advanced Research Centre for Power Metallurgy and New Materials (ARCI) is based in Hyderabad India. It is an industry centric, autonomous R&D centre of Government of India's Department of Science and Technology (DST) that became operational in 1996. It is involved in developing unique, novel and techno-commercially viable technology in the area of advanced materials and subsequently transfers them to industries. It has so far transferred 17 technologies to 30 entrepreneurs in India. It has technical collaborations with partners in 15 countries. Centre for Nanomaterials in ARCI has been created as the Centres of Excellence (CoE).

About SBP Aquatech Pvt. Ltd.: The Company was established in 2007 and registered in 2008. The company is Manufacturer / Exporters / Wholesale Suppliers of nano silver powder, domestic water filter, ceramic water filter, water purifier candle, drinking water purifier, drinking water filter, reverse osmosis systems, drip water filter, gravity water filter, nano silver water filter; having a turnover of approx. Rs. 0.5 to 2.5 Crore.

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Problems/Issues:

Although an overwhelming majority of the planet is composed of water, 97% of this water is constituted of saltwater. The freshwater that sustains human life is only 3% of the total amount of water on Earth. Of this 3%, slightly over two thirds is frozen in glaciers and polar ice caps. The remaining unfrozen fresh water is mainly found as groundwater, with only a small fraction present above ground or in the air. Fresh water is a renewable resource, yet the world's supply of clean, fresh drinkable water is steadily decreasing because of heavy pollution. The most common contamination of raw water sources is from human sewage and in particular human faecal pathogens and parasites. Most water require some type of treatment before use, even water from deep wells or springs. Appropriate technology options in water treatment include both community-scale and household-scale point-of-use (POU) designs. Presently there are various mechanisms of drinking water treatment such as reverse osmosis, sedimentation, membrane filtration, UV disinfection, ozone disinfection, distillation, use of activated carbon, etc. Though these technologies are used for the filtration of water, their requirement for water treatment is very high. Moreover, they cannot remove all the pathogens and for a country like India they are not very cost-effective. Hence, there is a need to develop a water purification system which will be cost effective, utilizes less amount of energy and has high efficiency.

Solutions:

Anti-microbial property of nano silver is a well-established fact. It is being used in many household equipments to get rid of bacteria. Therefore, using nano silver at ARCI, the conventional method of ceramic candle filtration has been combined with nanotechnology to produce nano silver coated

ceramic candle filters. Nano silver-coated ceramic filter candle for disinfectant water-filter application was developed by a group comprising of Dr. K. Murugan, J. Revathi, Neha Hebalkar and Tata Narasinga Rao. The main advantage of this water filters and water filter candles are that they remove bacteria and other diseases causing pathogens present in water thus making the water drinkable.

This technology was transferred to SBP Aqua Tech Pvt. Ltd. The company signed a know-how transfer agreement with ARCI in June 2007. The company is owned by an entrepreneur Mr. Venu Gopal Cheekoti. He is now producing nano silver ceramic water under the brand name *Puritech.* Apart from removing turbidity, presence of nano silver kills the bacteria present in the water. It is one of the cheapest water filters in the market providing a low cost option and convenient solution.

Generally water filter prices in India ranges from Rs. 2,000 to 5000. But price of a Puritech filter candle is Rs. 70 only. In outside India market, it is US$ 2.5 only. By fixing this filter candle in *Matka* (Clay pot) used in most rural households for storage of water, a low cost water filter can be made (Figure 2):

Figure 2: Puritech water filter candle fixed in *Matka* (Clay pot)

Field testing done in forty villages in Andhra Pradesh has shown that maximum probable number (MPN) of *E. coli* ranging from 30 to 1600 has decreased to zero MPN by these candles.

Concluding remarks:

Of the more than 800 consumer products ((food packaging materials and food supplements, odour-resistant textiles, electronics and household appliances, cosmetics and medical devices, water disinfectants, and room sprays) that contain nanomaterials, approximately 30% are claimed to contain silver particles. One of them is silver nanoparticles containing socks to kill the bacteria associated with foot odour. A recent study by *Benn et al. (2008*) revealed that the silver can easily leak into water during washing, thus potentially disrupting helpful bacteria used in wastewater treatment facilities, or endangering aquatic organisms in lakes and streams. They have also found that some brands of socks lose nearly 100% of their silver content within four washings, while some brands lost less than 1%. Use of Nano-silver in washing machines has recently been protested by Swedish Environmental Protection Agency, because wastewater may be contaminated with nano-silver. Recently, the United States Environmental Protection Agency (USEPA) has decided to regulate this specific form of

nanotechnology. Also, farmers are concerned that the antimicrobial activity of nano-silver will affect the beneficial bacteria in soil, which are essential for the soil used for farming. With this insight, there is a need to research and formulate the minimization of potential risks of nano-silver by collecting sufficient data on leaching of nano silver and to assess human health.

Case--study of a health-care company based on technology provided by National Metallurgical Laboratory (NML) - Eucare Pharmaceuticals Pvt. Ltd. Chennai

About NML:

The National Metallurgical Laboratory is one of the 38 laboratories of **CSIR**, formally inaugurated on the 26 November1950 by Jawaharlal Nehru "in a spirit of hope and faith in the future". NML was supported, in cash and kind, by (i) Tata Industries Ltd., (ii) Sir Ratan Tata Trust, and (iii) Sardar Bahadur Sir Indra Singh of Indian Steel and Wire Products (ISWP) Company. Dr. Balraj Nijhawan, the first Indian Director of the laboratory, set the pace for the rapid growth of the laboratory through the establishment of a number of pilot plants and R&D programmes.

About Eucare Pharmaceuticals, Chennai:

Eucare Pharmaceuticals was incorporated in 1996 as a Private Ltd. Co. registered under Indian Companies Act 1956. They are pioneers in collagen technologies and drug delivery system for burns, advanced wound management, surgical haemostasis and dental restoration. It has a manufacturing unit with WHO accredited cGMP facility, meeting ISO 9001: 2008 and ISO 13485:2003 Quality Management system with Class 10,000 Clean Room System and CE Marketing medical devices from DET NORSKE VERITAS Norway.Now they have entered into a new opportunity in dental and orthopaedic segment through tissue & bone regeneration.

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Problem/Issues:

Autogenous bone grafts are most frequently and routinely used filling up defects in dentistry. However, autogenous bone grafts are always associated with various adverse factors including donor-site morbidity and limited availability. The Xenograft although are available in abundance, there exists a risk of viral transmission, varied fusion and healing rates and other social factors. On the other hand, synthetic bone graft can have a desired consistency, particle size, porosity and strength with ready availability in sterile condition, totally eliminating donor-site morbidity and the risk of viral transmission with absolute social acceptance, thus preferred by the majority of surgeons as a material of choice.

Solution:

In the Material Science and Technology Division of NML, Jamshedpur, a biomimetic process was developed using globular proteins and synthetic polymers for the synthesis of (i) nano-sized hydroxyapatite, and (ii) bi-phasic nano-composite hydroxyapatite and beta-tricalcium phosphate. They transferred the know-how of these two nano crystalline products to Chennai based Eucare. These two products are under technology licence from CSIR - NML Jamshedpur, India. They are:

1. Synthetic Nanocrystalline Hydroxypatite which is being manufactured and marketed by Eucare as brand name SYBOGRAPH^{TM}
2. Synthetic Nanocrystalline Hydroxypatite and β-Tri-calcium Phosphate Composite, which is being manufactured and marketed by Eucare as brand name SYBOGRAPH^{TM}-Plus.

Both these products are: biocompatible as per EN ISO 10993 standards; non-toxic, non-allergenic, non-pyrogenic, has No BSE / TSE issues and are highly porous.

Concluding remarks:

Intellectual property is a big concern about novel unique discoveries. CSIR has positioned itself from being reactive to giving proactive IP protection by random patenting to planned patenting and designing patenting portfolios based on business plan with commercial and strategic considerations. It has filed 183 patents (unique inventions) in India and 404 patents abroad (multiple jurisdiction) during 2008-09. It now has a portfolio of 1910 patents in India and 2689 patents abroad

8.3. INDONESIA

Government initiatives:

Following the global trend, the Indonesian Ministry of Research and Technology has focused its attention on nanotechnology, with emphasis on its application in food and energy. With the advent of "Masyarakat Nano Indonesia (MNI) in 2005, the government of Indonesia started exploring the possibility of marriage between nanotechnology and bio-nanotechnology and initiated and invested in research in top universities and research institutes. The government laboratory, the Research and Development Centre for Material Science & Technology (RDCMST) has initiated the establishment of cooperative program in nanotechnology research.

With an intention of the Ministry of National Education to provide $26.5 million and the Ministry of Industry to contribute $1.59 million to promote the industrialization of R&D output on applications for industry including ceramics, textiles, food, environment, energy, and information technology and communications, Indonesia is well on its way for entering into the commercial arena. Following are institutions engaged in nanotechnology research covering areas like nanostructures, nano-encapsulation, Ag nanoparticles, nanocomposites and nano carbon**:**

- University of Indonesia, Jakarta

- Institute of technology Bandung (ITB)
- Institute of technology Surabaya (ISB)
- University of Gadjah Mada Yogyakarta (UGM)
- Indonesian Institute of Sciences (LIPI)
- National Nuclear Energy Agency for Indonesia (BATAN)
- Aeronautics and Space (LAPAN)
- Agency for the Assessment and Application of Technology (BPTT)
- Pusat Penelitium Elmu Pengetahuan Dan Teknologi (PUSPIPTEK)
- Eijkman Institute
- Mochtar Riady Centre (MRC)

About Mochtar-Riady Centre for Nanotechnology and Engineering (MRCNB):

The biggest investment in uplifting the status of nanotechnology in Indonesia, with an investment of US$ 20 Million, is by Mochtar Raidy & LIPPO group; to conduct innovative research on cancer prevention and new understandings of the cause, early diagnosis, control and cure of cancer. MRCNB is luring talents from Indonesia and overseas to conduct innovative research on cancer prevention and new understandings of the cause, early diagnosis, control and cure of cancer.

They founded Mochtar-Riady Institute of Nanotechnology (MRIN) with the aim to conduct innovative research in cancer. Their Scientific Advisory Board consists of members from USA, France, Singapore, Hong Kong, Australia and eminent scientists from Indonesia. The Centre also runs short term training courses and Ph.D. Program. This rich Centre has very well equipped labs and equipment. They have both international and national collaborations. International collaborations are with Shanghai Cancer Institute, Shanghai; Jiatong University, Shanghai; South East University, Nanjing; Hong Kong University of Science and Technology and Faculty of Medicine, National University of Singapore. National collaborations are with University of Indonesia, Jakarta; Cipto Mangunkusumo Hospital Jakarta, Hasanuddin University, Makassar; National Cardio-vascular Centre Harapan Kita, Jakarta, etc.

Case--study of a knowledge and technical help providing company - Nanotech Indonesia, Supported by PUSPITEK, Serpong

About PUSPITEK:

PUSPIPTEK was founded in 1976 with the aim to support the process of industrialization in

Indonesia. The Company then was designed to be a synergy between the educated and trained human resources, research tools and most comprehensive technical services in Indonesia as well as technology and expertise has been accumulated for more than a quarter century. It has a huge campus spreading over an area of 600 ha encompassing Research and Development, General Services, Housing and Environment as well as Utility Group; all having enough electricity and water supply and centralized solid and liquid waste processing systems.

MNI signed a MoU with research institution in PUSPIPTEK, with an intention to initiate research in nanotechnology. The result was a successful commercial set up – 'Nanotech Indonesia' - to provide support and knowledge related to nanotechnology.

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Problem/Issue:

Every country that has entered into the field of nanotechnology has felt the need of high quality nanotechnologists along with sophisticated equipment and their handling, especially to ensure the quality and capability of the national industries with the laboratory testing services.

Solutions:

Nanotech Indonesia was established with the purpose as a partner for the industries in supporting their growth and delivering technical solutions. With the support from experts and advanced facilities in PUSPIPTEK, Serpong, Nanotech Indonesia started following activities:

- **Laboratory Testing** – Using high-tech equipment, they provide (a) Microscopic Test – Optical, SEM and AFM; (b) Composition Test (Solid) EDS, XRF and XRD; (c) Composition Test (Solvent) – AAS, FT-IR and GCMS; (d) Particle Size Analysis; (e) Zeta Potential Test; (f) NDT (Non Destructive Test;) and (g) Mechanical Properties Test–Hardness, Bending, Impact, Tensile, Compression and Fatigue.
- **Technical Training** - Applied technical training services for enhancing technical capability:
- Failure analysis; (b) Risk base inspection; (c) API 579 and ASME 8; (d) SEM, GCMS, FTIR and PSA; (e) Nanotechnology training; and (f) Specific measurement instruments.
- **Technology and Management Consultancy** – (a) Product Development - PT. Gizi Indonesia; (b) Product Development - PT. Qolbi Herba Alami Sejahtera; (c) Processing machine for catechin in West Sumatera; and (d) Policy study for investment on electronic and automotive products.

Since founded in 2009, Nanotech Indonesia has become a partner for eighteen major industries in technology solutions and innovations. They are also in the business of trading nano machines and material processing.

Concluding remarks:

Efforts of Nanotech Indonesia are commendable, as they started the work with least funding and generated money through many training courses. They would have initially needed huge amount of spending on training equipments, but for that they took the help of PUSPITEK. Starting a R&D set-up is being supported by the government.

Case-study of a floor treatment company - NANOCORE Indonesia

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Problem/Issues:

Demand for hard, polished, smooth surfaces is rapidly increasingly. It is required for metal, cement, ceramic, plastic, mineral and glass surfaces. Apart from hard polished surface, there is a demand for better quality too.

Solutions:

To provide better floor, has been the aim of NANOCORE Indonesia. Today they are floor treatment specialists, with many innovative products developed with the help of nanotechnology. Some of their patented and *nano lithium* fortified products are:

- **Pentra-Finish™ (Li) -** This lithium fortified finish offers deep penetration, increased surface hardness and superior reflectivity. The reactive micro-impregnating Nano Lithium™ polymer creates greater protection and greater gloss with less labour. The unique treatment is environmentally friendly and meets CSMA floor polish slip resistance requirements employing ASTM test method.
- **Pentra™ Protective Coating -** It is a hybrid inorganic/organic Nano Lithium™(topcoat finish and surface hardener). This lithium-silicate water-based formulation has very low polymer odor and provides long-lasting surface protection. It is perfect for protecting concrete floors, ferrous metal, concrete block, aluminum/non-ferrous metal, asphalt and previously existing coatings.
- **Pentra-Sil (NL) – A concrete chemical hardener, sealer and densifier** is a Nano Lithium™ surface treatment. It forms a surface that is breathable, abrasion-resistant and extremely hard. It is excellent for concrete floors needing long-term protection against heavy wear and abuse, moisture, dirt and grime buildup, as well as protection against alkalinity and salt residue. Pentra-Sil (NL) is V.O.C. compliant and environmentally safe to use..
- **Pentra-Guard™ (HP) - High performance industrial flooring surface hardener and protective clear coat** is a "micro film forming hybrid inorganic/organic nano lithium™

surface treatment" that hardens and seals concrete floors, producing a very hard, dust repellent, chemical resistant and water tight surface.

Concluding remarks:

In a country where nanotechnology is in juvenile state of commercialization, efforts of NANOCORE and Nanotech Indonesia are unique and innovative. It has given a good start and boost.

8.4. ISLAMIC REPUBLIC OF IRAN

Government initiatives:

The Islamic Republic of Iran has realized that in the near future Iranian enterprises possess no option but to utilize novel technologies to increase its share of the future global market and to improve the level of nation's economy. To achieve this, in 2001 Iran has developed a comprehensive Iran Nanotechnology Initiative Council (INIC). Under INIC a National Nanotechnology Initiative (referred to as Future Strategy) was initiated in 2005, to support the nanotechnology development, which made significant leaps in nanoscience and technology advancement. Under this initiative, the national government is in charge of promotion of R&D and industrial production of nano-related products. An action plan for ten years that is up to 2015 has been chalked out.

This 10-year programme includes 33 activities divided into six categories:

1. **APAC** (Advocacy and Public Awareness Committee) is created to collect and distribute information regarding current and future potentials of nanotechnology to general public.
2. **HRDC** (Human Resources Development Committee) to promote manpower in the field of nanotechnology. More than 50 universities and research institutes are engaged in this.
3. **IRDC** (Research and Development Infrastructures Committee) to develop necessary infrastructures for the support of R&D in academic as well as industrial institutions. T
4. **INLN** (Iran Nanotechnology Laboratory Network) established in 2004 covers 42 advanced laboratories nationwide, and **INSC** (Iranian Nanotechnology Standardization Committee) and more than 10 patent offices in 2006 that has established Intellectual Property and Technology Licensing Office (IPTLO) in 2005 and Nanotechnology Standardization Committee in 2006.
5. **TDPC** (Technology Development and Production Committee) is in charge of promotion of research and development and industrial production of nano-related products.
6. **INBN (**Iran Nanotechnology Business Network) to support commercialization, investment, technology development, marketing, branding and the private sector start-ups entering into the market. Iranian funding between 2004-2008 has been US$ 135 million (US$ 40 million from State Fund, US$ 25 Million from Public Organizations and US$ 70 million from Private Fund). There are more than 50 active companies working in the field of nanotech in Iran, to them INBN provides both non-material and material support.

Following are the examples of research outputs:

- Hydro conversion of heavy crude oil into light crude oil using nanocatalysts. A pilot plant with a capacity of 200 barrels/day is being built.

- The Research Institute of Petroleum Industry (RIPI) is able to produce 8 kg CNT per day.
- Breast cancer diagnostic kit for the early detection of breast cancer is being produced and undergoing clinical test by NanoSina Co
- Nano additive for improving the performance of motor oil is already being produced and marketed by Pishgaman Nano Arya Co.
- Nano silver incorporated garments and textiles are being produced by two companies (Pars Nano Nssb Co. and Noavaran Catalyst Co.)
- Nanotechnology Systems Co is producing and exporting Scanning Tunnelling Microscope.
- Antibacterial nano products for treatment of air/water/soil, nano air-conditioning filter and photo-catalytic application are being produced by Nanopac Persia Co.

Case-study of instrumentation and devices company - Nanotechnology Systems Corporation (NATSYCO)

About the Company:

NATSYCO is a University based spin-off company formed by a group of scientists and researchers. It was supported by the Iran Nanotechnology Initiative Council (INIC) at various stages of development. Iran Nanotechnology Laboratory Network (INLN) has financially supported the manufacture of the advanced equipment needed for nanotechnology research.

Though initially NATSYCO was established as a research team in 2003, in 2006 it became a full-fledged production company involved in research, production and marketing of nanotechnology, instruments, devices and materials.

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Problem/Issue:

Growth and development of nanotechnology depends on availability of characterization facilities and equipment. Though earlier the concept of nanotechnology was not there, but nanotechnology was still existing and being used since 4th century B.C. Gold was not only known and exploited for its ornamental adornment but their sols and colloids were also a matter of excitation in the medieval age. "Soluble" gold appeared around 4th century B.C. in Egypt and China. This enigmatic behaviour of gold colloids led to the curious endeavour of using it as a pigment for coating glasses, enamel and chinaware in the mid-17th century. Andreus Cassius, a painter and sculptor, developed coloured solution of gold sol which was purple in colour and hence named it as "Purple of Cassius" which had been painted on the glasses of many houses and Churches. These special characters were due to nano

size. This was found out or rather seen after the discovery of electron microscope and many other supporting high-tech equipments.

Solution:

Importance of characterization devices and equipments cannot be emphasized enough. Without them nanotechnology would not have progressed. This realization was the reason for the genesis of Nanotechnology System Corporation (NATSYCO) which manufactures a wide variety of equipment and laboratory devices in the field of nanotechnology:

- Scanning Tunnelling Microscope – designed and produced by NATSYCO under the brand name NAMA-STM.
- AFM (Atomic Force Microscope)
- Nano-Bio-Sensor
- Magnetometer

The company has continued to gain an effective presence in hi-tech market outside Iran also due to these four products.

Concluding remarks:

Manufacture of highly specialized equipment like Scanning probe microscope NAMA-STM is a star product of Iran. It has given a very special status to the nanotechnologists of Japan. So much so that the Iranian President Mahmoud Ahmadinejad has presented it as official gift to Qatari Emir Sheikh Hamad bin Khalifa Al Thani of Qatar, Brazilian President and Venezuelan Presidents; during his visit to the respective countries.

Case-study of instrumentation and nano material producing company supported by INIC – Payamavaran Nanotechnology Fardanegar (PNF)

About PNF:

Payamavaran Nanotechnology Fardanegar (PNF Co.) was established in 2006 as a manufacturing company.

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Problems/Issues:

The previous company NATSYCO discussed above was about manufacturing equipments for characterization and visualization of nano materials. Obviously the next issue that comes to mind is how to make nano-materials. Should one depend on imported nano material and imported equipment for mass production of nano materials, was a major issue under consideration.

Solutions:

PNF is also in equipment manufacturing business related to nanotechnology. But they manufacture equipments for the synthesis of various forms of nano-particles. They manufacture equipment for the industrial mass production of various metallic and metal oxide nano-particles, i.e. Nano Colloid Maker and Nano Powder Maker. These are very high-tech precision machines. The design of these machines is the result of their various R&D projects in the field of nanotechnology processes and also modification of nano-products.

The *Plasma Nano Colloid Maker* is a special equipment by EEW technique in liquid media. It produces different ranges of metallic nano colloids. In this methodology using extra-high electric voltage or current, the metal wire is converted into nano metal oxide powder via explosive process.

Pulse Electrical Explosion (PEE) Maker is also by EEW technique in gas media and it produces nano metals and nano metal oxide in powder form. By this technology, any type of thin conducting metal wire can be transformed into nano particles. By using above mentioned methods, a wide range of nano powders and nano colloids have been produced by PNF Co.

Nano-Dispenser Machines developed by PNF are used to disperse dry nano powders in various kinds of liquid media to meet the requirement of high quality nano-products. The nano dispenser machines use the nano cavitations technology to de-agglomerate and disperse the nano particles in any liquid media.

Concluding remarks:

Nanotechnology Fardanegar Co., producer of electro-spinning and electrophoresis equipment, is supported in many ways by INIC. One of the goals of INIC is to introduce and present the latest scientific/technological achievements of knowledge-based Iranian companies at the international platforms. In order to support nanotech commercialization in Iran, 'Tech-Market Corridor' was established in 2010. It provides range of services to start-up companies, SMEs, large scale industries in the areas of nanoscience audit, IP, Technology Readiness Level Assessment (TRLA). business plans, licensing and tech-monitoring, market evaluation, venture capital, marketing, legal advisory and production consultation. INIC has made many promotional attempts for marketing the products.

Success of Nanotechnology in Iran is due to planned entry into the development area of nanotechnology. Infrastructure network was set up in 2004 covering 42 advanced laboratories nationwide and INBN was set up in 2007 connecting 110 nanotech companies. The embargo on Iran has motivated Iran industry to develop its own technology and products including STM, water purification system, air filters, industry scale quantity CNT and others

8.5. JAPAN

Government initiatives:

Comprehending the potential economic impacts of nanotechnology and the key challenges in its commercialisation, Japan was the first country in the world that started a major ten year

nanotechnology program (the Atom Technology Program) in 1992. The Japanese government invested a huge sum of US$ 250 million for R&D in various fields of nanotechnology. Today, it is at par with USA in the development of nanotechnology.

One of the most valued nano particle single walled carbon nanotubes and multi-walled carbon nanotubes were discovered by Japanese scientists Bethune (1993) and Iijima (1991) respectively. Even the word nanotechnology was coined by a Japanese scientist Norio Taniguchi. Umpteen numbers of carbon nanotubes and metal oxide companies mushroomed in Japan during the last two decades. The carbon nano tube companies of Japan boast of best quality products.

Two main funding Ministries of Japan are:

1. MEXT (Ministry of Education, Culture, Sports, Science and Technology) – It funds through JSPS (Japan Society for the Promotion of Science), JST (Japan Science and Technology Agency), NIMS (National Institute for Materials Science) and RIKEN (Institute of Physical and Chemical Research). JSPS supports basic research with grant-in-aid for scientific research, and JST coordinates challenging research which will need 10 to 20 years for industrial application. NIMS and RIKEN are mainly in charge of generic technology.
2. To encourage interdisciplinary, inter-organizational, and international collaboration among researchers, the Nanotechnology Support Project was started by MEXT in April 2002 and Nanotechnology Business Creation Initiative (NBCI) in 2004.
3. The Nanotechnology Researchers Network Centre of Japan is responsible for informational support, and 14 universities and national research institutes are responsible for common use facility support.
4. METI (Ministry of Economy, Trade and Industries) -METI has a funding agency, New Energy and Industrial Technology Development Organization (NEDO) and one research institute, National Institute of Advanced Industrial Science and Technology (AIST)]. Both organizations are in charge of flagship type research which will need 5 to 10 years for industrial application. The leading projects by METI are Focus 21, the nanomaterials and Processing Sub-Program by NEDO.

Strategic priority in R&D to basic research and 4 prioritized areas in funding are:

- Life sciences,
- Information and telecommunications,
- Environmental sciences, and
- Nanotechnology and materials science/technology

In 2001, nanotechnology and materials science, CSTP exemplified 4 fields:

- Nano-devices and materials for next-generation communication systems (information technology),
- Materials for the environment and energy-saving (environment),
- Nano-biology for new medical care technologies and biomaterials (biotechnology), and

- Underlying technologies such as fabrication and analysis/simulation technologies (generic technology), and novel materials with innovative functions (materials).

Case-study of a health-care compay started with the research efforts of University of Tokyo, Tokyo Women's Medical University and Jikei University - NanoCarrier (Japan)

About the Company:

NanoCarrier Japan was established in June 14, 1996 in Setagaya, Tokyo, with the purpose of applying new block copolymers to develop pharmaceuticals and put them into practice. In August 1997, it formed partnership with Nippon Oil & Fats Co., Ltd. (now NOF Corporation) on joint development and supply of a new block copolymer (afterwards entered into a supply agreement on exclusive manufacture and supply of polymer on December 2003). Head office and Lab in Chiba was started in October 1999 and a new Tokyo office was established in Chuo in July 2003. NanoCarrier got listed in Tokyo Stock Exchange in March 2008. At present its capital is ¥ 3,576 million (as of March 31, 2012). It has 29 employees involved in R&D and production of pharmaceuticals using micellar nanoparticles technology. The company has now planned to raise a capital in excess of ¥3.7 billion.

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Problems/Issues:

Prevalence of human suffering from dangerous diseases like cancer, and enhanced suffering due to increased doses of drugs has arrested the attention of scientists. There is a need to contribute to the betterment of human health of cancer patients by producing new drugs utilizing innovative nanotechnology.

Solutions:
This problem needed multidirectional research and approach
NanoCarrier's core technology, micellar nanoparticles technology, was proposed to tackle the problem and has been researched by Professor Kazunori Kataoka of University of Tokyo, Professor Teruo Okano of Tokyo Women's Medical University and Associate Professor Masayuki Yokoyama of the Jikei University. The aforementioned professors demonstrated that when drug-encapsulating micellar nanoparticles were intravenously administered, the particles could function as stable drug carriers in the bloodstream and they accumulated in cancerous tissues.

Prof. Kazunori Kataoka works on use of nano size (<100 nm) polymeric micelles as drug carrier for cancer therapy, in collaboration with Professor Teruo Okano whose research interests lies in the use of intelligent biomaterials for biomedical research applications such as micro-domain structured polymers, stimuli-responsive polymers, hydrogels, polymeric micelles, modulated drug release, targetable drug carriers, blood compatible polymers, cell engineering, tissue engineering, and artificial organs as well as others. Another research partner is Dr. Masayuki Yokoyama who is working on developing a nano-carrier system with novel polymer chemistry for the delivery of anticancer drugs and diagnostic imaging agents and immunity to nano-carriers, such as polymeric micelles, liposomes, etc.

Since oncology was the focus area of NanoCarrier and as pioneer of micellar nanoparticles technology, they jointly utilized the work of these three above mentioned Nano-Bio-technologists and entered into harnessing the potential of micellar nanoparticles technology to their product development. NanoCarrier Co. Ltd. was founded in 1996 by Dr. Nakatomi, CEO of the Company, together with Professor Kazunori Kataoka and Professor Teruo Okano. Their research resulted in January 2001 in the development of "Polymeric micelle containing cisplatin enclosed therein and use thereof" from the Centre for Advanced Science and Technology Incubation Ltd. (now TOUDAI TLO, Ltd.). Later in June 2002 they out-licensed Paclitaxel Micelle to Nippon Kayaku Co., Ltd.

NanoCarrier has been developing on advanced biomaterials and technologies for drug delivery using its proprietary technology called "Micellar Nanoparticles", invented mainly by Professors Kataoka and Okano. NanoCarrier has obtained over 40 patents, including worldwide substance patents to cover the use of polymeric micellar drug carrier as functional nanoparticles (Table 1). The company's product portfolio includes mainly intravenous formulations of various low and high molecular weights of therapeutic compounds, which in turn, improve the efficacy and safety profile of original drugs as well as patient's quality of life. It contributes to advance the treatment of cancer and other intractable diseases.

NanoCarrier has been continuously expanding their commercial horizon

In 2005 March and August, a partnership was signed with Debiopharm S.A. for DACH-Platin micelle (NC-4016), and with TOUDAI TLO, Ltd for "discovery and development of drugs with high usability for treatment of solid cancers" respectively.

In June 2006 NanoCarrier obtained exclusive license of "Electrostatic bonding type macromolecular micelle drug carrier and drug carried thereon" from TOUDAI TLO, Ltd. Another important step in 2006 August was in-licensed "Physical trapping type polymeric micelle drug preparation", for the research and development of paclitaxel micelle (NK105) with Japan Science and Technology Agency. In February 2007, a new block copolymer for preparation of pH-sensitive polymeric micelle and a production process thereof" from the University of Tokyo and TOUDAI TLO, Ltd was in-licensed.

According to NanoCarrier News - Orient Euro Pharma co Ltd. and NanoCarrier sign a new agreement on 7th November 2012 to conduct registration trials of Nanoplatin™ and to set up a manufacturing site in Taiwan province of China. By in March 2008, NanoCarrier Co., Ltd. became one of the leading biotech companies listed on Tokyo Stock Exchange (Code: 4751).

2008 was also a very fruitful year for NanoCarrier as it got exclusive license agreement signed with Toudai TLO, Ltd. on incorporated nucleic acids into micelles; license and co-development agreement of Nanoplatin (NC-6004) with Orient Europharma Co. Ltd.;and IND Application of Nanoplatin® for Phase I/II study was approved in Taiwan province of China. In-licensed "Cationic Polyamino Acids" from the University of Tokyo and TOUDAI TLO, Ltd was achieved in 2009.

In 2010, collaborative research agreement was signed with National Cancer Centre to initiate a preclinical study of Epirubicin Micelle (NC-6300).

In September 2011, worldwide license and co-development agreement of Epirubicin Micelle (NC-6300) with KOWA Company Ltd, and collaborative research agreement with Eisai Co. Ltd were signed. In 2012, they got Japan Substance Patent allowed for new DDS of VELCADE® and Docetaxel Micelle. In 2012, NanoCarrier has signed further extension of research collaboration with University of Tokyo.

It is worth mentioning the steady progress of clinical trials of their output that started progressing from 2006:

- In May 2006 they started phase I Clinical trial of Nanoplatin® (NC-6004) in U.K.
- In November 2007 Nippon Kayaku Co., Ltd. started phase II clinical trial (gastric cancer) of Paclitaxel Micelle (NK105).
- In March 2009 started phase I clinical trial of DACH-platin Micelle (NC-4016) in EU.
- In August 2010 Nippon Kayaku Co., Ltd. started phase I clinical trial (breast cancer) of Paclitaxel Micelle (NK105).
- In July 2011 started phase Ⅱ clinical trial of Nanoplatin (NC-6004) in Taiwan province of China and Singapore.
- In July 2012 Nippon Kayaku Co., Ltd. started phase III clinical trial (breast cancer) of Paclitaxel Micelle (NK105).
- In 2012 Phase III global clinical trial with Paclitaxel Micelle (NK-105).

Concluding remarks:

As compared to Nano carbon and electronic products using nanotechnology, application of nanotechnology in health care has been comparatively less in Japan. Efforts of NanoCarrier in collaboration with three research departments of different universities are a very good example of interdisciplinary research leading to commercialization. After a prolonged successful technical and commercial achievement, NanoCarrier has again extended the research collaboration with the Tokyo University showing the success of intention of Japanese government in the field of nanotechnology.

Table 1: Legal status of NanoCarrier's major patents

Pipeline	Title of the invention	Applicant/Patente	(R: registered; UP : under prosecution)
Paclitaxel Micelle (NK105	McKellar preparation containing sparingly water soluble anti-cancer agent & novel block Co-polymer	NanoCarrier Co. Ltd. Nippon Kayaku Co., Ltd.	R in 18 nations,including US & EU countries UP in 3 regions including
	Physical trapping type polymeric micelle drug preparation	Japan Science and Technology Agency	R in 12 nations including JP, US and EU countries
	Production process for polymeric micelle composition encapsulating a drug	NanoCarrier Co. Ltd.	R in 10 nations including JP, US and EU countries
	Production process for polymeric micelle composition encapsulating a drug	NanoCarrier Co. Ltd.	R in JP& 8 nations including EU UP in including US
	Lyophilizing composition of drug-encapsulating polymer micelle & method for preparation thereof	NanoCarrier Co. Ltd.	R in 23 nations including JP, US & EU countries
Nanoplatin® (NC-6004)	Polymeric micelle containing Cisplatin enclosed there in & use there of	TOUDAI TLO Ltd.	R in 23 nations including JP, US & EU countries
	Pharmaceutical composition & combined agent	NanoCarrier Co. Ltd.	Patent pending (PCT application)
DACH-Platin Micelle (NC-4016)	Coordination complex of DiaminocyclohexanePlatinum (II) with block polymer containing Poly Carboxylic acid segment & anti-tumour agent comprising the same	TOUDAI TLO Ltd.	R in 34 nations including JP & EU countries Accepted in 1 nation UP in US countries
	Process for production of polymerized coordination compound of Platinum complex.	NanoCarrier Co. Ltd. The University of Tokyo	R in 2 nation including US Accepted in 1 nation UP in 6 regions including JP & EU countries
	Coordination compound composed of DiaminocyclohexanePlatimum (II)&Block copolymer & anti-cancer agent comprising the same	The University of Tokyo	UP in JP, US & EU countries
Protein Micelle	Electrostatic bonding type macromolecular micelle drug carrier & drug carried thereon	TOUDAI TLO Ltd.	R in 11 nations including JP & EU countries UP in US
	Physiologically active polypeptide, polymer micelle having protein enclosed there in& process for production of the polymer micelle	Nanocarrier Co. Ltd.	Patent pending (PCT application)
siRNA Micelle	Electrostatic bonding type macromolecular micelle drug carrier & drug carried thereon	TOUDAI TLO Ltd.	R in 11 nations including JP & EU countries UP in US
	Composition containing fine particles as carrier for biologically active substance & method for preparing these	TOUDAI TLO Ltd.	R in 6 nations including JP and EU countries Accepted in US
	Polyethylene glycol/Polycation block	The University of	R in 3 nations including JP &

	copolymer	Tokyo	US UP in 3 regions including EU countries
	Copolymer including uncharged hydrophilic block&cataionicpolyamino acid block having lateral chain to which hydrophobic radical is partially introduced &use of copolymer	The University of Tokyo	Patent pending (PCT application)
	Cationic Poly amino acid & uses there of	The University of Tokyo	R in JP Patent pending (PCT application)
Sensor Linked Micelle	Active targeting polymer micelle encapsulating drug& pharmaceutical composition	NanoCarrier Co. Ltd.	R in JP accepted in 1 nation UP in 6 regions including US & EU countries
pH-Sensitive Micelle	Novel block copolymer for preparing pH-responsive polymer micelle& method for producing same	The University of Tokyo	UP in JP
	Block copolymer for drug complex & pharmaceutical composition	NanoCarrier Co. Ltd.	R in 12 nations including EU UP in 8 regions including JP & US
Docetaxel Micelle	Docetaxel polymer derivative method for producing same & use of same	NanoCarrier Co. Ltd.	Patent pending (PCT application)

Case-study of laser & optical equipment company in collaboration with University of Tokyo funded by METI & NEDO - Alnair Labs Corporation

Alnair Labs Corporation is one of the best examples of university and industry collaboration as well as the role of Japanese government in funding and promoting commercialization of nanotechnology based and related products.

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Problem/Issue:

With the advent of nanotechnology and the understanding that nano particles possess unique and novel optoelectronic properties, a need for advanced equipment was being felt.

Solutions:

Contribution of research by Prof. Kikuchi Kazuro, was thought of as a solution to the above problem. It was utilized by the visionaries of Alnair Labs Corporation. Prof. Kikuchi Kazuro was a specialist in optoelectronics and worked in the Department of Electrical Engineering and Information Systems and Department of Advanced Interdisciplinary Studies of University of Tokyo. His work has been on the

optical communication system. He is currently involved in all-optical signal processing devices and their applications to ultrafast optical communication systems. He is also interested in coherent optical communication systems that realize multi-level modulation formats with high spectral efficiency.

Alnair Labs Corporation was established on 29th August 2001 in Kawaguchi, Saitama-ken, Japan.(which later shifted to Tokyo in 2010) as one of the first venture companies to commercialize the photonics technologies developed at the University of Tokyo. Its capital increased to ¥200 million by December 2001. One of their directors is Prof. Kazuro Kikuchi of University of Tokyo. And their technical advisor Prof. Shinji Yamashita is also from University of Tokyo. In 2002 they got R&D grant from the Ministry of Economy, Trade and Industry for the *"Development and Practical Realization of Tunable Dispersion Compensating Devices", and in the same year Alanir Labs* released its first mode-locked pulsed fiber laser product based on proprietary carbon-nanotube technology.

In the second rounds, venture capital investment increased their capital to ¥320 million. In 2005 Alnair Labs got another R&D fund from NEDO for *"Development of 3D Measurement System using High Repetition Rate CNT Femtosecond Pulsed Fiber Laser"*. By 2007, its capital increased to ¥350 million and it got ISO 9001 certification. In 2008, its capital increased to ¥413 million. Looking at their very successful performance, NEDO again funded a venture R&D innovation grant to Alnair Labs, this time for *"Development of High-Precision E-field Sensing Systems for Near-Field Measurement of Electro-Magnetic Field Emitting Media"*.

Now Alnair Labs is the leading manufacturer of ultra-short pulse laser systems and solutions based on proprietary carbon-nanotubes photonic technology. Their products are:

- Optical measurement equipment for measuring the optical properties of nano materials (Optical sampling Oscilloscopes, Bit Error rate Tester, Short Pulse Autocorrelator)
- Lasers and amplifiers (Carbon Nano Tube Femtosecond Laser, 10 GHz Mode-locked Laser, Low Noise Optical Amplifier)
- Tuneable filters (Band-width Variable Wavelength-Tuneable Filter, Wavelength-Tuneable Narrow-band Filter, Wide-band Dispersion Compensator)

Concluding remarks:

Commercialization of these optoelectronic equipment using nano materials and for the characterization of nano materials is not only a joint effort of collaboration with university research centers but also involves funding by Japanese government. It should be followed by other countries for the growth and development of nanotechnology based industries.

Case study of nano carbon company - Nano Carbon Research Institute Co. Ltd. (NCRI); Shinshu University

About NCRI:

It is a nano-sized R&D company; hence has the smallest possible organization with only 3 employees. However, NCRI has powerful connections with academic and governmental research organizations all over the world. The Company was established and registered at the Hall of Chosei village, Chosei-gun, Chiba, on April 26, 2001. Later the registration was transferred to Ueda, Nagano. Its Capital value is ¥ 3,000,000. Prof. Eiji Ōsawa is the executive director and president (Professor Emeritus of Toyohashi University of Technology) of NCRI. The Company holds 4 patents related to nano Carbon and nano size particulate graphite.

The activity of the Company includes:

- Research and developments of nanocarbon materials
- Production and sales of nanocarbon materials
- Consulting in nanocarbon science and technology

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Web: http://nano-carbon.com

Problem/Issues:

Discovery of C_{60} in 1985 triggered a world-wide surge of research activities towards nano carbons. These invisible ultra-small particles are insoluble, non-volatile, non-melting, and non-subliminal gigantic molecules having extremely large surfaces of the orders of a few hundred m^2/g, are difficult to handle and purify. Hence, nanotechnology needs extensive research on the fundamental aspects of nanoparticles and then enter into commercialization.

It is realized by the scientists of the NCRI that for commercialization of carbon nano materials there will be four pre-requisites or issues: (i) low production cost, (ii) biocompatibility, (iii) high crystalline order in the atomistic structure, and (iv) the predictable existence of large market.

Solution:

The approach of NCRI in solving the above mentioned 4 problems were systematic:

1. To reduce production cost, Dispersed Ultra Nano-Crystalline Diamond (DUNCD) were isolated from soot produced by exploding a popular military explosive Composition B (TNT+RDX) in water or other inert media. Note that the expired military explosives have negative price.
2. To confirm biocompatibility, careful studies on the cytotoxity were undertaken, which confirmed total absence of cytotoxicity in DUNCD.
3. To get ordered atomic structure, the primary particle of DUNCD was found suitable because it is a single cubic diamond crystal containing about 5000 carbon atoms. With such a large number of constituent atoms, DUNCD was found to retain most of the properties known to bulk diamond. Due to the closest packing, diamond has long been rated as the best general-purpose industrial material known on earth, especially excelling in hardness, Young's modulus, transparency, chemical inertness, thermal conductivity and doping possibilities.
4. Marketability – Since the dispersed single-nano diamond particles or DUNCD retain most of the properties of bulk diamond, and are still amenable to the known processing technology of nanoparticles, it will prove to be a highly versatile material for a variety of applications, thus making it a marketable possibility.

So we can see that the DUNCD satisfies all the four requirements as mentioned above.

In November 2011, NCRI was authorized as the private research organization by JSPS, entitled to apply competitive funding for international programs of exchanging researchers.

Their products include:

- Dispersed single-nano diamond particles of 4 nm average size – it is produced by detonation method using TNT+ RDX/water as raw material. It is NCRI's breakthrough achievement.
- Ultra High Quality Carbon Nanotubes (both MWCNT and SWCNT).

NCRI markets their products through two Japanese agents, namely New Metals and Chemicals Corporation Limited and Bravus Japan Corporation Limited.

Concluding remarks:

This set up is more like a University's effort of entering into production through a company that is marketing its products through agents. Shinshu University's Faculty of Engineering Textile Science and Technology and Education, School of Medicine, and Institute of Carbon Science and Technology, is actively involved as the leader in research and development of smart devices using nanocarbon (i.e., to create new composite materials using carbon nano tubes and other carbon materials, energy applications, composite platings, development and practical application of composite materials, as well as bio applications and to construct new devices in collaboration with Yamagata University, Matsumoto Dental University and Nagaoka University of Technology.

8.6. REPUBLIC OF KOREA

Government initiatives:

Government's awareness and activities to advance the nanotechnology R&D and production became evident more than a decade ago in 2000 when Korean National Nanotechnology (NT) Initiative was started and approved by the National Science and Technology Council (NSTC) in December 2001 and finally the Nanotechnology Development Promotion Act was passed in 2002.

Within five years of first phase (2001 – 2005), with the help of nearly four thousand researchers, 214 nanotech based companies and KRW 277.2 billion investments by 2005, the Republic of Korea came up with 1431 paper publications and 979 foreign patents (*Korea NT Annual 2005, KISTI*).

They are continually increasing funding R&D and basic research in nanotechnology since then in the areas that include terabit-class nano devices, nano-structured materials technology, nanoscale mechotronics and manufacturing, NT-based core technology development, basic research for nano semiconductor instrument development.

The Republic of Korea has 5 nanotech related projects supported by US universities and European institutions.

According to Korea NT Annual 2007, KISTI, by 2007 there were 274 nanotechnology-related companies (37-large, 92 small to medium and 145 venture companies) with an investment of Korean Won 281 Billion, 2236 publications and 1769 foreign Patents.

Korean nanotech policy and assessment and funding agencies are:

- Ministry of Science and Technology (MOST)
- Ministry of Education and Human Resource (MOEH)
- Ministry of Commerce, Industry and Energy (MOCIE)
- Ministry of Information and Communication (MOIC)
- Ministry of Health and Welfare (MOHW)
- Ministry of Environment (MOE)
- Ministry of Defense (MOD
- Ministry of Agriculture (MOA)
- Office for Government, Policy Coordination (OGPC)

Excluding Japan, the Republic of Korea has been the highest funding country for the development of nanotechnology. The Republic of Korea likewise is a good mix of high government and corporate nanotech spending levels and strong technology development, with 16 percent of GDP from high-tech manufacturing and 3 percent of GDP invested in R&D

Case-study of nano health-care Company, a venture company of Gwangju Institute of Science and Technology (GIST) - Anygen CO. LTD.

About GIST:

GIST is eventh in the QS World University ranking 2012. It ranks No. 1 in Asia and No 1 in the Republic of Korea for last five consecutive years. It was founded in 1993 by the Korean Ministry of Science and Technology to meet the nation's demand for advanced research and enhanced higher education in science and engineering. In 2010, it started undergraduate courses. GIST is situated in the Gwangju Science and Technology Park in northern suburb of Gwangju, i.e. about 200 miles south of Seoul.

GIST is having research collaboration and partnership with many universities and research institutes of Australia, China, Finland, France, Germany India, Israel, Japan, Malayasia, Romania, Turkey, Ukraine, Uzbekistan and Viet Nam. Recently GIST scientists have reported polymer light emitting diodes (PLEDs) with a solution-processable graphene oxide (GO) interlayer. The GO layer with a wide band gap blocks electron transport from an emissive polymer to an ITO anode while reducing the exciton quenching between the GO and the active layer in place of poly(styrenesulfonate)-doped poly(3,4-ethylenedioxythiophene) (PEDOT:PSS).

About AnyGen Co. Ltd.:

It was established as the first bio-venture company in 2000 by professors at the Gwangju Institute of Science and Technology (GIST). The company focuses on developing new bio drugs and essential materials based on physiologically active peptides, biologically functional materials, and chemical nano materials. The company got registered in September 2005. Today AnyGen provides services to facilitate the research efforts of investigators at both academic institutions and pharmaceutical/biotechnology companies, with 50-100 employees. It has an annual turnover of US$ 5,000,001 - 10,000,000.

The company obtained two ISO certifications (ISO 2001, ISO 14001), and the company was awarded the "INNO-BIZ" award by the Korean government for its innovative products.

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Problem/Issues:

AnyGen has established itself well as manufactures of highest purity peptide available in the market (98% vs. 95% for most competitors) and specialist in difficult and long sequences for peptide synthesis. ISO certified, it is the first Korean peptide manufacturer to obtain GMP (Good Manufacturing Practice) status for its production facility. Looking at the expertise available with them through GIST scientists, and their interest in cancer therapy they were in search of more comfortable cancer therapy.

Solution:

AnyGen's passion to develop bio-new drugs and essential materials, especially new drug candidates based on physiologically active peptides, biologically functional materials, and chemical nanomaterials resulted into production and sales of nano medicine - oral anticancer drug. "Peptide-based drugs offer the advantage of low toxicity, no complications, low therapeutic costs and high-biological activity," said Dr. Jae-Il Kim, C.E.O. of AnyGen. Peptides have the inherent ability to block and/or enhance signal transfers in the human body.

Support from GIST was their great asset. GIST – according to 2012 QS GIST - is world's 7th in university ranking and in Asia 1st for 5 consecutive years. To support for successful commercialization of and application of basic research capabilities into the region specific industries in Gwangju and the Cheonnam province, in 2005 GIST Technology Institute (GIT) was founded.

Their IPR status (Table 2) is also commendable with the following patents:

- PCT/KR/2005/000209 – Korean
- 10/586,780 (Registered0 – USA
- 2006-550940 (Applied) – Japan
- 05710825,0 (Applied) – Europe

However, for their nano medicine - oral anticancer drug - that contains Paclitaxel their Intellectual PCT is as follows:

Domestic: 0791414(registered),
0766820(registered)
US: 11/847,237 (applied)

Table 2: Present patent status of AnyGen

R&D field	Domestic registered	Domestic applied	International registered	International applied	Subtotal
Compound/Nanomedicine	9	2	3	5	19
New peptide medicine	2	3	1	4	10
Peptide/Protein manufacturing technique	3	4	0	1	8
Total	**14**	**9**	**4**	**10**	**37**

Some of their other achievements are:

2008	AnyGen got occupancy agreement for Jeollanam-do Nanobio Research Center
2009	AnyGen was selected for small business technology transfer development (200 million for 1 year) and investment from KDB capital, Nexus investment, Hyundai patented technology venture investmen and, CKD venture capital firm.
2010	Selected as "the top 20 best venture company" in Korea venture investment.
	Relocated their headquarters to Jangseong-gun. Jeollanam-do.Jeonnam Nano Bio Research Centre was selected for product technology development industry of small business.
	Completed GMP factory in Jangseong-gun, Jeollanam-do.Jeonnam Nano Bio Research Centre.
2011	Received peptide APIs GMP certification for the first time in Korea and got selected for Small and Medium Business Administration Technology Innovation Development Project (700 million for 2 years)

Concluding remarks:

Nanotechnology is a multidisciplinary field, which recently has emerged as one of the most propitious field in cancer treatment. Nanotechnology is a medical boon for diagnosis, treatment and prevention of cancer disease. It supports and expands the scientific advances in genomics and proteomics and builds on our understanding of the molecular underpinnings of cancer and its treatment.

Case-study of a nano health-care company supported by SMBA - Advanced Nano Products Co. Ltd.

About SMBA:

The Small and Medium Business Administration (SMBA) founded in 1996, is a major policy player in promoting growth of SMEs and the Korean economy at large. Republic of Korea's SME policies have supported the increase in SME's R&D activity and the growth of the venture business. SMBA has developed a variety of SME promotion measures, combining financing, marketing, technology, business start-up, micro-enterprises, etc. In terms of jurisdiction, SMBA belongs to the Ministry of Knowledge Economy. However, it has its own jurisdictional authority as a semi-independent agency. Above all, those programmes designated to SMEs are under the responsibility of SMBA. The focus of SMBA's technology policies includes reinforcement of industry-academia-research institute networks, commercialisation of developed technology and establishment of digital infrastructure. The main policy initiatives decided by SMBA in 2011 are (a) raising the role of SMEs and strengthening their core capacities, (b) creating fair business environment, (c) increasing the self-sustainability of small merchants and manufacturers, and (d) creating jobs and stimulating the foundation of new business.

About ANP (Advanced Nano products Co. Ltd) :

ANP is a company that manufactures and supplies chemically processed crystalline nano materials (metal and metal oxide, ultra-fine powders, sol, paste and coating solution) as well as their chemical precursors for coating and powder processing applications.

ANP Corporation, a SME company that started in 2000, knew or rather realized that the Small and Medium Business Administration (SMBA), since its foundation in1996, has been in the driver's seat of Republic of Korea's SMEs-led innovation. SMBA has developed and implemented SME promotion systems, combining financing, marketing, technology, business start-up, micro-enterprises, etc. It received the Excellent Technology Award from Techno-Business-Incubator Association and got an Encouragement award from the venture enterprises exhibition and contest by SMBA.

Looking at the brief history of ANP Corporation, it becomes clear that the Korean government's planned financial support to new innovative field of nanotechnology has played a pivotal role in its advancement and success. ANP received support from Technological Credit Guarantee Fund, started its own R&D and completed ITO powder and sol development within a year in 1999 which is an example of further support received by SMBA.

By 2001, ANP established its R&D Centre having 950 m^2 R&D analysis labs equipped with ICP, BET, Particle size analyzer, UV-VIS Spectrophotometer, Rheometer, Zeta potential, 3D surface analyzer and thickness measurement system, cell efficiency analyzer, etc. There are 32 R&D engineers involved in the research activities related to:

- Basic research for procuring original technique of nano material
- Application research for product development and industrialization
- New process development research for cost effectiveness

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Problem/Issues:

Increased demand for specifically synthesized nano materials, especially metals and their oxides in powder, slurry or paste form for various devices was being felt in late 1990s. The demand for nano metal oxides is on rise as it has found wide variety of applications like anti-microbial activity, Li-ion batteries, as catalysts, in ceramics, etc

Solutions:

Based on their own research output ANP has successfully completed commercialization of nano size material products for manufacture of metal and metal oxide, ultra-fine powder, paste, sol and coating

solutions. They are marketing the CMP slurry for STI application as well as the hydrophobic and antibiotic coating solution.

Same year they developed ITO paste, ATO paste and TRB paste (for window-films application), that was followed by ITO sputtering target and got registered as CleanANP brand in 2003.

CMP slurry that they had developed in 2001 was developed as slurry for ILD application in 2004 and got selected as the Promising Export Small Business in 2005. The following nano-items are listed in their product list:

- Indium TIN oxide, Indium Gallium Zinc Oxide,
- ZrO_2 nano powder (5-10nm)/slurry (15 nm),
- TiO_2 Powder (5-10nm)/slurry (15 nm),
- Aluminium Zinc OxideAl_2O_3/ZnO;
- GZO (Gallium Zinc Oxide)/ ZnO Target**,**
- CeO_2 Powder (40, 80,120 nm),
- Silicon oxide, and
- Silver paste

These products are being used for

- Materials for display (ITO, IGZO, Target, ITO Tablet,ZrO_2& TiO_2)
- Materials for solar cell (ITO, Sputtering Target, ZnO & TiO_2
- Materials for semiconductor (CeO_2 Slurry)
- Materials for functional-material (TRB paste, Silver paste, ATO & ITO)
- Materials for printed electronics (T Silver paste, Silver paste (offset), Silver-jet ink)

Concluding remarks:

The achievements of this company show that apart from technical support, the financial and policy support by the Government is equally important and has resulted in faster commercialization of R&D outputs.

8.7. MALAYSIA

Government initiatives:

Realizing that the key drivers of growth are labour, knowledge and innovation**,** nanotechnology has been identified as one of the new sources of economic growth by the Government of Malaysia. The following initiatives were taken in this regard:

- Malaysian National Nanotechnology Initiative (NNIM) was officially launched in September 2006 with a budget of MYR 20 million.
- The fund injected by the Government in nanotechnology in Malaysia during 2006-2010 was US$35.26 million.
- In2010, the National Nanotechnology Directorate (NND) was officially formed under the Ministry of Science Technology and Innovation (MOSTI).

- The Academy of Sciences Malaysia (ASM) is now a focal point for nanoscience and nanotechnology. Malaysia has also set up the National Nanotechnology Technical Committee, with SIRIM Berhad as its secretariat. The country currently has 300 researchers in the field of Nanotechnology.
- Efforts have been made to identify nanotechnology experts from overseas to collaborate with Malaysian researchers.
- Malaysia is in the process of setting up its National Nanotechnology Centre (NNC) having its research focus on nanoparticles, CNT, dendrimers, aerogel, OLED, quantum dot, nano-magnetic, single electron transistor and DDS.
- Malaysian agencies in nanotechnology were formed to integrate all existing local nanotechnology activities; coordinate and plan the R&D activities; prepare a platform for commercialization and transfer of new technology to generate economic returns for the general public; develop educational resources, skilled labour, expertise and nanotechnology infrastructure; and provide facilities and nanotechnology research support services. These agencies comprise of:

    a) Institute of Micro-engineering and Nano-Electronics (IMEN),
    b) University Kebangsaan Malaysia (UKM) is focussing on MEMS, nanowire and sensors
    c) IbnuSina Institute for Fundamental Science Studies (IIS), involved in nanochemistry and nanostructures materials,
    d) University of Technology Malaysia (UTM) working in the field of nanocatalysts, CNT, nanoelectronic devices,
    e) University Malaya (UM) - (i) Combinatorial Technology and Catalysis Research Centre Catalysts (COMBICAT) (ii) Glycolipids Research Centre (GLYCOLIPIDS), (iii) Advances Materials Research Centre (AMREC), SIRIM Nanomaterials, Processes (iv) Berhad School of Physics and School of Medical Science, Organic LED, Molecular Nanobiotechnology,
    f) University Sains Malaysia (USM) with interest in CNT, Drug, Delivery System (DDS), Sensors,
    g) Institute of Advanced Technology (ITMA),
    h) University Putra Malaysia (UPM) working in the field of nanocomposites, electronics and nanomedicinE

Malaysia Nanotechnology companies are developing CNT nanocomposites, biosensors, nano-catalysts and biofertilizers. At present, the funding is conventional collateralized by tangible risk capital, particularly assets venture capital.

Case-study of silver nano material producing company in collaboration with Japan and Republic of Korea - Nano Silver Manufacturing Sdn Bhd (NSM)

About the Company:

NSM was established in June 2004. It is a high technology Company which focuses on research, development, production and marketing of nanotechnology products. NSM Research and development team consists of expertise from Malaysia, the Republic of Korea and Japan, of which five members of the team are full time research professors specializing in nanotechnology. They have successfully applied nanotechnology in the field of agro-based products, poultry, water treatment and others.

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Problem/Issues:

Even though ordinary or bulk silver is known to have superior antibacterial and antibiotic characteristics, there has been limitation on the application because of its darkening at high temperature and high cost. Whereas now-a-days nano-silver is a synonym with anti-bacterial technology, according to Samsung the silver nano technology sterilizes over 650 types of bacteria

Solutions:

Nanotechnology or rather nano sized silver, solved all these two problems at the same time and retains its anti-microbial activity. Nowadays, nano silver technology is used in coating the surface of electronics, carbons or carbon blocks, textiles, metals, woods, ceramics, glass, papers, mixing with plastics resin, using in fiber and many others. Utilizing these unique qualities of nano-silver, NSM has come up with a range of healthcare products such as dressings for burns, scald, skin donor and recipient sites, acne and cavity wounds, and female hygiene products – panty liners, sanitary towels and pants. Some of the nano-silver products of NSM are:

SilverSol™ is the colourless, tasteless, and odourless colloidal solution suspended in the distilled water. It is between 3-5 nano meters (nm) as compared to common colloidal silver which is 8nm-10micron. NSM produces more than 20 tons of nano silver a day at very low cost.

Silver sol coated carbon - Activated carbon has been widely used in water purification due to its high adsorption rates and capabilities. The inherent drawback of carbon materials, however, is that they

have excellent biocompatibility with bacteria. To address this problem, NSM has developed a safe and effective product - silver sol coated carbon having 99.9% antibacterial and antifungal activities.

NanoGreen™, a natural antibacterial agent produced from natural minerals through the use of nanotechnology. It is free from harmful chemicals, thus not jeopardizing the human body, animals as well as plants. It can be a replacement for chemical fertilizers to be sprayed on plants and crops. Moreover, NanoGreen™ is also a unique product for wastewater treatment.

ECS has enhanced antibiotic efficacy and is used for feeding the broiler chickens.

Concluding remarks:

NSM's effort in manufacturing colloidal silver along with many nano silver related agro-products is a commendable effort. This is done with the international collaboration involving scientists from Japan and the Republic of Korea. However, environmental concerns relating to nano silver should not be ignored. Recently The German branch of Friends of the Earth, Bund fürUmwelt und Naturschutz Deutschland (BUND), has criticized the use of nano silver as it has a toxic effect on different kinds of living cells and they may be a threat to soil, water and human health.

Case-study of photocatalytic coating material producing company - Arc Flash Corporation (M) Sdn Bhd

About the Company:

Arc Flash Corporation (M) Sdn Bhd., is a Malaysian owned trading company which has been appointed by a Japan based manufacturer as the sole distributor of the brand, NanoYo PHOTOCATALYST Coating, from Malaysia. The Company was established in 2004. The Company is having 15 – 30 employees and has ISO 9001:2000 Management Certification.

Problem/Issues:

Before entering into commercialization of any new field or product it is important to know whether it will be accepted in the market or not?

Solution:

Arc Flash Corporation (M) Sdn Bhd. took up the role of exploring the task of distributing, promoting and expanding the market for the NanoYo photocatalyst products and services in its allocated regions. One year later, the company reported to the manufacturer, stating that the product actually has great potentials locally in Malaysia as well as the rest of the countries in this region. Therefore, the company was offered the role of sole distributor of the brand and product in the region.

The company started marketing the product from the end of 2005 in Malaysia. Within six months, the company had managed to gain its access in three other countries in the region (Indonesia, Brunei and Cambodia). Now they are exporting to other countries also. Their total annual sales volume is now < US$ 1 Million and export percentage is 71 – 80%.

As mentioned above, they are trading photo catalyst coating under brand name, NanoYo (NanoYo is a Japanese company founded more than 18 years ago).

It is a liquid paint and contains an active ingredient, an n-type semiconductor TiO_2 (Titanium dioxide) nano particle that is responsive to light. When it is sprayed on the interior and exterior surfaces of buildings, and when it is exposed to light or even normal room temperature, it acts as self-sanitizing-bacteria and viruses, deodorizer, anti-fungal agent, anti stains and is self-cleaning.

Concluding remarks:

Trading a product that is manufactured by some other country, may not exhibit the countries progress but it does help in the economy of the country, especially when it is exporting >70%. However, little is known about the toxicity of titanium dioxide nanoparticles, In an experiment conducted by *Saber et al (2012),* using titanium dioxide nanoparticle UV-Titan L181 ($NanoTiO_2$), pure or embedded in a paint matrix showed pulmonary inflammation and DNA damage in mice instilled with sanding dust from $NanoTiO_2$ paint; however, pure $NanoTiO_2$ caused greater inflammation than $NanoTiO_2$ embedded in the paint matrix. Whereas, *Servin et al (2012)* has shown entry of Nano TiO_2 in cucumber plant roots. The impact of TiO_2 on the plant is still to be researched.

8.8. PAKISTAN

Government initiatives:

To promote nanotechnology a National Commission on Nanoscience and Technology (NCNST) was formed (*APCTT-ESCAP, 2010).*

On 1st January 2006, the Ministry of Science and Technology of Pakistan approved a project worth Rs 195.867 million for research and fabrication of scientific devices by application of nanotechnology and also to contribute to human resource development by imparting higher education in the area of nano-materials to meet the needs of this emerging sector. Many universities have upgraded their curriculum to introduce nanotechnology.

Another fund of Rs 3.2 billion was allocated for new-materials and nanotechnology in the Medium Term Development Framework (2005-2010). Obviously the multifaceted utility of nanotechnology has been well recognised by the Pakistan Government.

Moreover, Pakistan Council of Scientific and Industrial Research (PCSIR), which was established in 1953 has now a fully functional Nanotechnology Centre, mainly focusing on R&D activities related to nano-coatings, nano-materials and nano-powders and plans to undertake cooperative research with local and foreign R&D organizations and commerce-industrial outfits (*Paper by Mr. Shahzad Alam, Director General, PCSIR, Lahore, APCTT-ESCAP, 2010).*

Apart from PCSIR, Pakistan Institute of Nuclear Science and Technology (PINSTECH) and Pakistan Atomic Energy Commission (PAEC) have also been roped in for time bound R&D work.

Some of the leading institutes working in this area are:

- Pakistan Council of Scientific and Industrial Research (PCSIR);
- NINVAST, Quaid-e-Azam University, Islamabad;
- Commission on Science and Technology for Sustainable Development in the South (COMSATS);
- University of the Punjab-Solid State Physics Departure;
- University of Engineering and Technology, Nanotechnology Research Centre, Department of Physics,
- Some other universities are also coming forward (*Source: partly from APCTT-ESCAP, 2010*).

R&D efforts of Pakistan have come up with outputs that can be thought of as commercial venture, e.g. aluminum-diamond nano-composites, Al-SiC composites, Zinc Ferrite Nanoparticles (ZnFe2O4), electrolytic synthesis of thin sheet of nano-porous alumina, electro-deposited nano structured Ni-Zn and Ni-W alloys, etc. But at present they are in infancy and still conducting seminars and conferences as well as proposing recommendations for commercialization of nanotechnology. Emphasis is being given to international collaborations. Commercialization of research output from Pakistan has yet to fully reach the industries. In the demanding fields of nanotechnology like therapeutics, diagnostics and carbon nanotechnology hardly any work is being done at commercial level. At present they are mostly involved either in importing the desired material and equipment directly or through the traders. Three main traders of Pakistan are:

- **Cloud 9 –** A trading company is one of the supplier company form Lahore, which apart from nano calcium carbonate (the only nano product they deal with) also supplies caustic soda flakes 99%,caustic soda, soda ash light, caustic soda liquid, corned beef, calcium carbonate, calcium carbonate, hard calcium carbonate and plastic. This company has about 11 – 50 employees. Their main customers are - Halliburton's, Kuwait Petrochemical Company, Ashaye Chemicals Japan and they have an Annual Sales volume of US$ 2.5 – 5.0 million. They are having HACCP & ISO 9001:2000 Management Certification.
- **Maira Trade International -** A trading company from Lahore are supplier of carbon nano fibre. It is in professional exporting and importing business for nearly three decades, running as a marketing company with government's license. Apart from carbon nano fibres, their mail products include valves, fittings, pipes, sheets, stainless steel products, mild steel products, thermocouples, felts, carbon products and high temperature products. They boast of having trade relations all over the world in order to bring best products and services for customer in Pakistan. They are dealing with more than 50 countries like Germany, England, Sweden, USA, Canada, China, Dubai, Ireland, Norway, Italy, etc.
- **Global Traders -** A trading company is supplier of TiO_2 l Photocatalyst Sol coating imported from Shanghai.

Concluding remarks:

A report published on 7th May 2012 ENn (Flickr/nic221) will perhaps summarize the delay in Pakistan's entry in commercialization of nanotechnology.

[KARACHI] Nanotechnology research in Pakistan, which had shown a trend of higher publication numbers over the last decade, has suffered from the country's present financial crisis, a study said.

In 2008 the government did not extend the term of the National Commission for Nanoscience and Technology, initially set up in 2003 for three years and later extended for two more years.

The study, published online on 29 March inScientometrics, said research publications in the field had grown from seven in 2000 to an impressive 542 papers in 2011, registering a 29 per cent annual growth rate.

This is higher than the average annual growth rate of 23 per cent registered globally, said RizwanSarwar Bajwa, research associate at the Preston Institute of Nanoscience and Technology in Islamabad who, together with his colleague KhwajaYaldram, had carried out the study.

Much of the contribution came from 13 universities while only two state-owned research and development institutions in the country participated in nanoscience and nanotechnology research.

The study attributed the spurt in research and publications to heavy government spending on manpower training and procuring the latest equipment for laboratories working in the field.

"Unfortunately, the present financial crunch faced by the country could have a negative impact on the progress achieved so far," the study concluded.

"The publication shows that despite availability of funding, the research and development institutes contributed very little in the field of nanoscience and nanotechnology,"

Bajwa, lead author of the study, told *SciDev.Net*

8.9. THE PHILIPPINES

Government initiatives:

The government's awareness and initiation of efforts are visible in their intention to enter in this new field. The government bodies of Philippines that are involved in promoting nanotechnology includes: Department of Science and Technology (DOST) and Philippine Council for Advanced Science and Technology Research and Development (PCASTRD).

The DOST has identified scientists interested in nanotechnology and nano-biotechnology research. The priority area that the Government has chalked out encompasses:

- Nanomaterials and nano-composites,
- Solar energy devices,
- Nano-designed sensors and actuators,
- Nano-based delivery systems,
- Nano-composite films and membranes,
- Nano-sensors,
- Nano-porous filters, and
- Nano-based environmental remediation systems.

PCASTRD through various government agencies has funded many nanotechnology related projects viz.

- Development of nanosensors for antibiotic, based on molecularly imprinted polymer coupled with piezoelectric quartz crystal (ITDI-DOST);
- Development of gold (111) and platinum (111) single-crystal substrates for
- nanomaterials – preparation, characterization and applications (UST);
- Synthesis and characterization of carbon-based nanostructures using horizontal
- vapour phase deposition (DLSU);
- Production of recycled polycarbonate/organoclay nanocomposites (ITDI-DOST);
- Imaging of quantum-dot labelled mouse embryos using multi-dimensional spectral microscopy (UP Diliman);

Engineering Research and Development for Technology (ERDT)-funded nanotechnology-related projects are:

- Nanomaterials from indigenous sources of the semiconductor and electronics industry (UP Diliman); and
- Production of CNTs in the presence of magnetic field and other external factors by microwave-enhanced vapour deposition (DLSU)

There are some Universities and Research Centres, which are involved in various aspects of nanotechnology related research like molecular modelling, quantum dots, nano-sensors, synthesis of polymers, dendrimers, etc. Researchers in the public and private sector, faculty and graduate students are also involved in Nanotechnology R&D.

- Universities (Ateneo de Manila University, Mindanao State University-Iligan Institute of Technology, De La Salle University, University of the Philippines-Diliman, University of the Philippines Los Baños, University of Santo Tomas); and
- Government research institutes (Industrial Technology Development Institute, Metals Industry Research and Development Centre, Surfaces and Coatings Research and Development Centre).

Case-study of developing a commercially viable technology for sensor using SnO_2 Nanowire by De La Salle University (DLSU)[1]

About DLSU:

DLSU-Manila has also been recognized as one of the best universities in the world and within Asia at the start of the new millennium. The De La Salle University Science Foundation serves as DLSU's repository of research funding providing research grants to faculty and scholarship grants to students.

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Nanotechnology R&D:

The Physics Department is recognized by the Commission on Higher Education (CHED) as a Centre of Excellence. The Department is chaired by an eminent Physicist Dr. Gil Nonato G. Santos. Fabrication and characterization of Nanomaterials is one of the forefront researches of the department.

The Solid State Physics Research Laboratory of DLSU, under the leadership of Dr. Gil Nonato C. Santos has been able to establish a good research laboratory with suitable staff. This group is mainly concentrating on synthesis of various metal oxides, sulphides, nitrides etc and trying to study their applications. This group has been able to:

i. Develop C-Ag Composite for making an electrode in a battery.
ii. C-Ag Composite was grown on carbon rod using horizontal vapour phase crystal growth technique. The precursors were flame annealed prior to HVPCG for higher yield of deposited nano materials thus improving battery characteristics.
iii. To synthesize semi-conducting nanowire of SnO_2 using Wang et al's (of Georgia Institute of Technology) HVPG method. This very thin nano wire of tin oxide can be used as a biosensor, for which they have taken one patent.

[1] *This case study has been prepared on the basis of information and material collected by APCTT during a study visit.*

iv. Apart from nano wires they have also synthesized nano belts and cluster like nano-cauliflowers of SnO_2

Some of their other research activities in the field of nanotechnology are:

- Characterization of nanomaterials including different nano forms of carbon, ZnS, SnO_2, ZnO, CdO, In_2O_3, Fe_2O_3, TiO_2, GaN_3, Gold, MgB_2, Ag-C composite, Bi_2S_3, etc
- Understanding the growth behavior and characteristics of nanomaterials
- Device fabrication of photoluminescence nanomaterials for:
    - Environmental nanomaterial sensors
    - Bio nanomaterials
    - Solar nanomaterials
    - Nanocoatings

Researchers from several other departments of the De La Salle University are also actively engaged in research and development activities related to nanotechnology applications. The departments are – Biomedical Physics Department, Molecular Biology Department, Chemistry Department, and the Chemical Engineering Department.

The intellectual property policy:

De La Salle University-Manila acknowledges the necessity to provide policies to promote and encourage excellence, creativity and innovation in research and other scholarly works by identifying and protecting the rights of the University, its faculty, staff and students. These policies are intended to provide the basic framework for the treatment by the University of Intellectual Property Rights (IPR) They are stated in broad terms in order for the details of the policies to evolve from their interpretation and application in individual cases.

The DLSU Intellectual Property Office (DIPO) acts as the Technology Licensing Office (TLO) of the University established to implement the IP policies of the University. The DIPO assists researchers in the drafting of contracts, agreements, affidavits, patent applications, and other documents which are necessary to protect the intellectual property rights of the University. The office also assists in the evaluation of the commercial potential of research works, technology commercialization activities, and in the negotiation of licensing agreements, joint ventures, spin-offs, and other similar contracts referred to it by the University.

Concluding remarks:

But at present, the entire work is at the research level only, though it has a great commercial potential and possibility. DLSU has put in place a policy framework for the protection and commercialization of intellectual property.

Nanotechnology R&D at the Industrial Technology Development Institute (ITDI), Philippines[2]

About ITDI:

The Industrial Technology Development Institute or ITDI is one of the research and development institutes (RDIs) under the Department of Science and Technology. ITDI is multidisciplinary with a unique blend of scientific disciplines, enabling the Institute to carry on its role as one of the active leaders in the country's industrialization program. Its R&D programs are anchored on its vision of propelling development while addressing the national call for job creation to help alleviate the plight of the less-privileged sector of society. R&D activities are focused on seven major areas, namely: food processing, materials science, chemicals and minerals, electronics and process control, fuels and energy, microbiology and genetics, and environment. The Materials Science Division (MSD) of ITDI is engaged in R&D activities related to the development of several nanotechnology-based value added products.

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Web: http://www.itdi.dost.gov.ph

Nanotechnology applications:

ITDI has developed several nanotechnology applications through intensive R&D efforts. Some of those are briefly described below:

- **Biodegradable nanocomposite films for green packaging:** The nanocomposite films are made from cornstarch and local-nanoclay to form the biodegradable nanocomposites. These are cost-effective barrier materials, intrinsically biodegradable and suitable for food packaging applications.
- **Halloysite nanoclay-filled epoxy molding component for integrated circuit packaging:** The nanoclay fillers for epoxy molding compounds (EMCs) are made of local halloysite

[2] This case study has been prepared on the basis of information and material collected by APCTT during a study visit.

nanoclay. It has applications in the IC packaging with improved thermal properties of IC packages.

- **Recycled polycarbonate-layered silicate nanocomposites:** The polycarbonate-layered silicate nanocomposites (PLSN) have been developed from recovered post-consumer waste compact discs (CDs). They were reinforced with locally synthesized nanoclay for prototype products, i.e., plastic tiles/slabs, plastic caps for current voltage equipment and printed circuit boards (PCBs). These products find wide application in the manufacturing sector.
- **Local bioactive polymer nanofibrous scaffold for tissue engineering:** Through the application of nanotechnology, third-generation biomaterial for in-situ tissue regeneration and repair has been developed. The biodegradable nanofibrous scaffold using local carrageenan and polycaprolactone was processed by electrospinning. It is efficient, low-cost and uses local, indigenous raw materials. The scaffold is used in medical procedure/operations and needs only minimally-invasive surgery for treatment. It is a welcome development for tissue engineering.
- **Nanostructured fibrous membrane for wastewater treatment:** This product is fabricated from polymethyl/methacrylate impregnated with local nanoclay. The technology offers option for the treatment of wastewater that may contain organic contaminants.
- **Nano-inorganic mineral filled self-cleaning paint for architectural applications:** A new self-cleaning organic paint/coating suitable for exterior concrete walls and structures is currently being developed. The formulated paint, when applied on exterior concrete panels/walls forms paint films on the surface of the concrete after drying. The dry paint film modifies the surface of the concrete into becoming more hydrophilic which prevents adhesion or accumulation of airborne contaminants such as lipophilic dirts, oils, emission gases, dust particles, etc.
- **Water purification system using ceramic pot-type filter (WPS/CPF):** The CPF is specially formulated with red clay and coated with nano anti-microbial agent. It is used to purify tap water, deep well water, and raw water from ponds and springs. The CPF-filtered water samples are claimed to confirm to the Philippine National Standard (PNS) for drinking water.
- **Nano-clay – A multifunctional nanomaterial additive for nanostructured polymer-based nanocomposites:** Synthesized from bentonite ore, the nanoclay is a nano filler in polymer-based nanocomposites for different matrices such as thermoset, thermoplastic and rubber. It has applications in the automomotive industry (bumpers, interior and exterior panes, etc), construction industry (panels, boards, etc), electronics industry (electrical housing, printed circuit boards, etc), and packaging industry (packaging films, containers, etc).

Technology transfer and commercialization:

ITDI is a recognized player in technology generation through R&D, technology transfer and a reliable provider of technical services. The institute offers traing and technology transfer services under various schemes. ITDI has fostered collaborations and partnerships with academic institutions, professional organizations and industry associations at local and international levels.The networks and linkages have bolstered research collaboration, capacity building, among others, for the benefit of the researchers and the institute in general.

The Technological Services Division (TSD) of ITDI has been established to: diffuse, transfer Institute's generated technologies, promote public awareness of the Institute's technologies/new services, establish and main linkages with mass media,scientific and technology-based institutions and other organizations involved in industrial development for the promotion and transfer of technologies, enhance and maintain databases/documentation system of original ITDI research outputs and related researches from other sources for global access/information service and contribute in the planning and implementation of the Institute's programs/projects.

Technical support to industry:

The Institute provides various services or interventions to industry to help modernize the production sector and improve their productivity:

- **Research and Development (R&D):** Multidisciplinary applied research in the fields of industrial manufacturing, mineral processing, energy and environment, using local raw materials.
- **Technology Transfer and Contract Projects:** Transfer of mature technologies with techno-economic viability, from product/process development to techno-assessment to commercialization.
- **Tests and Analyses**: Recognized as the national agency for tests and analyses, ITDI plays a critical role in product standardization and testing by providing analytical and testing services to industry and government agencies for various products and materials. The government's Department of Science and Technology recently established the ADMATEL (Advanced Device and Materials Testing Laboratory), a national center for advanced materials characterization for the Semiconductor and Electronics Manufacturing Industries. This center houses new/advanced facilities which will be used for materials analysis/characterization and product development of nano-based products for the electronics and semiconductor sector and other industries. The Laboratory will benefit not only the local semiconductor industry but also attract potential investors seeking for a more conducive business environment. This would ensure shorter turn-around times especially for companies who cannot afford to put up their own FA (failure analysis) and characterization laboratories. This would be less expensive for manufacturers who need not have to send their materials and samples abroad.

Concluding remarks:

The nanotechnology R&D activities being conducted at ITDI are mostly demand-driven from the industry. This provides a good opportunity for the Institute to forge research collaboration with the industry to develop and commercialize nanotechnology-based applications. The mechanisms for intellectual property protection and technology transfer have been put in place by the Institute. The competency level of researchers involved in nanotechnology R&D at ITDI appears to be fairly good.

Case study of environment-friendly nano product company - INERGI Philippines, Inc.

About the Company:

INERGI Group, founded in 2005, was initially an energy management and engineering services company. But now it has changed its focus to an effective green solutions provider. This privately held company has 1-10 employees. Inergi has two divisions (i) Agro sciences, and (ii) Green lighting.

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Problems/Issues:

The world is facing "climate destabilization" caused by man-made emissions of greenhouse gases onto the atmosphere, and the gradual contamination of our arable land and water resources through rampant use of toxic chemicals in agriculture and industries. Food supply and safety had been a cause for concern in climate deterioration. Food safety is very much affected because of the use to chemicals at toxic levels. There is not only a need to develop effective pollution prevention and energy efficiency solutions to our environment but also to enhance the food safety and productivity.

Solutions:

Focused on delivering "positive changes" to "climate destabilization, the INERGI Group has managed to combine innovative products and services to deliver effective pollution prevention and energy efficiency solutions to our environment.

Efforts of innovative researches of *INERGI AgroScience Corporation Limited*, has brought non-toxic, environmentally friendly products to enhance food growth and quality whilst at the same time, encourage sustainable farming to reduce the damage done by the use of conventional toxic agrichemicals to the arable lands. The product that they have developed is NutraGreen™.

NutraGreen™ is a concentrated colloidal micelle solution engineered from a mixture of food safe, environmentally friendly bio-based chemicals. It is highly soluble in water and applied in recommended dilution range with water. It has no known toxicity to the environment, nor ill health to humans, animals and marine life. NutraGreen™ contains micelle structure at nano-scale size less than one nano-meter. Together with bodies of chemicals that predominantly contribute to NutraGreen™, i.e. fatty acids, organic alcohols and various forms of glucose that combine to promote plant cell metabolism so as to allow plants to grow and reproduce, maintain their structures and respond to their environment more effectively. NutraGreen™ facilitates photosynthesis which converts carbon

dioxide from the atmosphere into simple sugars – the main building blocks that form the key structural component of plants.

The other division of this company is Green Lighting Nanoflex Limited, which is producing Nanolux®. This technology of energy efficient green light was developed in Hong Kong for bringing quality illumination for the built environment. Nanoflex provides high efficient optical reflectors and reflective components that raises the system efficiency of light fixtures by 15% to 30% depending on the light source, while improve the quality of reflecting light distribution.

Concluding remarks:

Keeping agriculture and environmental concerns like reducing electrical consumption is a very befitting approach for a developing country like Philippines. Hang Seng Bank has used Nanoflex lighting system in their building and in a press release they have credited Nanoflex® technology in reducing their electricity consumption of ATM by 330,000 kWh per year, an energy saving of 33 percent.

Case study of a health care company - G-CORE Group Inc

About the Company:

G-CORE Group Inc has 70 years of experience in the field of business and industry management. It is dedicated to find solution of relieving pain. GCORE is a marketing corporation duly registered with the Securities & Exchange Commission with a License to Operate granted by the Bureau of Food and Drugs. G-CORE is the exclusive marketing partner of CAStech Research and Development Company which is responsible for the design, research, development and manufacturing of patented invention products related to health, energy conservation, alternative fuels and environmental protection.

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G-CORE Group Inc
South triangle, Quezon City - 1103
Manila, Philippines

Problems/Issues:

Since this company already had interest in natural products derived from plants, they also felt the need of a safe, side effect free all natural therapy for relieving the pain. Nanotechnology in medicine involves application of nanoparticles currently under development, as well as longer ranges research that involves the use of manufactured nano-robots to make repairs at the cellular level (sometimes referred to as nanomedicine). Moreover, since most of their products are plant based, their interests were also on a nanotechnology supported plant growth material.

Solutions:

The use of nanotechnology in medicine offers some exciting possibilities. Some techniques are only imagined, while others are at various stages of testing, or actually being used today.

Approach of G-CORE Group Inc. was to create a medicine for relieving pain utilizing the nanotechnology and natural products. The theory behind their approach was that nanoparticles can be easily taken up and body can assimilate and absorb it faster, thus speeding up the process. They also wanted an access to profitable and stable business that will answer to their financial worries. The application makes G-CORE products more effective. According to their claim, it also helps in alkalizing the more oxygen into the cellular matrix. Moreover, their products are affordable to most Filipinos.

The product they have developed consists of basic and naturally fundamental elemental process-energized by the latest most advanced science-lab techniques e.g. fluid thermodynamics, biotechnology, nanotechnology and hydrogenics.

The resultant products are first of its kind conglomeration of inventions, marvels in health food supplements, energy conservation, alternative fuels, pollution control, bio-cosmetics, physical revitalizer and pheromones, all of state-of-art quality from package to processing.

Now their main products are: instant pain reliever, nanotech energy booster, memory enhancers, immune system booster, hair re-growth natural solution, slimming product, beauty secrets in 10 minutes, smart drops, height enhancer and pheromones, etc.

In these natural products where nanotechnology was used are:

- *Beauty Secret Astringent* - that uses state-o-art nanotechnology energized water instead of alcohol.
- *Slim Pro* – produced by using nano-sized particles of minerals that due its size easily gets absorbed by the body with an ionic effect. This allows slimming process to rapidly take effect, causing body fats to burn faster to make the body slim.

As mentioned above, their interest lies in plants and plant growth and they are pioneers in marketing high quality products processed through nanotechnology. One such agro product is SeedGROWTH. As mentioned above, their interest lies in plants and plant growth and they are pioneers in marketing high quality products processed through nanotechnology. One such agro product is SeedGROWTH, the first liquid organic fertilizer/soil conditioner processed through nanotechnology.

Nutrients of SeedGROWTH are processed by tri-atomic processors to become one billion times smaller than a meter. This gives SeedGROWTH the capability to penetrate plant cells three times faster than other farm inputs. This also rapidly neutralizes soil acidity and balances soil pH level, especially when applied during land preparation.

SeedGROWTH has been found to be very good for rice, corn and other grains, vegetables, fruits, fruit-bearing-trees, flowers, orchids and many other crops.

Concluding remarks:

Climate change, urbanization, sustainable use of natural resources and environmental issues like runoff and accumulation of pesticides and fertilizers are the hot issues for today's agriculture. Efforts of G-CORE to combine the nanotechnology and natural products by Philippine's extraordinary product like SeedGROWTH is commendable.

8.10. SRI LANKA

Government initiatives:

For promoting nanotechnology, the Sri Lankan government took a unique step and created SLINTEC.

Case study of Sri Lanka Institute of Nanotechnology (SLINTEC)[3]

About SLINTEC:

The Sri Lanka government took a unique step and created SLINTEC for promoting Nanotechnology in the country with the help of 5 joint public private partnerships namely.....

1) Brandix Lanka Ltd. – 409, Galle Road, Colombo – 3, Sri Lanka
2) Dialog Telecom Plc. - DTL Cooperate building, Union Place 475, Colombo 00200, Western Province, Sri Lanka
3) Hayleys Plc. - Hayleys Group, No.400, Dean's Road, Colombo 10, Sri Lanka
4) Loadstar Ltd.- Load star Pvt. Ltd. Head office, regents Court, 218 Minuwangoda Road, Ekala, Ja Ela, Sri Lanka
5) MAS Holdings Plc –AS Holding Pvt. Ltd., No. 7th Lane, Off Borupana Road, Kandawala Street, Ratmalana, Sri Lanka…….

In 2007, to implement the National Nanotechnology Initiative (NNI) the Cabinet of ministers approved the setting up of the Sri Lanka Institute of Nanotechnology (SLINTEC) and the Nanoscience Park, with a Government commitment of Rs. 5.6 billion over a five year period and by April 2008 it was incorporated. After completion of infrastructure and installation of equipments, science projects commenced on 12thAugust 2009 and in the same year their website was also launched. Today it has a production facility called NANCO. There is a strong effort in "Concept to Commercialization", by formulating strategies and policies keeping in mind the challenges to be met. Members of the National Nanotechnology Committee (NNC) were involved in the following nanotechnology policy development objectives:

- To develop a world class environment for nanotechnology research, innovation and commercialization;

[3] *This case study has been prepared on the basis of information and material collected by APCTT during a study visit.*

- To develop human resource needed for a viable and innovative Sri Lankan nanotechnology industry;
- To promote industry oriented collaborative R&D through public private partnership to transform the generated knowledge into innovative products/services & provide a competitive edge to the local nano-industry;
- To significantly increase the Sri Lankan intellectual property in nanotechnology and establish a framework to safeguard and exploit these for economic development; and
- To establish a regulatory framework for promotion of nanotechnology to suit the needs of our society and industry while paying attention to ethical, environmental and safety aspects with regular monitoring, evaluation and public debate.

After a visit to SLINTEC in 2009, the World Bank Reported that the SLINTEC model is: "Leveraging high technology to drive innovation and competitiveness in key export industries & building the Sri Lankan knowledge economy".

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Web: http://slintec.lk

Nanotechnology R&D and commercialization:

The research focuses of SLINTEC are based on the market demands of the industries that has supported it formation. They are:

- Textile and apparel;
- Solid tyres;
- Fertilizer;
- Rubber gloves;
- Activated carbon;
- Biosensors;
- Blue sky project; and
- Nanomaterials

However, looking at the research interest and research publication, it is certain that they will enter into other domains of nanotechnology based products.

To promote research:

- SLINTEC and the Nagarjuna Fertilizers and Chemicals Limited of Nagarjuna Group India entered into a strategic collaboration of US $ one billion to develop the next generation of Nanotechnology based plant nutrition solutions. SLINTEC will carry out research and Nagarjuna will develop the product.

- With an intention to enter into market driven developments in Nanotechnology, SLINTEC has signed a deal with Japan International Cooperation Agency's (JICA). JICA will provide expertise as well as equipments.
- On 28th October 2009, SLINTEC signed an agreement for collaborative research with the Research Organization of the Science and Engineering of the Ritsumeikan University, Kyoto, Japan.

The unique and novel efforts of SLINTEC has been appreciated by all the experts and world leaders in science who visited their establishment e.g. Dr. Mashelkar from India, Hans Wijayasuriya from Sri Lanka, Hugo Van de Wiele from Luxembourg, Wim Swyzen from Netherlands and Prof. A.P. de Silva of Belfast. Even Nano-Globe has written in its column that "I am most impressed by the Sri Lanka Nanotechnology policy is its emphasis on private - public partnership (PPP) and incorporating responsible development and regulatory framework.(*http://www.nano-globe.biz*)

Due to fast track research activities, SLINTEC's has acquired five international patents in nanotechnology in its first year of operations in a drive to commercially exploit the technology. The first IPP – 4 – 2010 was files on 12th August 2009 and four more provisional patents in December 2010; two in the area of agro-chemicals (that include carbon nanotubes, nano fertiliser), one relating to solid rubber tyres and another of self-cleaning antibacterial fabrics (*Lanka Business On-line, 22.4.2011*).

Having considered the fact that many research findings arising from research and experimental development projects are confined to laboratories without progressing into commercial applications and also with a view to develop an entrepreneurial culture among researchers, scientists, engineers in the research institutes and universities, the grant scheme "Support for start-up businesses based on novel Technologies (Start Ups)" is established by the National Science Foundation of Sri Lanka. The scheme provides an opportunity for researchers/scientists/engineers to start up businesses by establishing start-up companies or spinoffs using their university/institute-based new technologies

Concluding remarks:

With the efforts of SLINTEC, other Government organizations and their collaboration with Indian company and Japanese University, Sri Lanka would very soon be introducing many industries based on nanotechnology products. With this first movement of nanotechnology, Sri Lanka believes that nanotechnology will facilitate the differentiation of Sri Lanka's commodity exports and will also shift towards a knowledge based economy. It will soon redefine Sri Lankan industry and establish them as the trailblazers of our age.

For a country which has limited funding from the government [i.e. only 50% funding from Sri Lanka National Science Foundation (NSF)] has shown its commitment in developing nanotechnology with a unique –public-private partnership and passionate scientists.

Case study on the development of nano-coated self-cleaning ceramic tiles for commercialization by Industrial Technology Institute (ITI)[4]

About ITI:

The Industrial Technology Institute (ITI), Sri Lanka is engaged in the applied research and development in the area of nanotechnology. The Materials Technology Section of ITI, initiated a project for the development of a nano-coated self-cleaning ceramic tile in collaboration with a reputed tile manufacturer in Sri Lanka. In this mutual agreement the Materials Technology Section of ITI was identified as the technology research and development group whereas the ceramic industry as the financial support and materials and infrastructure provider of research and development until the technology transfer. The initial concept and the project proposal were prepared by the Institute. The project duration was three years starting from October, 2006.

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Nanotech R&D:

ITI performed all preliminary lab trials within a period of 18 months. In addition selection of suitable material for coatings, coating trials, firing and characterization and property analysis etc. were also tried out. ITI researchers attempted to adopt a coating technique suitable to the factory since designing of a new processing unit was expensive. Yet, adapting a method to the factory requirements created some problems because of high kiln temperature at the main factory. Some other basic requirements for coating were also not available at the factory. The factory allocated another site for low temperature firing. This has led to find new raw materials to suit the low temperature kiln which took more than a year.

Pilot scale trials at the factory level were carried out for the coating technique using new raw materials as per the agreement with the industrial counterpart. The technology transfer, however, was delayed as there were new trials with new formula.

[4] *This case study has been prepared on the basis of information and material collected by APCTT during a study visit.*

Industrial experience:

The experience of ITI researchers in working with their industrial counterpart during the factory level trials includes the following:

- *Occupational problems* - Because of limited facilities and potential health hazard of nano-materials based spray coating, the factory requested for an alternative coating method other than that developed by ITI. The Institute optimized the factory's available method for coating tiles through laboratory and pilot trials.
- *Development of new formula* - A new formula was developed suitable for the coating method that was available at the factory. Additional chemicals were also used in the new method thus optimizing the formula.
- *Change of the new formula* - Due to unavailability of chemicals, the factory again requested ITI to change the formula using new chemicals. The laboratory optimization was initiated before pilot trials.
- *Change of the coating technique* - The management requested to try out another coating technique also that is available in their factory to study as there were some problems of the appearance of the tile edge. ITI researchers realized that and the process optimization was again carried out.
- *Property analysis* - After successful pilot trials, upon request of the factory management, the ITI researchers conducted studies to prove the effectiveness of self-cleaning properties of the tiles in an actual situation. However, the industry has requested for a second commercial trial at their new kiln premises before the technology transfer is made.

Concluding remarks:

ITI is currently developing guidelines for the development, protection, and commercialization of its intellectual property. The draft has been approved by the ITI Board. ITI has signed a MoU with SLINTEC to share the research facilities on payment basis. There is a need to build capacity of the nanotechnology researchers of ITI in the areas of intellectual property protection and commercialization, and collaboration with industry.

8.11. THAILAND

Government initiatives:

The National Science and Technology Development Agency (NSTDA), a cell of Ministry of Science and Technology (MOST) of Thailand realized the importance of this emerging field of nanotechnology and founded National Nanotechnology Centre (NANOTEC) in August 2003 as an autonomous body committing US$ 25 million during 2004-2008. NANOTEC's missions were to create nanotechnologies that would enrich Thai industries, give rise to niche innovative products, processes and competitiveness in the global market, they have decided to concentrate on following objectives:

- Conduct and promote R&D in nanotechnology as enabling tools to improve the competitiveness of Thai industries;
- Develop human resources in the field of nanotechnology;
- Establish R&D collaboration among academics, industry and government – bothon a national level and internationally; and
- Promote public awareness and understanding of nanotechnology.

The responsibilities allotted to NANOTEC are:

- To work as a national R&D centre;
- To fund R&D work pertaining to nanotechnology;
- To provides services in nano-scale measurement and characterization using state-of-art equipment to the academics, industry and government;
- To serves as the Secretariat of National Nanotechnology Policy Committee chaired by the Prime Minister;
- To provide direction, strategy, research plan and development of Nanotechnology; and
- To do the assessment of risk and nano-safety, and accordingly provide information on regulations, standards or procedures of nano-safety to key stakeholders. They would also collaborate with national and international organizations to ensure safety.

Their priority area of nanotechnology research are food packaging; cosmeceuticals - (nano-emulsion and nano-capsule, skin care nano-emulsion with Thai herbs service, controlled sustained release technology, textile (technical and functional, bio-component fibres for medical application, apparels and nonconventional), Flexible polymer solar cells, Health-care (therapeutics, drug delivery system and diagnostics)

NANOTEC has:

- In-house central laboratory, including 11 labs, 65 scientists and 200 other staff;
- University-based Centres of Excellence (COEs) in 8 leading universities, focused networks on textile (in 3 universities), cosmeceuticals (in 5 universities) and computational nanoscience;
- Research grants are given to universities and other agencies for > 30 projects
- Moreover, NANOTEC operates 11 laboratories in Thailand Science Park.

The output of NANOTECH in 2009:

- Published 92 articles in international journals;
- Filed 21 patents (mostly domestic);
- Signed 14 contracts with industries;
- Held 57 discussions with industries; and
- Provided services to industry/labs (~13,000 tests)

To regulate the standards of nanotechnology applications in different fields, the following bodies were made responsible:

- Thai Industrial Standards Institute (TISI)
- Thai Food and Drug Administration (Thai-FDA)
- Office of Consumer Protection Board (OCPB)
- Metrology National Institute of Metrology Thailand (NIMT)
- Testing Labs National Electronics and Computer Technology Centre
- National Metal and Materials Technology Centre
- National Synchrotron Research Centre (NSRC)
- Thailand Textile Institute (THTI)

Concluding remarks:

Good efforts have been made by the Thai government however, commercialization has not picked up the speed but some companies have entered in this arena with great success.

Case study of a company involved in nanotechnology for industrial and consumer products – Creative Technology Solutions Co.Ltd. (CTS)

About the Company:

CTS were established in 1996. The company specializes in die-cutting services assembly and business services of industrial products. In die-cutting services, they produce a wide range of components and parts for electronic equipment, automotive, audio visual products, construction, and other industrial components. Material used are plastics, felt, paper, fiber, tape, EVA, rubber, polyester film, EPDM, polyurethane form (PE & PU), PVC, copper (foil and embossed), and other materials requested by their customers.

With the vision of creative technology, in the year 2004, CTS started to study and cooperate with well-known research labs in both Republic of Korea and Thailand to come up with world-changing products using their licensed Nano Technology and in 2004, the CTS GROUP was established in Thailand and pioneered nanotechnology in various industries simultaneously.

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Problems/Issues:

2004 was the year when NANOTEC of Thailand Government decided to create nanotechnologies that would enrich Thai industries, give rise to niche innovative products, processes and competitiveness in the global market. It was the same year when CTS decided to enter into a new nanotechnology based product.

Solution:

Confirmation that nano particles of silver have anti-bacterial, anti-fungal, anti-molds, anti-viral and deodorizing (VOC reduction) properties, CST decided to produce various consumer goods utilizing the nanotechnology approach:

- Filters for the air conditioner and air purifier. They developed a nano-silica core with nano silver and coated it onto the mesh of the filter. Apart from nano silver; nano copper, nano gold and photocatalysts were also used.
- Nano Silver Masterbatches is another product that CTS offers; it is anti-microbial with a wide variety of applications across many industries.
- Nano silver solution and
- Nano-ceramic balls.

Following are the companies that are using nano-filters or other products manufactured by CTS: Toshiba / Carrier (Thailand) , Hitachi Consumer Products (Thailand), SMS Aluminium (Thailand), SaijoDenkei (Thailand), Thai Thavorn Metal (Thailand), Samsung Electronics Malaysia), LiproSdnBhd (Malaysia), JK Wire Harness SdnBhd (Malaysia), Matsushita Electronics (Malaysia), Kyoshin Sdn Bhd (Malaysia), Hill Industries Sdn Bhd (Malaysia), Gallant Electronics Sdn Bhd (Malaysia), Sanden Air Conditioning (Malaysia), Tan Chong Motor (Malaysia), Honda Auto Parts MFG (Malaysia), Gallant Electronics Sdn Bhd (Malaysia), Teck See Plastics Sdn Bhd (Malaysia), Daiei Interplas (M) Sdn Bhd (Malaysia) Creative Technology (Singapore) and PCA Technology Ltd. (Singapore).

Concluding remarks:

Whenever use of nano metal particles is discussed, the darker side of the nanotechnology comes to mind, which usually industries do not want to talk about. If we look at one of the recent research that has confirmed that fish exposed to very low concentrations of nano particles, within 48 hours after being exposed exhibited brain damage that resembles Alzheimer's disease. This remark is not only for CTS Co, but all those companies involved in nano particles that have ani-biological activity. It is imperative that leaching of nano-particles and their impact must be taken into consideration.

Case study of a company involved in manufacture of nanoparticles for industrial applications – Nano Materials Technology Co., Ltd

About the Company:

A company known as Navapatarakit Co., Ltd. has operated zinc business since 1994. Later the company jointed business with Dr. Pachernchai Chaisit, of Science faculty, Ladkrabang King Rama Five University, and researched the manufacture of zinc oxide nano particles with spray pyrolysis method. It becomes Zinc oxide (ZnO), which have nanometres molecules. The research result succeeded in 2007, and the Company then got registered under a new name Nano Materials Technology Co. Ltd. in 2008. Since then it is in manufacture and

distribution of ZnO nano particles. Nano Materials Technology Co., Ltd synthesized ZnO of micrometers molecule level also by French process method. The result of process is zinc oxide in 0.5 micrometers molecule level with high purity in premium grade for the manufacture of rubber, polymer, ceramic, plastic and animal feedstuff industries.

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Problems/Issues:

Since ancient times, ZnO was referred to as Calamine in Egypt, which is a natural mineral Smithsonite with $ZnCO_3$ as its main compound. But the mode of action of ZnO in curing the disease was not known, though its use was prevalent. Hence it always had a big market. With the global changes in the situation, it has become necessary for industries to develop products having increased efficiency. Nanotechnology has come to the rescue or one can say a better solution to such problems.

Solutions:

One of the reasons of higher efficiency of nano particles is its higher surface to volume ratio (SVR). All the chemistry happens at the surface of the molecule. Hence, the concept of SVR is enhanced when the size of the material is very small. Hence, the concept of SVR is enhanced when the size of the material is very small and higher numbers of sites are available for bonding with other molecules. Moreover, nano-size is known to alter the melting point of the substance, it has higher photocatalytic rate, altered optical and magnetic properties, etc.

Keeping these novel properties in mind, Nano Materials Technology Co., Ltd entered into developing a methodology to produce nano particles of ZnO with the help of a scientist Dr. Pachernchai Chaisit.

They developed an innovative spray pyrolysis method to produce ZnO nano particles. It was manufactured for its use against fungus, bacteria and also protection from UVA and UVB. Zinc oxide is a stable material in terms of anti-bacterial agent, which in nature is not poisonous. Instead of just killing the bacteria, the entire purpose is to prevent bacteria from happening in the first place, which lets bacteria have no opportunity to transform. As a result, ZnO has become one of the major forces for inorganic anti-bacterial agent. Synthesis of ZnO is also being done by co-precipitation, sol-gel and hydrothermal methods.

Nano Materials Technology Co., Ltd is marketing their products as:

- Transparent ZnO nano colloids for coating of clothes, for UVA-UVB protection and anti-fungal as well as anti-bacterial properties;
- ZnO white seal micro-fined powder; and

- Zn oxide NP Powder having photocatalysts properties, which decomposes organic products that cause fouling dirt, degrade and eliminate odour.

Concluding remarks:

At the end it can be said that 'Smaller is Better and Faster.' Nanotechnology is an enabling technology that allows doing new things in almost every conceivable discipline from electronics to medicine.

> ***In thinking about Nanotechnology today what's most important is understanding where it leads, what Nanotechnology will look like after we reach the assembler breakthrough.***
>
> ***K. Eric Drexler***

9. Status of IPR policies affecting nanotechnology in Asia-Pacific countries

9.1 What is IPR?

Intellectual property (IP) is a legal concept which refers to creations of the mind for which exclusive rights are recognized. Under IP law, owners of the creation or discovery are granted certain exclusive rights, such as discoveries and inventions; musical, literary, and artistic works; words, phrases, symbols and design, etc. Under IPR the owner can get copyright, trademarks, patents, industrial design rights and in some jurisdictions trade-secrets. Except for trademark, intellectual property law is needed to promote progress.

Industrial property includes patents. A patent is a IPR granted by an inventor "to exclude others from making, using, offering for sale, selling and importing the invention" for a limited time, in exchange for public disclosure of the invention when the patent is granted. Differences in the patenting systems do result in subtle economic differences, e.g. the Japanese patenting system is designed in part to promote greater intra-industry knowledge spillovers than the U.S. system. At present patent remains the most preferred form of IPR protection of nanotechnology innovations.

Is there a need for a new patent regime in Nanotechnology? This has been a consideration in many countries and has been tackled differently by different countries depending on their existing IP laws.

9.2 IPR considerations for nanotechnology in Asia-Pacific countries

Since this report revolves around the commercialization of innovative nanotechnology research, it is imperative to discuss the techno-legal aspects of nano-related innovations to aid their effective integration into businesses. There are several available definitions of nanotechnology pertaining to IP related issues one of the most accepted one is:

"*The term nanotechnology covers entities with a geometrical size of at least one functional component below 100 nanometres in one or more dimensions susceptible of making physical, chemical or biological effects available which are intrinsic to that size. It covers equipment and methods for controlled analysis, manipulation, processing, fabrication or measurement with precision below 100 nanometres."*

All the available definitions underline three characteristics of nanotechnology:

- Materials or processes for which minimum one component is of nanometre-scale.
- The control, handling and manipulating at nano scale, excludes all "accidental" nanotechnology.
- Acceptance of the fusion of nanotechnology and adjacent scientific disciplines, e.g. biotechnology.

Input of almost all the branches of science, viz. chemistry, physics, engineering, electronics, health care related biosciences and agro-science are accepted in nanotechnology and this makes formulating a IPR policy for nanotechnology all the more complex. Many believe that when it comes to patents, nanotechnology does not differ much from other technologies, hence, there is no need for a new patent regime in nanotechnology. The next few paragraphs are a peep into the IPR policies of nanotechnology developed by different countries.

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9.2.1 China

Up to 1977, Chinese dissemination of R&D results for commercialization was totally controlled by the government. Protection of IP law has been established by government legislation, administrative regulations, and decrees in the areas of trademark, copyright and patent under a comprehensive legal framework to protect both local and foreign IP. Despite this, copyright violations are common in China. The legal framework for protecting intellectual property in the PRC is built on three national laws passed by the National People's Congress: the *Patent Law*, the *Trademark Law* and the *Copyright Law*. By the beginning of eighties, the government realized the importance of Open Door Policy and started de-centralizing R&D and engineering, and universities and research institutions became more autonomic. Though in comparison to other industrialized countries, the Chinese government still substantially affects its domestic innovation system. China has realized that foreign companies would not transfer their technological knowledge to China without offering legal protection for their IP. Hence in 1980, the Chinese Patent Administration was founded and in 1985 China joined the World Trade Organisation (WTO); in 2002 China acceded to the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).

9.2.2 India

In India, the involvement of the Department of Science and Technology (DST) with nanotechnologies started in 1997/98., and in October 2001, DST launched a Nano Science and Technology Initiative (NSTI) as national funding programme. In March 2007, the Bureau of Indian Standards (BIS) established a Nanotechnologies Sectional Committee (MTD 33) comprising of DST, Department of Information Technology (DIT),different CSIR laboratories, some academic research outfits and a few private sector corporations to work with the International Organization for Standardization's Technical Committee on Nanotechnologies (ISO/TC 229).

A data of 2007 shows that Indians held 167 patents on nanotechnology, 39% of these patents are held by government institutions, 27% by industry, 22% by individuals and 6% by academic institutions, with the remainder being joint patents between government institutions and industry.

In a "National Conference on Nanotechnology and Regulatory Issues" organized by TERI in January 2009, and attended by various experts from industry, civil society and science, it was decided that "*No new law on nanotechnology is needed but amendments to relevant legislation are necessary and no new regulatory authority is needed but that an expert committee should be formed".*

Nanomaterials risk assessment in India is so far mostly limited to a few individual toxicity programmes and studies.

9.2.3 Indonesia

It has been difficult to enforce IP laws in Indonesia. The experts have given following reasons for that:

- The origins of the existing IP regime in Indonesia does not lie and has never been developed in Indonesia, but rather in Western countries that have different economic interests and cultural norms from those of Indonesia.
- The IP laws are incompatible with *Adat* (an extensive system of Indonesian norms).
- The weak legal enforcement in the field of IP law.
- The laws are not appropriate for their economic and technological development.

However, according to the report, Indonesian authorities made positive efforts in 2011 to strengthen IPR protections, and some rights holders reported good cooperation with enforcement authorities.

9.2.4 Islamic Republic of Iran

The Islamic Republic of Iran has not signed the PCT (Patent Cooperation Treaty). PCT is an international patent law treaty, which provides an integrated procedure for the filing, searching, and examination of applications for the protection of inventions and for rendering special technical services. However, in 2011, Iran has been granted almost 70 patents in the United States and Europe and 37% of all patents belonged to the nanotechnology field.

Iran Nanotechnology Initiative Council (INIC) launched a programme to overcome existing shortcomings and encourage nanotechnology researchers to protect their inventions in the country and particularly, overseas. In 2008, the patent law was reformed and the new law entitled "Patent, Industrial design, Trademarks Act" was created. According to the new law the inventor has the right to claim priority, based on a prior filing in any Paris Convention member state. But the government will have the right to grant a compulsory license under certain conditions.

9.2.5 Japan

Japan is signatory to most of the international treaties concerning IPR. Some of them are:

- Trade Related Aspects of Intellectual Property Rights 1994
- Paris Convention for the Protection of Industrial Property 1883
- Patent Cooperation Treaty 1970
- Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure 1997
- International Convention for the Protection of New Varieties of Plants 1961
- Nice Agreement of International Classification of Goods & Services for the Purposes of Registration of Marks 1991
- Trademark Law Treaty 1994
- Protocol Relating to the Madrid Agreement Concerning the International Registration of Marks 1989
- Berne Convention for the Protection of Literary and Artistic Works (Paris Act) 1971
- Universal Copyright Convention 1971
- Rome Convention for the Protection of Performers, Producers of Phonograms and Broadcasting Organizations 1961
- Geneva Convention for the Protection of Producers of Phonograms against Unauthorized Duplication of Their Phonograms 1971
- WIPO Copyright Treaty 1996
- WIPO Performance and Phonograms Treaty 1996
- Convention Establishing the World Intellectual Property Organization 1967

In Japan the term of a patent is generally 20 years from the date of application. IPR in Japan primarily consist of (1) patents (2) utility model rights (3) design rights (4) trademark rights, (5) copyrights (6) protection of trade-secrets and (7) protection from unfair competition.

9.2.6 Republic of Korea

Republic of Korea's nano industry came into existence in 1990s and by 2002 Nanotechnology Development Promotion Act was legislated and in 2002, and in 2003 Enforcement Decree of the Nanotechnology Development Promotion Act was passed. Koreans applied for 979 International

patents during 1990-2003 making them world's 5th nation. And by 2004 (according to a report of the WIPO the Korean Intellectual Property Office) it became the third largest recipient in terms of the number of patent application, i.e. next to Japan and USA. The IP system in the Republic of Korea includes patent, utility, trademark, design and copyright system. The Republic of Korea has been continually improving their patent system of 1961 by removing unreasonable elements and for complying with international patent systems and principles and harmonizing with them. Such efforts make the patent system in the Republic of Korea hold several features: (i) to enlarge patentable

subject matters; (ii) to increase effectiveness of patent examination; (iii) to strengthen patent protection such as extension of patent protection term; (iv) to control misuse of patent right; (iv) to join international agreements on patent; and (vi) to comply with international trend for patent protection.

9.2.7 Malaysia

The Patent Act of 1983 and the Patent Regulations of 1986 was revised in 1995 to speed up the processing and granting of patents in accordance with the Paris Convention and to extend the protection of patent rights. The Act was again revised in 2000 to extend coverage from 15 to 20 years to incorporate Malaysia's accession to the multilateral TRIPS Agreement to allow for parallel imports and to limit the Government's power to exploit patents only during emergencies. The Act was revised in 2003 to enhance the management of IPR. A new multilateral agreement is being negotiated with the USA by Malaysia to adopt a much harsher IP policy on offenders.

9.2.8 Pakistan

As far as Science and Technology is concerned, the global system of IPR is designed to protect the scientific discoveries, technological innovations, and traditional knowledge by Pakistan Council for Science and Technology (PCST), Ministry of Science and Technology, Government of Pakistan. It ensures financial benefits for individual inventors and R&D organizations. The IPR regime in Pakistan has been strengthened after signing the agreement on TRIPs under WTO. The Intellectual Property Organization (IPO) of Pakistan was established in 2005 and its legal position was defined through an Ordinance of the Government of Pakistan in 2007.

9.2.9 Philippines

State Policies to protect IP according to Philippine Constitution is provided in Art. XIV, Sec.3. The IP Code R.A, 8293 of the Philippines, is an act prescribing the IP code and establishing the IP office, providing for its powers and functions. Other laws protecting IPR are Protection of Layout Designs of IC, i.e. R.A 9150, Optical Media Act R.A. 9239 and Plant Varieties Act R.A. 9168. So far no specific code is given to nanotechnology. Hence it is assumed that standard S&T policies of IPR is applied to nanotechnology. The Philippines IPR includes: copyright and related rights, trademarks and service marks, geographic indications, industrial designs, patents, layout designs (topographies) of integrated

circuits, and protection of undisclosed information. Now the the Bureau of Patents, Trademarks and Technology Transfer has been replaced by the Intellectual Property Office of the Philippines (IPO) for the implementation of the Intellectual Property Code.

In a unique development in 2003, the University of Philippines formulated its own guiding principles and policies on IPR. It is bounded by the constitutional mandate to maintain the academic freedom of its faculty and of the university as a whole and the provisions of the Intellectual Property Code (Rep.

Act No. 8293, 1997) and other laws pertaining to intellectual property rights such RA 9168 etc.

9.2.10 Sri Lanka

The current IP system in Sri Lanka is governed by the IP Act No 36 of 2003 which makes provisions for a variety of IPR and their acquisition, management and enforcement. The law relating to the registration and enforcement of patents in Sri Lanka is contained in the Code of IP Act No.52 of 1979, which is modelled on the WIPO Code. In 1991, the Governments of the USA and Sri Lanka signed an agreement for effective protection and enforcement of IPT in patents, trademarks, copyrights, trade secrets, and layout designs for integrated circuits. Though Sri Lanka has amended the code of IP in 2001 to suit IT industries, no such amendment has yet been noted for nanotechnology.

Sri Lanka conducted a detailed review and orient the Sri Lankan IPR regime with a special focus on nanotechnology innovation led economic growth. The challenges faced by them were low number of international patents filed from Sri Lanka and absence of an efficient framework for IP management with sufficient controls and necessary facilitation so that Sri Lanka could benefit from nano patents.

9.2.11 Thailand

National Committee on IP Policy was established in 2009 under the Ministry of Commerce to protect IPRs, Reform & Modernize IP laws. IP Law encompasses Patent Act, Trademark Act, Optical Disc Act, Geographical Indications Act, Trade Secret Act, Copyright Act, Protection of layout design of integrated circuit act and traditional knowledge.

Following are the international treaties signed by Thailand:

- Berne Convention (Copyright) in July 1931
- WIPO Convention in December 1989
- TRIPS Agreement in January 1995
- Paris Convention in January 2008
- PCT (Patent Cooperation Treaty) in December 2009
- Madrid Protocol - to be member by 2015 under ASEAN Economic Community (AEC) Blueprint
- Hague Agreement (Industrial Design)

.*Nanotechnology is not yet included in their strategic sector*. However, Science, Intellectual Property and Energy Policy (Section 86) is formed.

9.3 Conclusion

Intellectual Property Rights (IPRs) have a vital role in the knowledge and technology transfer, and commercialization of new technologies. Introduction of new products to market needs successful knowledge, and technology transfer from universities and research laboratories to "high tech" companies, and technology utilization in these companies. The commercialization of new technologies provides a potential source of income for universities and research organizations, thus promising to reduce their dependency on public funds. In many countries, these institutions encourage their scientist employees to make and disclose inventions, which can then be patented and licensed to commercial firms, and/or to organize spin-off firms. Moreover, there is a need to look into and avoid patent thicket and a patent monitoring system specific to nanotechnology should be there for an applicant to search prior to applying for a patent. Commercial nanotechnology, however, is at a nascent stage. Patents are already shaping the rapidly evolving field of nanoscience and nanotechnology and will play a critical role in the success of the global nanotechnology revolution

There is no doubt that creativity is the most important human resource of all. Without creativity there would be no progress, and we would forever be repeating the same patterns."

– Edward de Bono

References

1. Sumio Ijima (1991), "Helical microtubules of graphitic carbon", *Nature*, Vol. 354, pp. 56 - 58
2. Foster S.S.D & Chilton P.J. (1993), "Ground Water System in Humid Tropics: An Overview", In IHP Technical Document in Hydrology No. 52: UNESCO – Paris, pp. 441 – 468
3. Benn, T. M. and P. Westerhoff (2008), "Nanoparticle silver released into water from commercially available sock fabrics", *Environmental Science and Technology*, Vol. 42(11): pp. 4133-4139
4. The United States *Environmental Protection Agency* (*USEPA),* Nanosilver - a threat to soil, water and human health?
5. Saber A.T., Håkan W. & Ulla V. (2012), "Current status of nanosafety, DET Nationale Forskningscenter for ARBEJDSMILJØ
6. Servin A.D., Castillo-Michel H., Hernandez-Viezcas J.A., Corral-Diaz B, Peralta-Videa J.R. & Gardea-Torresedey J.L. (2012), "Synchrotron Micro-XRF and Micro-XANES

Confirmation of the Uptake and Translocation of TiO_2 Nanoparticles in Cucumber (*Cucumis sativus*) Plants", *Environmental Science and Technology*, Vol. 46 (14), pp.7637- 7643