NANOTECHNOLOGIES: OVERVIEW AND ISSUES

ANDREW D. MAYNARD*

Chief Science Advisor, Project on Emerging Nanotechnologies,
Woodrow Wilson International Center for Scholars,
One Woodrow Wilson Plaza, 1300 Pennsylvania Avenue NW,
Washington DC 20004-3027, USA

Abstract: Nanotechnology – the manipulation of matter at near-atomic scales to produce new materials and products – is a reality now, and our ability to produce evermore sophisticated materials, processes, and products by engineering at the nanoscale will only increase over the coming years. Yet our understanding of the potential health, safety, and environmental impacts of these emerging technologies is rudimentary at best. Current knowledge is sufficient to indicate that some nanotechnologies will present new risks. What we still lack is information on how to assess and manage these risks. The challenges to the scientific community are significant: Which nanotechnologies present a significant hazard? What are those hazards and how do they relate to risks to health, safety, and the environment? How can risks be identified and controlled effectively? These and similar questions will require the risk research community to devise new strategies, new thinking, and new funding if answers are to be found. Above all, new partnerships will be needed to address potential risks – between researchers, agencies, stakeholders, and governments. However, by finding ways to work together effectively within a strategic framework, there is every chance that beneficial, sustainable, and safe nanotechnologies will emerge.

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1. Introduction

In 1959, the celebrated physicist and Nobel Laureate Richard Feynman challenged the scientific community to think small – not to restrict its vision,

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* To whom correspondence should be addressed.

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but to imagine what could be achieved if we were able to manipulate matter at the nanoscale (Feynman 1959). To many, this was the beginning of the dual concepts of nanoscience and nanotechnology. Now, more than 40 years later, nanotechnology is a multi-billion dollar research field that crosses many areas of research and development.

The rapid rise of nanotechnology – spurred on by an increasing ability to probe and control matter at the nanoscale – has led some to call it the next industrial revolution. Certainly, it has stimulated new research and innovative thinking throughout the scientific world. But it has also raised concerns. Within the scientific community, there are those who question the validity of this "new science" – citing centuries-old technologies based on nanostructured materials. Others have expressed concerns over the safety and societal impact of new, emerging technologies. Will these technologies lead to innovations that challenge the very basis of modern societies – such as artificially enhanced intelligence and longevity? And will the unique properties and behaviors of nanotechnology-enabled products lead to new risks to health and the environment?

In previous industrial revolutions, technologies were developed ahead of most thoughts about the possible consequences – and many would say we are still paying the price of a lack of forethought. However, the scientific and social climate within which nanotechnology is being developed is very different. High-profile technologies such as nuclear power and genetically modified organisms have demonstrated the need to balance risks versus benefits on a grand scale, if long-term rewards are to be reaped. But they have also highlighted the role of responsible science in society, and the power of social acceptance to change the course of a technology's development: Science and technology are now developed at the pleasure of those who will use them, benefit from them, and potentially suffer by them.

Just as the impact of nanotechnology has been surrounded by considerable hype, the potential risks have also been overemphasized at times. The idea of a "grey goo" – out-of-control self-replicating nano-bots overtaking the world – still captures the imagination of some. This is little more than fantasy at the moment. Yet, nanotechnology does raise the possibility of risks to health and the environment that do not occur with more conventional technologies. Fundamentally, nanotechnology is about developing products that behave differently through controlling their makeup at the nanoscale. These same properties will challenge the way we understand and address potential risk in some cases. We may not be facing a grey goo challenge in the foreseeable future, but managing the risk of products where nanostructure and chemistry conspire to create new properties is presenting sufficient challenges of its own.

Current research into the risks presented by engineered nanomaterials is rather limited. It is sufficient to alert us to the fact that some engineered nanomaterials do indeed behave differently to their more conventional counterparts, and may present new and unusual risks. But we do not yet have the knowledge to understand fully the nature of these risks, and how to manage them.

This would perhaps not be of great concern if nanotechnology were a technology of the distant future. However, it is happening now, and answers on how to assess and manage risk are needed urgently. Lux Research estimates that US$32 billion worth of nano-enabled products were sold in 2005, and this will rise to US$180 billion by 2008 (Lux Research 2006). In the consumer marketplace, nearly 400 products are currently being sold that purportedly use nanotechnology – everything from computer chips to cosmetics to food supplements (PEN 2006). The reality is that people and the environment are being exposed to nano-enabled products on a daily basis, and information is urgently needed on how safe these products are.

A recent report by Lux Research stressed the importance of industry taking action on the environmental, health, and safety risks of nanotechnology, if these technologies are to succeed. The report concludes that, while there is ambiguity over the real risks presented by nanomaterials, "the hard data is simply too worrying for companies to gamble that nanomaterials won't cause harm" (Lux Research 2006). They also highlight the importance of perceived risk in determining the success or failure of products, and stress the need for companies to openly communicate what they are doing to ensure the safety of nanoproducts.

It is against this backdrop that the risk research community is struggling to understand what the key challenges are, who should be addressing them and how. In the remainder of this paper, I explore what nanotechnology is from the perspective of risk research, what the key risk challenges are, and how we might respond to them.

2. Nanotechnology – An Overview

Despite current interest in nanotechnology, there is no one definition of the field that has been universally accepted. Richard Feynman did not use the term specifically, but referred to "manipulating and controlling things at a small scale" (Feynman 1959). In his book *Engines of Creation: The Coming Era of Nanotechnology*, Eric Drexler explores the idea of manipulating matter at the nanoscale to build new materials and products atom by atom – molecular manufacturing (Drexler 1986).

This idea of having control over matter at the nanoscale is reflected in more recent definitions. The US National Nanotechnology Initiative (NNI) defines nanotechnology as "the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications" (NSET 2004). In 2004, a UK government report commissioned from the Royal Society and Royal Academy of Engineering (2004) separately defined nanoscience and nanotechnology:

Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale.

Nanotechnologies is the design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanometer scale.

Within these concepts and definitions, common ground emerges: an ability to control matter at the nanoscale, to visualize nanometer-scale structures, and the practical application of unique properties arising from these abilities and structures.

Within such boundaries, nanotechnology is more of a concept or philosophy than a discrete field of study: it is an idea that crosses traditional scientific boundaries, and is finding a home in research areas as diverse as solid state physics and medical diagnostics, and applications ranging from microprocessors to dietary supplements. A recent survey of nano-enabled consumer products identified early adoption of the technology in electronics goods, sports equipment, clothing, cosmetics, over-the-counter drugs, and food supplements (PEN 2006). Close to market applications are high-performance batteries, inexpensive, flexible solar cells, highly sensitive compact sensors, and water treatment/remediation technologies. More sophisticated applications including nano-engineered medical treatments, high-efficiency energy storage and transmission, faster and more powerful computers, and high-performance prosthetics are anticipated in the near future. This is not a technology that lends itself easily to sharply delineated categories, but rather represents a merging of ideas and abilities across many different areas.

The Royal Society and Royal Academy of Engineering understood this when they coined the term “nanotechnologies” – representing the enormous diversity of possible technologies based on manipulating matter at the nanoscale (The Royal Society and The Royal Academy of Engineering 2004).

With an increasing ability to manipulate matter at the nanoscale comes the opportunity to utilize material properties and behavior that are specific to engineered nanostructures. Some of the most dramatic changes in going from the macroscale to the nanoscale occur in metals and metal oxides. Gold, for instance, loses its “gold” color when separated into nanometer-diameter particles, and becomes red. Although the chemistry was not understood at the time, colloidal gold nanoparticles were used to color medieval stained-glass windows red. Titanium dioxide and zinc oxide on the other hand shift from being opaque to visible light at the macroscale, to being transparent at the nanoscale. Semiconductors such as cadmium selenide exhibit a property known as quantum confinement at the nanoscale – where the Bohr radius of an electron-hole pair exceeds the diameter of the particle. This leads to some very interesting behavior, in which particles fluoresce with a wavelength that is determined by their physical size, rather than their chemistry.

Other materials show unusual behavior that is only accessible by engineering at the nanoscale. Single-walled carbon nanotubes, for instance, are in essence a single sheet of graphite wrapped into a tube around 1.5 nm in diameter, but up to hundreds of nanometers long. Yet the properties of the nanotubes – whether they are highly conducting or semiconductors for instance – may depend on the precise offset of the graphite sheet as it is wrapped into a tube (chirality).

These are just a few examples of first-generation nanomaterials. As our ability to manipulate matter at the nanoscale becomes increasingly sophisticated, more complex structures, materials, and devices are anticipated (Roco 2004). For instance, artificial "transport molecules" – or nano-cars – have been made by attaching C60 molecules (the wheels) to rodlike molecules (Shirai et al. 2005). The resulting devices show directional motion across surfaces, and may form a basis for constructing inorganic systems to transport molecules in a manner analogous to biological systems. Indeed, the more advanced generations of nanotechnology are anticipated to lead to ways of mimicking biological systems and functions.

These may seem trivial examples, but nanotechnology is all about discovering something that is different, and using it to develop a competitive edge. So gold nano-shells are used as the basis for targeted cancer treatments; TiO_2 nanoparticles are used widely in sunscreens that are transparent to visible light but opaque to UV; CdSe "quantum dots" are developed into medical diagnostics and treatments, and various photoelectronic applications; and single-walled carbon nanotubes are considered in applications as diverse as electronic displays to high-strength composite materials to hydrogen storage. In each case, it is the unique material behavior that comes from engineering at the nanoscale that is being exploited.

3. Identifying Nano-Specific Risks

By its very nature, nanotechnology challenges how we understand and manage risk to human health and the environment. Commercial nano-enabled products rely on what is different and unique about engineered nanomaterials, raising the question: Are there also different and unique risks associated with these same properties? This is a valid question, but is insufficiently bounded to lead to specific solutions. For instance, it makes little sense to compare the risk to health of an electron microscope (a nanotechnology-based tool) with the risk to health from free single-walled carbon nanotubes (a nanotechnology material); or the environmental impact of nano-electronics printing equipment (a nanotechnology-based process) with unbound TiO_2 nanoparticles. Clearly, different nanotechnologies will entail different risks.

If the potential risks of nanotechnologies are to be addressed systematically, we need to understand what is unique about these risks, where conventional understanding and approaches might fail, and how to discern between technologies presenting a greater or lesser potential risk.

Nano-specific risks will depend on individual technologies, and how they are implemented. There is one common element – and that is the role of structure, as well as chemistry – in determining the behavior of many nanomaterials. This immediately places evaluations of engineered nanomaterials outside the realms of conventional chemical-based regulations and oversight. To address the potential impact of an engineered nanomaterial, we must understand how its structure will determine behavior within the environment or the body, as well as its chemistry. This brings with it additional challenges: while chemistry might remain the same through the life of a product, structure may change, and this in turn may alter the potential of a nanomaterial to cause harm. For instance, airborne nanoparticles agglomerate into larger particles with complex structures; discrete nanoparticles may be encapsulated into a composite material; machining and grinding nanomaterials might lead to the release of respirable particles with unusual nanostructures; the degradation of nanoproducts at the end of their life may lead to previously encapsulated nanostructured materials being released into the environment. At each stage, changes in material structure may enhance, or even suppress, the potential to cause harm.

If the structure of nanomaterials plays a role in determining impact, and yet conventional approaches to addressing risk rely on chemistry alone, the possibility of misassessing risk arises. For instance, the Manufacturers Safety Data Sheets for some carbon nanotubes have listed the material as synthetic graphite, and referenced safety precautions for use with materials having this chemistry. Yet, the desirable properties of carbon nanotubes are far removed from graphite, and it is likely that the health impact will be also. Likewise, there has been a tendency to assess the potential risks associated with TiO_2 on a chemical basis alone, even though some TiO_2 nanoparticles exhibit a distinctly different physicochemical behavior to larger particles (Oberdörster et al. 1994).

Structure can also affect exposure and dose in very fundamental ways. A given nanoparticle may not have a greater intrinsic hazard potential than a larger particle, but if it is more able to enter the body or be dispersed in the environment, it may have a greater real hazard potential. For instance, diameter affects where airborne particles deposit in the lungs if inhaled (Maynard 2006), and there is evidence that the small size of nanoparticles enables them to penetrate cells, migrate along olfactory nerves (Elder et al. 2006), and cross from the lungs to the blood and subsequently to other organs (Kreyling et al. 2002). There are also indications that some nanoparticles might be able to penetrate to the dermis if applied to the skin (Tinkle et al. 2003; Ryman-Rasmussen et al. 2006), although this seems to depend on particle type and size, and the carrier medium.

The physical shape and structure of nanostructured materials might also be responsible for specific impacts. Asbestos is known to cause disease because of its structure as well as its chemistry: although the analogy is applied to engineered nanomaterials with caution, it is likely that some materials will show a similar dependency. Studies on carbon nanotubes in the lungs have already demonstrated unusual responses that appear to be associated with material structure (Shvedova et al. 2003, 2005; Lam et al. 2004; Warheit et al. 2004). There is also evidence that nanometer-scale particles can lead to oxidative stress by virtue of their size, as well as their chemistry (Brown et al. 2001).

The challenge we face is how to discern between nanotechnologies and nano-enabled products that present a significant risk to the environment and human health, and those that present a lesser risk. Here, it is useful to start from the classical risk assessment framework – describing risk in terms of both exposure and hazard. To present a significant risk, a nanotechnology must lead to a material with the potential to cause harm, and a route for significant exposure to occur in a form where the *hazard potential will be realized*. This qualifier is necessary to distinguish between different contexts that might apply to a nanomaterial throughout its life. For example, consider a hypothetical use of single-walled carbon nanotubes in an epoxy-based composite material. Assume that exposure potential is high during handling the unprocessed carbon nanotube material, and finishing components made from the nano-composite by grinding. Both processes may lead to nanotubes being inhaled, but the full hazard potential of the material is more likely to be realized when inhaling agglomerates of unprocessed nanotubes, rather than respirable particles of resin-encapsulated nanotubes.

Maynard and Kuempel (2005) address the question of identifying nano-materials which may present a unique risk to human health through the following criteria:

1. The material must be able to interact with the body in such a way that its nanostructure is biologically available.
2. The material should have the potential to elicit a biological response that is associated with its nanostructure.

These provide a useful working framework for distinguishing between materials and products that are more or less likely to present a health risk, as well as separating materials that present a unique risk from those that behave in a conventional way. Although Maynard and Kuempel were considering human exposure, the criteria also work well when considering environmental impact.

When linked to human exposure via the skin, respiratory system and gastrointestinal system, categories of materials and sources begin to emerge that may present a greater risk under some circumstances. These include unbound nanometer-diameter particles (in powders, aerosols, and liquid suspensions); inhalable agglomerates and aggregates of nanometer-diameter particles – where nanoscale structure-based functionality is retained; aerosolized liquid suspensions of nanomaterials; and the attrition of nanomaterial composites through various mechanisms (Maynard 2006).

The same categories of nanomaterials will be relevant when considering potential environmental impact. In addition, the release of what might be called active nanomaterials – for want of a better phrase – into the environment over a product’s lifetime must be considered. These will include nanomaterials that result from the transformation of nano-enabled products through wear and tear, as well as chemical and biological actions.

4. Responding to the Challenge

Managing the risks presented by some emerging nanotechnologies will require new ways of addressing risk. These will ultimately need to be based on new knowledge – “safe” nanotechnologies will first and foremost be built on sound science. The challenge to the science community – including policy-makers and research managers, as well as the researchers themselves – is how to develop an understanding of the potential health, safety, and environmental risks presented by emerging nanotechnologies in parallel with the technologies’ development and implementation.

This is not an easy challenge. It will require collaborations and partnerships that cross traditionally rigid boundaries. It will depend on realistic funding levels for risk-based research. And it will need a strategic steer to ensure that right research is pursued at the appropriate time.

The challenge is real, and it is urgent. Nano-based products are a reality now, as demonstrated by nearly 400 products identified by a public web-based inventory published by the Project on Emerging Nanotechnologies (PEN 2006). Many researchers and nanotechnology industry workers are already producing and handling engineered nanomaterials on a day-by-day basis, with little information on assessing and managing risk (Maynard and Kuempel 2005). These products and materials are being released into the environment (intentionally or unintentionally) with little understanding, at least in some cases, about what the long-term impacts might be. Even if the term "nanotechnology" goes out of vogue, our increasing ability to manipulate matter at the nanoscale will lead to ever more sophisticated technologies over the coming decades, that demonstrate new and unusual behaviors.

So how do we respond to the challenge? First and foremost, strategic, prioritized research is needed to address immediate issues – including the safe use of nanomaterials under development and already in commercial use. Research is also needed to build capacity and understanding that will enable future challenges to be met, including an ability to predict the impact of emerging nanotechnologies. Finally, global coordination, cooperation and partnering between researchers, producers and users will be essential if relevant solutions are to be developed and adopted around the world.

In recent years, a number of groups have published lists of the research needed to address potential risks of engineered nanomaterials. These include government agencies, independent reviews, industry groups, user groups and academics (The Royal Society and The Royal Academy of Engineering 2004; Chemical Industry Vision 2020 technology Partnership and SRC 2005; Dennison 2005; EC 2005; EPA 2005; HM Government 2005; Maynard and Kuempel 2005; NIOSH 2005; Oberdörster et al. 2005). A review of research recommendations in nine such publications by Maynard showed considerable consensus over what still needs to be done (Maynard 2006). Thirteen overarching categories of research needed to better understand and manage potential risks associated with nanotechnology were identified:

- **Human health hazard:** how nanomaterials get into and behave within the body, and how toxicity can be tested for and predicted.
- **Health outcomes:** disease resulting from exposure to engineered nanomaterials within the workforce, the general population, and sensitive groups such as children and the elderly.
- **Environment:** how engineered nanomaterials enter the environment, where they go and how they behave once there, the impact they have, and how they might be controlled.
- **Exposure:** sources of engineered nanomaterials exposure, exposure measurement, and how changes in nanomaterials with time might affect exposure.
- **Characterization:** significant characteristics of engineered nanomaterials, such as size, shape, surface area and surface chemistry, to be measured when evaluating risk.

- **Control:** identifying where engineered nanomaterials might potentially escape into the environment or workplace and ways of preventing such escapes, and research into the efficacy of personal protective equipment (including respirators).
- **Risk reduction:** new ways of assessing risk, and new ways of working safely with engineered nanomaterials.
- **Standards:** the development of appropriate nanotechnology standards – and in particular, standards that develop an appropriate language for describing nanomaterials, standards for measuring exposure and standard materials for toxicity evaluation.
- **Safety:** the potential for engineered nanomaterials and nano-products to cause physical harm, such as through explosion and fire hazards.
- **Informatics:** how to collect, sort, and use the vast and diverse amount of data being generated on engineered nanomaterials that is relevant to understanding risk.
- **Research approaches:** how to plan and carry out risk-based research effectively.
- **Transportation:** containment requirements, labeling, the potential for release, and the exposure hazard for different types of engineered nanomaterials, as they are moved from one place to another – in raw, intermediate, or highly processed forms.
- **Emergency responders:** how to respond effectively and safely – and in particular how procedures and protocols may differ from incidents involving conventional materials – to spills and other accidental releases of engineered nanomaterials.

These categories are useful for pointing to where progress needs to be made in support of safe nanotechnologies. But outside the context of a strategic research framework, they offer little guidance on what needs to be done when.

Strategic research requires prioritization, which is never easy, and always contentious. However, the danger of not prioritizing is that limited resources are spread too thin, irrelevant research is pursued at the expense of necessary research, and answers to specific questions on risk are not forthcoming. One possible framework within which risk-focused research can be prioritized is to consider criteria for immediate, medium-term, and long-term needs:

- ***Immediate needs*** – ensuring that current nanotechnologies are as safe as possible, appropriate workplace practices for handling engineered nanomaterials exist, and appropriate ways of using and disposing of nano-based products are understood.

- ***Medium-term needs*** – establishing associations between nanomaterial exposure and disease or environmental impact, and developing an understanding how to minimize impact. This research would include human health outcomes, ecotoxicity, toxicity screening, risk management systems, control methods, lifecycle assessment, and exposure methods.
- ***Long-term needs*** – developing ways of predicting and preemptively managing the potential risk of emerging nanotechnologies, including mechanistic toxicology; predictive risk assessment and management of later generation nanotechnologies; and emergent behavior and convergence between different technologies.

These criteria were used in (Maynard 2006) to identify critical research priorities for the next 2 years. Identified short-term goals fell into five categories:

- **Risk assessment:** this includes research methodologies, risk assessment tools, and information management.
- **Environmental impact:** high-priority research goals include identifying routes of release and exposure, and measurement methods.
- **Human health impact:** high-priority research goals include exposure measurement methods, controlling release of material and preventing exposure, and developing toxicity screening tests.
- **Predicting hazard:** the ability to predict the hazard of a new engineered nanomaterial, and even to reduce its toxicity through careful engineering, is a long-term goal than needs an initial research investment now.
- **Materials characterization:** an ability to characterize nanomaterials appropriately when evaluating potential risk will require investment in basic research now.

These goals recognize that medium- and long-term research needs will only be successfully addressed if necessary capacity is developed in the short-term. This includes developing a solid science foundation on which to build new knowledge, and developing an expertise and facilities base that is capable of offering new knowledge. Investment needed now in medium- to long-term research areas includes addressing environmental impacts, developing a systematic approach to understanding and managing risks from nanotechnologies, and developing the capabilities to better predict risks posed by new nanomaterials. In addition, the global research community needs to be energized and challenged to tackle the potential dangers of some nanotechnologies – and to this end, Maynard et al. have issued five grand challenges to developing "safe nanotechnologies" (Maynard et al. 2006).

Effective partnerships will be essential if these goals are to be achieved. At a fundamental level, the complexity of nanotechnologies demands interdisciplinary collaboration, if risks are to be assessed and managed effectively. Oberdörster et al. (2005) have emphasized the need for toxicologists to work with physicists, chemists, and engineers in characterizing engineered nanomaterials. Similar cross-disciplinary collaborations will be needed when addressing other aspects of risk.

At a higher level, organizations overseeing risk-focused research will need to cooperate and coordinate if holistic research strategies are to be developed, that respond to oversight needs. Just as risk-based research cannot be compartmentalized for nanotechnologies, management of research and oversight will be ineffective if there is no overarching plan for integrating areas such as human health and environmental impact. This degree of coordination is essential within government. Yet, it must also extend out into the private sector, and to organizations representing the interests of end users and the environment. By ensuring tripartite oversight of nanotechnology risk-focused research, there is a greater chance of ensuring that research is relevant and responsive to real needs.

Finally, global partnerships will be essential to the long-term success of emerging nanotechnologies – whether these are between individual researchers, industries, or governments. Nanotechnology presents global challenges to addressing risk, and information will need to be shared openly if global solutions are to be found. Certainly, an ability to develop safe nanotechnologies in one country should not be used to develop a competitive edge. Conversely, we need to avoid a situation where a lack of concern over risk in some sectors provides an (albeit short-term) economic advantage. In this sense, a global nanoeconomy will benefit from a global-level playing field when it comes to understanding and managing risks.

Developing such global solutions will require globally coordinated research. Resources for risk-focused research are always likely to be limited. However, by ensuring that international research programs are complementary rather than duplicative, these limited resources can be leveraged to maximum effect. This in turn will require combined efforts from regions around the world to develop partnerships and act in concert.

5. Summary

Nanotechnology is a reality now, and our ability to produce ever-more sophisticated materials, processes, and products by engineering at the nanoscale will only increase over the coming years. Yet our understanding of the potential health, safety, and environmental impacts of these emerging technologies is rudimentary at best. While it is by no means certain that emerging nanotechnologies will present a significant risk, we can be sure that inaction in addressing risk will pave the way to public distrust and the potential for serious harm to occur.

Current knowledge is sufficient to indicate that some nanotechnologies will present new risks. What we still lack is information on how to assess and manage potential risks. The challenges to the scientific community are significant: Which nanotechnologies present a significant hazard? What are those hazards and how do they relate to risks to health, safety, and the environment? How can risks be identified and controlled effectively? These and similar questions will require new strategies, new thinking, and new funding within organizations and groups addressing the risks of emerging nanotechnologies.

Above all, new partnerships will be needed to address potential risks – between researchers, agencies, stakeholders, and governments. By finding ways to work together effectively within a strategic framework, there is every chance that beneficial, sustainable, and safe nanotechnologies will emerge.

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