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Spotlight

Nanotechnology

The influence, risks and opportunities of a rising technology

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Abstract

This *Spotlight* examines the social and ethical implications of nanotechnology in Ireland. The use of nanotechnology is continuing to grow through the development of new products, this is shaping the development of our economy, society and how we interact with the environment. This paper provides an overview of sectors, such as manufacturing, medicine and agri-food, where the use of nanotechnology and nanomaterials are likely to have a significant impact and considers the challenges associated with the technology and its materials.

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The influence, risks and opportunities of a rising technology

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Glossary

0D, 1D, 2D Materials – classes of nanomaterials categorised by the primary dimension of their shape, such as 0D spherical, 1D cylinders and tubes, 2D surfaces and planes.

Additive manufacturing – a description of technologies that build 3D objects by adding layer-upon-layers of material. Such materials include plastic, metal, concrete or biological materials. Additive manufacturing contains a wide set of technologies including 3D printing, rapid prototyping, direct digital manufacturing, layered manufacturing and additive fabrication.

Carbon nanotubes – tubes made of carbon with diameters typically measured in nanometres.

Circular Economy – an economic system with the goal of eliminating waste and reducing dependence on new resources. Circular systems employ reuse, repair, recycling and linked value chains in manufacturing to create a closed-loop system.

European Green Deal – a set of policies by the European Commission with the aim of making Europe climate neutral in 2050.

Internet of things – describes a network of physical objects and devices, embedded with sensors, software, and other technologies that can connect and exchange data with other devices and systems over the Internet.

Lateral flow tests – are simple devices to detect the presence of a particular substance in a liquid sample without the need for specialized and costly equipment, for example pregnancy tests.

MRI – magnetic resonance imaging is a medical imaging technique that uses strong magnetic fields to produce images of features with the body.

mRNA –messenger ribonucleic acid is a single-stranded molecule of RNA, (DNA is a double strand). It is the encoded genetic sequence of a gene used to produce proteins.

Nano – the prefix for one billionth. From the Greek root – *dwarf*. It is broadly used to describe objects and effects whose properties are influenced by properties at the nanoscale.

Nanoform – a form of a natural or manufactured substance containing nanoparticles as described by the European Commission recommended statistical definition of a nanomaterial.

Nanomaterial – material with any external dimension in the nanoscale or having an internal structure or surface structure in the nanoscale.

Nanomedicine – the application of nanotechnology in medicine and healthcare with a view to making a medical diagnosis or treating or preventing diseases. It exploits the improved and often novel physical, chemical and biological properties of materials at nanometre scale.

Nanometre – a length scale of one billionth of a metre, $1nm = 1 \times 10^{-9}$ m.

Nanoscale – lengths between 0.1 – 100 nanometres.

nm – nanometre.

OECD – Organisation for Economic Co-operation and Development.

PET – positron emission tomography is an imaging technique that uses radioactive materials known as radiotracers to visualize and measure processes within the body.

REACH – Registration, Evaluation, Authorisation and Restriction of Chemicals - EU regulation that addresses the production and use of chemical substances, and their potential impacts on both human health and the environment.

Semiconductor – material with an electrical conductivity value falling between that of a metal and an insulator, the primary material used to produce computer chips.

Smart nanomaterials – advanced nanomaterials that actively respond to external stimuli such as physical, mechanical or chemical.

Introduction

Nanotechnology is an enabling technology that already lies at the heart of many of the technologies taken for granted today. Ireland has economically benefited from the use of nanotechnology in information and communication technologies, and there is potential for strong growth in areas including medicine and agri-food. However, for future leadership in these sectors, there is a need to adapt the development of nanotechnology to reflect the pressing demands of environmental sustainability. Sustainable practices could be promoted by publicly funded research considering the lifecycle of materials, and further secured by active engagement to produce effective regulation of nanomaterials, with long-term goals for critical issues such as health and waste.

Nanotechnology - an Overview

Over the past twenty years, nanotechnology has quietly gone from a subject of largely academic interest, to a hidden standard expected in everyday products. There is no single "nanotechnology industry" however, but rather a shared collection of materials and practices that add value across a wide range of existing industries. Nanotechnology thrives at the interface between traditionally different disciplines. As such it can be difficult to appreciate the broad scope of where nanotechnology is used, and where it can be applied.

Nanotechnology seeks to control and use materials at the smallest achievable scale, and this approach has revolutionised the way we live in unnoticed ways. It is at the core of products upon which we have become deeply dependent, for example, it is the materials and engineering at the heart of modern computing and communications. The rollout, from laboratory to commercial products, has been led by certain industries, such as computer chip manufacturing and chemical industries. Rapid development in the field over the past last two decades has included the discovery of new classes of materials suitable for nanotechnology that can be exploited for a range of applications.[1].Today the specialist tools and materials developed for nanotechnology are being applied to more areas like construction materials, medicine and agriculture.

It is useful to consider nanotechnology as an enabler of technology. This means that nanotechnology is generally only part of a product, but a part which provides that product with crucial functionality for a specific application or purpose that would not be otherwise possible. As a result, it is not unusual to have very different products for very different purposes using the same or similar nanotechnology and materials. While scientific research has been at the forefront of progress, the scope of possible nanotechnology applications is still largely unexplored. Nanotechnology is broadly stimulating innovation and evolving applications are being explored in academic and commercial research and development (R&D).

The growth in nanotechnology has been greatly helped by the recognition of its importance to industry by funding bodies that support research and innovation. Industry within the European Union (EU) provides one in five jobs and generates 80% of its exports, so innovation is essential to remain competitive.[2] It was recognised 20 years ago that knowledge and capacity in nanoscience, the field of science underpinning nanotechnology, was a limiting factor to the development of nanotechnology in Europe.[3] Since then innovation in nanotechnology and nanoscience have been promoted through development programmes, like the EU's Horizon 2020 Framework Programme for Research and Innovation, which ran from 2014–20.[4] Nanotechnology was recognised as a key enabling technology in Horizon 2020, and acknowledgement of its importance has continued to grow, to the extent where it was recently named as a technology to help fight the coronavirus pandemic, in a publication by the European Parliamentary Research Service (EPRS).[5] The global nanotechnology market is expected to exceed USD$125 billion by 2024.[6] In addition, industries that rely on nanotechnology are expected to be developed further. In a European Commission joint declaration, it was recommended that 20% of the European Recovery and Resilience plans should go to the digital transition, which is up to €145 billion over the next two to three years.[7]

European and national investment have helped fuel the growth of Ireland's nanotechnology capabilities. Between 2001 and 2009, Ireland spent approximately €282 million on nanotechnology across the commercialisation value chain.[8] In 2010, Ireland was ranked in the top 10 globally in materials science, of which nanoscience was a strong component.[9] This was in part enabled through initiatives such as the establishment of Centre for Research in Adaptative Nanostructures and Nanodevices (CRANN) in Trinity College Dublin[10], which Ireland's first purpose-built research institute for nanoscience research. Ireland has won over €1 billion in funds from the Horizon 2020 programme.[11] Tyndall, which is national institute for photonics and micro/nanoelectronics, has participated in 56 Horizon 2020 projects since 2014 with total value of €370m, including significant co-funding by industry partners.[12]

This year sees the launch of the EU's latest innovation programme, 'Horizon Europe', with a budget of more than €95 billion.[13] It has five missions related to cancer, carbon-neutral cities, climate change, oceans and waters, and soil health. The previous programmes, such as Horizon 2020, were concerned with building basic capacity. Now focus has broadened and in this latest programme nanotechnology is no longer visible as an innovation theme, but it is a key aspect of the technologies needed to turn the ideas of the 'Global Challenges and European Industrial Competitiveness' pillar into reality. Other initiatives such as the digitisation of industry, following the European Digital Single Market policy, are only possible with reliable nanotechnology enabled computer infrastructure.[14]

Successes in the development of nanotechnology should not be mistaken for a complete or fully mature technology. The developed infrastructural and knowledge capacities need to be supported and maintained if nanotechnology is to continue enabling innovation. Nanotechnology is a young and expanding technology and rapid innovation can be difficult to manage and regulate. A review of the regulatory landscape of nanotechnology, produced from the 2019 Global Summit on Regulatory Sciences, stated:

> *"Nanotechnology and more particularly nanotechnology-based products and materials have provided a huge potential for novel solutions to many of the current challenges society is facing. However, nanotechnology is also an area of product innovation that is sometimes developing faster than regulatory frameworks."*[15]

If the regulatory frameworks fail to keep pace with scientific developments it could slow commercialisation, weakening our ability to compete, and if neglected it could lead to long-term health or environmental hazards. Regulation becomes an issue of greater importance as the use of nanotechnology in products becomes more implicit. In addition, to protect longer-term innovation it is important that the fundamental science, the source and support of many advances, is not overshadowed by changing trends in funding as nanotechnology becomes more established and its uses mainstreamed. To guarantee that the future uses of nanotechnology are sustainable and safe, maintaining an open discussion on the topic is essential. Being aware of the scope of nanotechnology is invaluable in understanding today's technological developments and guiding them to support Irish interests.

What is Nanotechnology?

The term “nanotechnology” has been around for nearly 50 years, and while it basically describes technology at a very small scale, there is no agreement on a standard definition.[16] A useful definition of nanotechnology was set out in Ireland’s Nanotechnology Commercialisation Framework (2010)[17] in line with international alternatives:

> *“The purposeful engineering of matter at scales of less than 100 nanometres (nm) to achieve size-dependent properties and functions.”*

The important points of this definition are worth examining in closer detail, as follows:

- **Purposeful engineering:** This indicates design intent – many ordinary materials and products will have nanoscale features that are not considered.
- **Scales of less than 100 nanometres (nm):** “Nano” means one billionth, so one nanometre (nm) is one billionth of a metre in length. The precision and structures of nanotechnology are on the nanoscale. The nanoscale describes a length scale close to the atomic scale and corresponds to fractions of a thousandth of the width of a human hair. The generally accepted range in sizes is 0.1-100 nm.

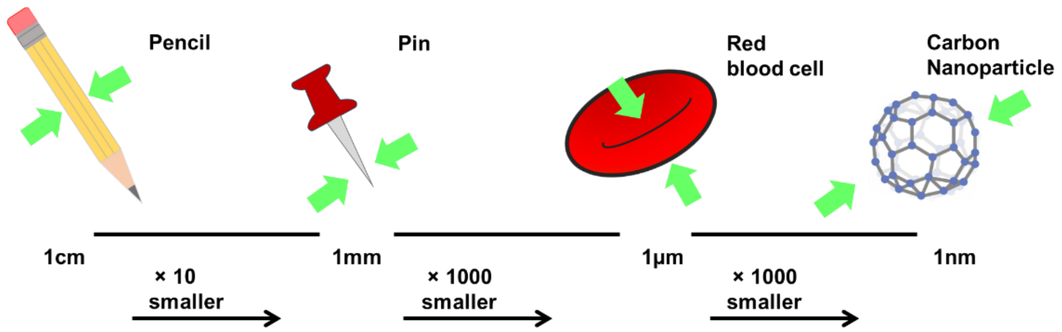

Figure 1. Understanding the nanoscale from the human scale

- **Size-dependent properties and functions:** Size-dependent properties are the essential factor that make nanotechnology novel and useful. The materials and structures are not only small, but small and different. The novel properties that are only apparent and achievable at the nanoscale are often the motivation to design products with features at this scale and incorporate nanoscale materials into the design of new products.

> An advantage of working at the nanoscale is that there are more possibilities to tune the physical properties of materials for applications.

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This includes a near endless list of physical and mechanical attributes, including electrical conductivity, thermal conductivity, thermal stability, hardness, tensile strength, chemical stability, transparency, and light wavelength dependent responses. Combinations of these properties determine whether a material is good for specific uses. To understand why a material might be selected, it is worth considering the following examples:

- Thin nanoscale materials are often flexible and strong, if the electrical properties change when a material is bent, the material might be suitable for sensors to detect vibrations – for example in wearable health monitoring devices; and
- Nanoscale materials have large surface areas relative to their small "nano" volumes. This allows them to interact with more chemicals on their surfaces, This large surface area is useful for more efficient catalysts, and allows quicker delivery of medicines reduced to nanoscale dimensions. These surface interactions can change the electrical properties of the material. An electrical change in response to a gas can indicate the material is useful for sensing dangerous gases, enabling better gas sensors.

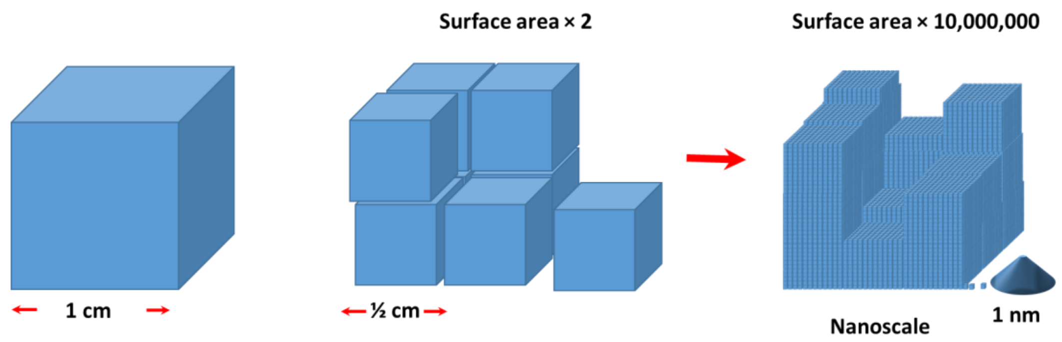


Figure 2. The surface area available for reaction increases as dimensions get smaller

Nanomaterials

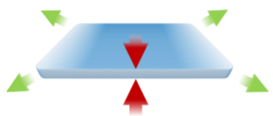
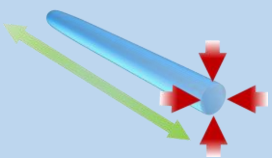
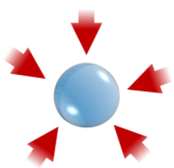
Materials with nanoscale dimensions are generally referred to as nanomaterials. The study of nanomaterials is the core of the subject of nanoscience. Nanotechnology, which is the application of nanoscience, includes not only devices engineered at the nanoscale but also the materials that make up the devices. However, it is important to note that not all nanomaterials are purposefully engineered. Some are naturally occurring like volcanic ash, while others are by-products of human activity, such as carbon nanoparticles within soot produced by the burning of fuels, and particles produced by degradation of plastics.[18] The same nanoscience techniques and tools used to study these "incidental" nanomaterials are those used generally in nanotechnology.

Nanomaterials come in a variety of shapes or forms – sheets, wires or fibres and particles. As the properties of the nanomaterials are often associated with their form, it is often useful to group or classify them according to whether the dimensions are limited to the nanoscale. Table 1: *Classes of Nanomaterials*, gives an overview of these shapes, the common types of nanomaterials and a selection of potential uses and applications where they might be found. The nanomaterials can be part of a surface coating or film and not just freestanding. These materials can be combined to build metamaterials which are more complex composite structures.[19]

The chemical composition of nanomaterials is another crucial factor that influences the properties of nanomaterials. However, the chemical and physical properties of nanomaterials are often very different to those of the same chemical materials in their larger forms. For example, graphene[20] – a single layer of graphite (the "lead" in a pencil) – is the strongest material ever tested (unlike so many broken pencils because the layers, while strong, can easily be separated), and many metal nanoparticles are highly chemically reactive much more so than the bulk materials, in part due to the increased surface area.

A final type of nanomaterial is when a surface or a material is textured at the nanoscale. These sorts of nanoscale patterns also exist in nature such as the colourful reflective wings of a butterfly.

Table 1: Classes of Nanomaterials

Dimension	Types and Names	Applications[21]
2-D Materials  Nanoscale thickness but large area	Nano-flakes Nano-sheets Nano-films	Anti-reflective coatings for windows, phones and solar panels; touch screens; flexible electronics, battery electrodes; water filters and desalination; vibration sensors; weather resistant paint
1-D Materials  Long and nanoscale thin	Nano-wires Nano-tubes Nano-ribbons	Material reinforcement in wind turbine blades, airplanes, sports equipment, construction materials and body armour; filters; biological sensors; x-ray sources; antibacterial textiles; wound healing products
0-D Materials  All dimensions are nanoscale	Nano-particles Quantum Dots Nano-capsules	Surface coatings such as cosmetics, sunscreen, paint scratch resistant coatings and antibacterial coatings; solar cells; lasers; reinforced plastics; fuel cells; medical technologies such as vaccines, pharmaceuticals and wound dressings

Seeing and working at the nanoscale

Many nanomaterials cannot be seen with traditional optical microscopes, their nanoscale dimensions are too small to be resolved with light. Alternative approaches are needed to observe the materials and provide information on the properties. To overcome this problem a number of techniques have been developed and are employed. Some commonly used methods include[22]:

- **Electron microscopy:** Electrons are used to see the surfaces rather than light, a technique that has been refined since the 1930s.
- **Scanning probe microscopy:** A sharp tip feels and traces the surface, like an atomically sharp record needle.
- **X-ray analysis:** x-rays are smaller than light and can probe much smaller features.

These microscopes are typically able to resolve nanoscale features and individual atoms. Such microscopes are used in both industrial and academic settings. For research purposes they allow detailed examination of the structures on nanomaterials, necessary for development and classification. While in industrial settings they are widely used for failure analysis.

The past decade has seen the capabilities of Irish microscopy facilities in universities grow considerably with investment by European and Irish funding sources. Ireland now has some of the most powerful microscopes in the world. State of the art electron microscopes, costing in excess of €5 million, have been installed in both the Advanced Microscopy Laboratory in Trinity College Dublin and the University of Limerick.[23] These microscopes are part suite of instruments in the universities that are accessed by both academics and industry for imaging, patterning and analysis.

Seeing materials at the nanoscale is only a single but vital step in their production and use in nanotechnology. Nanotechnology research is capital intensive, that is material- and nano-scientists require a variety of specialised tools to fully characterise the properties of new nanomaterials and test quality at this scale.[24] A 2017 OECD publication, on the implication for governments and business of the 'Next Production Revolution', recognised it is almost impossible to gather all nanotechnology infrastructure in a single institute or even a single region, due to expense and expertise.[25] Nanotechnology requires increased partnership across institutions and sectors. For example, some larger more specialised tools are available only on a collaborative basis, such as through European neutron source facilities.[26] This fundamental research and development, often within universities, is an essential step before the materials can be produced on an industrial scale or brought to market. The OCED publication recommended that public funded research programmes should encourage the collaboration of academia and industry, due the operational and capital costs. In Ireland, the National Technology Transfer system is a route that enables the transfer of commercially valuable research outputs from academia into industry.[27]

Applications of Nanotechnology

The application of nanotechnology is often associated with high-tech electronics, but its uses go far beyond this. Nanotechnology is largely a product of materials science, and sits where technology, biology and information converge.[28] This makes it a subject of great interest to researchers and of great use to innovators. Academic research is often a pipeline to industry, particularly as nanotechnology research and development is costly and small firms can struggle to buy equipment.

The development of nanotechnology products requires both infrastructure and expertise. While larger multinational companies may have access to research and development divisions, small and medium enterprises (SMEs) can benefit from access to university facilities for technology transfer.[29] Maintaining a pool of highly educated workers is important, one of the main reasons many multinational companies choose to locate in Ireland is the availability of science graduates.[30] Demand has led many Irish universities to offer specific degree and postgraduate programmes for nanoscience. Nanotechnology in both industrial and in academic settings has had a positive effect on the Irish economy. Between 2007 and 2016 Ireland's leading nanomaterials research centres, CRANN and AMBER, generated €505 million in gross national output,[31] a return of five Euros for every one invested.

The example applications discussed here loosely follow sectors of interest within Irish research priority areas[32] and expand on wider possible future uses. The applications are in areas where the use of nanotechnology has brought or is likely to bring transformative changes. Where appropriate the regulation of nanotechnology and nanomaterials is also examined. The sectors are:

- Information and communication technologies
- Manufacturing
- Medicine, and
- Agri-food.

Information and communication technologies

Computer circuits have become smaller steadily since the 1960s. Now, for more than a decade, the electronics within computers are being designed and built at the nanoscale – this is nanoelectronics. Manufacturers can now squeeze more than 100 million transistors, the basic building blocks of computing, into each square millimetre of a computer processer.[33] This means more computing power with components that take up less space and have lower energy demands. Nanoscale semiconductors, the materials from which computer processors are built, are found today in almost every electrical device, from cars to mobile phones and networks, and monitoring equipment. They are the infrastructure of digital innovation, needed to develop the digital economy and smart devices, and are the systems on which software technologies, such as artificial intelligences, are built. The properties of these materials and devices shape the abilities of the products in which they are used – including in areas such as security, privacy, energy-performance and safety. Innovation in this sector effects how others develop and sets the physical limitations on what is possible in a digital world.

The global semiconductor market, which includes computer manufacturing and communication technology, is worth €440 billion.[34] Currently the EU's share of this market is a relatively small 10%, which it intends to grow to 20% by 2030. The importance of the industry was highlighted by a joint declaration on "a European Initiative on Processors and Semiconductor technologies" by the European Commission in December 2020, inviting member countries to cooperate in developing the industry together. [35] The declaration stresses that a well-developed semiconductor industry is necessary to secure Europe's ability to compete across a wide range of sectors.

The semiconductor industry has a large impact on the Irish economy, and the sector has continued to grow since the first wafer fabrication facility was established in 1976.[36] This growth has been due to the presence of international technology companies such as Intel. Since arriving in Ireland over 30 years ago, Intel has invested USD $15 billion in its site in Leixlip, and it is currently spending an additional USD $7 billion on expanding its facilities.[37] This is to produce the next generation of computer chips, with transistors as small as 7 nm. The semiconductor industry spends heavily on research and development, and as a percentage of revenue it is among the highest of any industry - usually between 15 and 20%. Sustaining the high level of research and development in the semiconductor industry is only possible with a highly skilled and educated workforce. Ireland's ability to attract and retain such companies has been supported by the education system, which is currently ranked within the top 10 globally as meeting the needs of a competitive economy, and the number of people holding doctorates has doubled in recent years.[38] The presence of established technology companies creates an environment and value chain that makes Ireland attractive to other technology companies.

Nanotechnology will continue to be important for the future of computing. Nanoscale electrical circuits and components have improved the performance of computers, but there is a limit to how small these can become. Rather than electrical signals, the future of computing may be based on the quantum properties of materials, which are only achievable at the nanoscale. Quantum computing, which uses these properties, could soon revolutionise computing as it can solve types of complex problems that simply cannot be done with today's computers.[39] The rapid development of quantum computing comes with the concern that it could make standard encryption, for secure computer communication, ineffective.[40] However, the use quantum properties also offer the most secure way protect digital communication.[41]

The future of nanoelectronics is not simply ever smaller and faster computer chips. Rather, a much a wider range of non-traditional electronics is possible using nanomaterials, such as optical computing and flexible electronics. Low power flexible electronics with additional functionalities are made possible with 2D materials such as graphene and 1D materials like carbon nanotubes. "Wearable microgrids" that can harvest energy from the sweat and movements of the human body, and store it to power small electronics have been demonstrated.[42] These can be used with extremely responsive sensors to monitor the health of the wearers, by measuring oxygen levels, testing for glucose, caffeine and alcohol, and determining their blood pressure from their pulse.[43] These sorts of small, sensitive and low-power nanotechnology devices are the basic building blocks, or smart technologies, that make up the "Internet of things". The nanomaterials in these flexible electronics can be produced at low cost, and this will likely lead to an expansion of their use.

Manufacturing

Manufacturing is a central pillar of the Irish economy, employing over 227,000 people.[44] The industry in Ireland is diverse, and within it the main engineering sectors include automotive, aerospace, chemicals and advanced materials, medical devices, industrial automation and engineering services. International companies in the industrial technology sector based here generate €4.7 billion in exports annually. For example, Henkel is long established in Ireland, and is considered a cornerstone of the high tech and high value chemicals manufacturing sector. [45] The development of better composite materials can lead to significant improvements in manufacturing.

It is worth considering that engineering in Ireland is typically associated with development and design leadership, rather than heavy industry. Nanotechnology has the potential to help enable innovation in manufacturing, through the digitisation of industry known more generally as Industry 4.0, and by a deeper understanding of materials leading to improved practices, such as those of the circular economy which seek to recover and preserve the embedded value in materials, components, and products.[46] A more direct use of nanotechnology, however, is the use of nanomaterials in innovative manufacturing processes such as additive manufacturing.

Additive manufacturing and 3D printing

A 3D printed object is produced by depositing a material under computer control, and usually without the need for significant cutting or machining. 3D printing, more generally known as additive manufacturing, is a simple idea but a disruptive technology. A disruptive technology is an innovative enabling technology that is capable of fundamentally changing existing markets and methods of production.[47] This shift away from traditional industrial methods makes manufacturing accessible to many more users. Since 3D designs can be customised easily on a computer, printed models can be adapted quickly to suit specific user needs. An example of where this responsive design has been particularly successful is for personalised prosthetics.[48] The flexibility of design through a computer interface means 3D printing is also a tool that can be used within digitised industry.[49] For industry, this means designs can be more responsive to consumer needs and that prototypes can be produced in less time, shortening the overall timeframe for product development. There are practical uses across a wide range of industries, including medical, aerospace, automotive and defence. The global market for 3D printing is projected to be worth as much as €491 billion by 2025.[50]

The most common domestic 3D printers use plastics to produce their models, although additive manufacturing is not necessarily limited to just one material. It is also possible to print metals and ceramics. An ongoing topic of research in nanotechnology is the development of nanomaterials and advanced composites that could be used for printing.[51] The use of nanomaterials can improve quality and expand the variety of materials or inks for printing. For example, using inks containing electrically conductive nanomaterials, it is possible to print cheap thin flexible circuits on paper, which could be used as disposable electronic tags in packaging.[52] Controlling and combining the types of nanomaterials in the inks allows the printing of more complicated circuit components, such as sensors and even batteries.[53]

It is also possible to print using biological compatible materials for medical implantation, enabling better cosmetic reconstruction. These techniques are used for nanomedicine applications.[54]

Structures can be printed from nanomaterials that act as supports for the growth of tissue.[55] There is even the possibility of using cells as a printing material by tagging them with magnetic nanoparticles, these printed cell structures can then be used to simulate conditions inside a body for testing new drugs.[56] Considering the medical applications of 3D printing, it is suggested that Ireland is ideally positioned to benefit from opportunities in implantable devices.[57] Ireland's medical technology sector is already a leading cluster for medical device products globally, with such products and devices making 8% of Ireland's total merchandise exports. To maintain this competitive environment, it is important to actively engage with the use of nanotechnology in medicine.

Additive manufacturing is not without its nanoscale problems. It has been shown that desktop 3D printers can produce ultra-fine nanoscale plastic particles that may be inhaled.[58] The concentration, size and harmfulness of these particles will depend on the material being printed and the printing process.[59] Guidance by the European Commission on the protection of the health and safety of workers from the potential risks related to nanomaterials at work considers exposure such particulate matter.[60] However, with the expanding domestic use 3D printers, and the scope for printing novel nanomaterials, further specific emission standards and guidance for printers may need to be considered.

Nanotechnology in medicine

Medicine is an area that affects us all. Advances in medicine are important to society as a whole and enterprise in Ireland has benefited from investments by biomedical companies. In planning for future developments in the health sector, the Department of Enterprise, Trade an Employment identified four priority areas for research and innovation under the theme of 'Health and Wellbeing', these were[61]:

- Connected Health and Independent Living
- Medical Devices
- Diagnostics, and
- Therapeutics.

The use of nanotechnology is already driving innovation in these areas. An OECD review of trends in technologies noted a growing link between nanotechnology and biotechnology.[62] Nanomedicine, the use of nanotechnology in medicine, is a fusion of these technologies. However, while there is a need for clear regulatory guidance, it struggles to keep pace with technological developments and in particular efficient classification of new technologies.

What is nanomedicine?

European Union Definition of Nanomedicine

Nanomedicine is defined as the application of nanotechnology in view of making a medical diagnosis or treating or preventing diseases. It exploits the improved and often novel physical, chemical and biological properties of materials at nanometre scale.

This is a wide-reaching definition, covering uses such as the medical applications of nanomaterials and biological devices, to nanoelectronic sensors for measuring biological processes, and even possible future applications such as machine interfaces with the brain[63] and nanoscale machines that use biological components to function.[64]

A major advantage of nanotechnology in medicine is its size compared with the cells of the human body.[65] Biological processes, including those necessary for life, occur at the nanoscale. Nanoscale devices and materials used for nanomedicine can be one hundred to ten thousand times smaller than human cells. This puts them on the same scale as viruses or large biological molecules such as antibodies, enzymes and receptors, which are responsible for biological processes. Devices circulating in the body that are smaller than 50 nm can easily enter most cells, while those smaller than 20 nanometres can move in and out of blood vessels.[66] This access gives the potential to detect disease and deliver treatments in unprecedented ways.

Nanomedicine has the potential to impact all aspects of medicine. The application of nanomaterials in medicine has already led to the development of diagnostic devices, contrast agents for imaging, analytical tools, physical therapy applications, and enhanced drug delivery.[67]

The applications of nanomedicine are both outside and inside the body. Outside of the body nanomedicine is greatly improving diagnostics.[68] There is an ever-expanding range of sensitive non-invasive lateral flow tests, similar to pregnancy tests and breathalyser tests. However, its internal uses could revolutionise healthcare, by enabling personalised, targeted and regenerative medicine through the delivery of new drugs, treatments and implantable devices.

The future of nanomedicine is of global interest. A longer-term aim of nanomedicine researchers at the Innovation Center of NanoMedicine Japan is the development an effective “in-body hospital” using nanotechnology.[69] This would involve dispersing nanomachines into the body, to perform detection, diagnosis and treatment, which can communicate wirelessly with physicians who would monitor and direct treatment. However, such technologies are still at an early stage of development, but the high level of automation possible could make this a cost-effective approach. This would enable wider availably and more affordable delivery of medicines and treatments, and would be particularly suitable for managing the medical demands of an aging population.

Stakeholders in Nanomedicine

The European Technology Platform for Nanomedicine (ETPN) is an initiative set up to address the application of nanotechnology in healthcare. It acts as a ‘Think Tank’ for nanomedicine in Europe. It has been led by industry since 2005 and was set up together with the European Commission. In 2015, the ETPN became an independent association and now has more than 125 members from 25 different Member States, with stakeholders from academia, SMEs, industry, public agencies, and representatives from national platforms and the European Commission.

How would nanotechnology change medicine?

Diagnostics

Outside the body nanotechnology is being used to develop more sensitive medical tests and simpler diagnostic tools, such as "lab-on-a-chip" lateral flow test devices that can combine several laboratory tests on a simple single integrated chip – allowing better automation and higher-throughput screening. These sensors can be included in wearable medical devices,[70] which enable personalised digitised medicine such as remote health monitoring or e-Health.[71] Rapid testing is vital for stopping the spread of highly infectious diseases. To improve sensitivity, there is also the possibility of nanotechnology diagnostics tools within the body, where nanoparticles would mark or highlight issues such as cancer at an early stage.[72] Earlier detection can enable earlier intervention which is linked to better patient outcomes and lower costs.

Example: Alzheimer's disease is currently diagnosed with brain scans after patients start to show symptoms, but by the time symptoms are visible treatments are less effective. Recently, a nanomedicine-based blood test was developed that could detect Alzheimer's years before symptoms appear.[73] Similar tests are been used in the fight against the COVID-19 pandemic. For these rapid tests, Covid-19 antibodies selectively bind to the surface of gold or magnetic nanoparticles, which triggers a colour change that can be used for reliable identification in minutes.[74]

Nano-therapeutics

Nanotechnology can be used to "recognise" specific parts of cells or tissue within the body. Cells or tissue within the body can be marked with nanoparticles and then targeted for treatments. This allows drugs to reach damaged tissue while avoiding healthy cells. This more targeted approached would reduce treatment times.

Nano-therapeutics also includes controlled and efficient drug release. Nanotechnology can be used to change how a drug is delivered but also more accurately control the quantity and rate at which it is delivered. In some treatments, nanomaterials can be used to deliver multiple drugs at once, which could reduce treatment times, such as for cancer and tuberculosis.[75] Some treatments are currently problematic to administer, for example insulin for diabetes needs to be injected, but nanomedicine may provide more convenient alternatives such as inhalers or tablets. Another approach is the real time monitoring of insulin levels with wireless communication to release supplies within the body.[76] Such advances would reduce patient distress and improve quality of life.

Example: There are already a number of approved cancer drug therapies that use nanotechnology.[77] Consider the poor survival rates of pancreatic cancer, a new treatment being tested uses iron nanoparticles absorbed by cancer cells to selectively heat the cells allowing the drugs to target the cancer cells more effectively.[78]

Medical imaging

Specialised nanoparticles can be used to mark features of interest so they can be studied in higher detail and more accurately targeted for treatment.[79] Nanoparticles can deeply penetrate tissue, and so can be used to enhance contrast and improve clarity in medical images produced by ultrasound, magnetic resonance imaging (MRI) and positron emission tomography (PET). The use of nanomaterials brings higher sensitivity and a reduced dose of radioactive materials for PET imaging.[80] Imaging enhanced with nanotechnology helps further medical research by providing better understanding of biological processes and provides more certainty in diagnosing problems.

Example: Producing clear images of problems within the body, such as the pooling of blood or inflammation, is essential for the treatment of cardiovascular problems so that the correct medical action can be taken.[81] For cancer treatment, it is possible to combine different medicines with nanoscale encapsulated tracers, so as to visually assess and monitor drug release within the body in real-time, enabling selection of the most effect medicines.[82]

Vaccines

Nanomedicine can be used for disease prevention. Vaccines that use only sections of genetic code (mRNA) rather than the whole virus or its DNA are the most recent generation vaccines. This approach is considered safer as mRNA is not infectious and cannot be integrated into the host genome, and allows vaccines to be modified more quickly to respond to different seasonal strains.[83] Nanoparticles are a safe way to stabilise the mRNA which would otherwise degrade, and others can also be used to better handle pieces of DNA.

Example: Lipid nanoparticles – nanoscale droplets of fatty biomolecules – are an important stabilising ingredient used for the mRNA *Moderna* and *Pfizer* COVID-19 vaccines.[84] The ability to safely deliver mRNA into the body is a key challenge, and being able to so opens up a variety of other treatments, such as immune system based cancer treatment[85].

Regenerative medicine

Nanotechnology is already used to improve the quality of implants and prosthesis. Nanomedicine aims to go further by using tissue engineering to repair injuries and damaged organs. This could be done using scaffolds that mimic the structure of tissue at the nanoscale, and would enable the printing of artificial skin, the engineering of bone and cartilage growth to repair damaged knees, or tissue growth for bladder replacements.[86] 'The use of specialised 'bio-inks' would encourage the body's growth of blood vessels around the new bone and tissue.[87] Such developments are aimed at personalising treatments, meaning a lower chance of rejection and better long-term outcomes, which would also reduce disability associated with aging and injury.

Example: For joints damaged by osteoarthritis, Irish scientists are developing personalised 3D-printed biological implants designed to regenerate diseased joints rather than replacing them.[88] Repairing nerve injuries is particularly difficult, Irish scientists have had improved success in overcoming this challenge with the use of the 2D material graphene to enhance nerve cell growth.[89]

Safety and regulation of nanomedicine

Safety

Nanotechnology is relatively new, and as such, information on the long-term risks associated with exposure to nanomaterials is limited. Furthermore, despite the many potential uses for nanomaterials in medicine, most are still in early stages of development. Understanding the risks associated with nanomaterials is a vital step towards their use in medicine. While there are real risks associated with some nanomaterials, it is also important to recognise that there is nothing inherently dangerous about nanoscale objects. There are countless harmless everyday nanoscale objects, such as droplets of sea water made by the crashing of waves. However, there are some specific nanomaterials such as carbon nanotubes that have the potential to damage DNA, or due to their shape, pose risks of lung damage similar to asbestos.[90]

The possibilities offered by breakthrough technologies like those used in nanomedicine need to be weighed against the potential toxicity or persistence risks.[91] Some nanomaterials have been found to persist in the body - gold nanoparticles were found in the human body for months.[92] This introduces the concern that nanomaterials that cannot be broken down may accumulate within the body. Plastic and silver nanoparticles have the potential to cross the placenta during pregnancy and enter the brain.[93] Such deep penetration may be advantageous for some treatments[94], but repeated cumulative exposure to unwanted materials could lead to health complications, even at apparently safe doses through consumer products. Due to their ability to disperse within the body, there is the potential for silver nanoparticles to harm organs such as the liver and lungs and interfere with the immune system, nervous system and reproductive development.[95] However, there is an immense variety of nanomaterials and there is little data on long-term effects.

It is known that the uptake and passage within the body of nanomaterials is highly dependent on the physical and chemical properties of the particles, including size, surface properties and chemical composition.[96] Most engineered nanomaterials considered for use in nanomedicine are chosen for their low toxicity. In many cases the purpose of using nanomaterials is to reduce risk, for example to deliver drugs more safely. It was noted by the US National Cancer Institute,[97]

> *"Certainly, the nanoparticles used as drug carriers for chemotherapeutics are much less toxic than the drugs they carry and are designed to carry drugs safely to tumors without harming organs and healthy tissue."*

The responsible management of nano-enabled products within nanomedicine requires an understanding of intended product uses and possible side effects. Similar to other aspects of medicine, this means science-based assessments of potential risks, and clear communication of the health and environmental information needed for their safe handling, use and ultimately disposal.

Regulation

From the diversity of applications, it is clear that nanomedicine is a complex and rapidly evolving topic, and this has made it difficult for regulation to keep pace. In turn, uncertainty in regulation has slowed the uptake and use of nanotechnology in medicine. To facilitate communication between developers and users of nanotechnologies in healthcare, there has been some standardisation of the vocabulary used (ISO/TR 17302:2015).[98] However, currently separate EU regulations exist to regulate medical products such as devices and drugs. Depending on how they work, nano-enabled health products are regulated at a European level either as medicinal products (Directive 2001/83/EC) or medical devices (Regulation (EU) 2017/745).[99] The purpose of the product and the applicable regulation is clear for some cases, for example external diagnostics or nano coatings on artificial joints to enhance durability are clearly devices. However, many nanoparticles and other nanotechnology products used in nanomedicine often have more than one purpose, they can act either as a device or a drug, or both. This and specific concerns of nanomaterials can make the route the approval therapies that use such products within the body difficult.[100]

Currently, there is no specific regulatory framework for nano-enabled health products. In the REFINE white paper published by the European Commission in 2019, it is acknowledged that additional guidance may be needed in order to fully cover the special challenges of such products.[101] However, due to the fast progress in nanomedicine there is often limited data available on the long-term safety of nano-enabled products.

The report also notes that more engagement is needed with researchers to develop regulations.

> *"More efforts are needed to take up translational and regulatory science into academic research and educational programmes in order to support the development of regulatory structures that can be adaptive to increasingly complex innovative health products"*[102]

Another issue recognised by the white paper is the need for harmonisation of regulatory practices, as standards and terminology in nanomedicine differ worldwide. This is an important factor to be considered within the context of Irish medical exports. A lack of shared practices and guidelines would limit market access.

It is clear that active participation in the creation of guiding regulations for use nanomaterials would support innovation within the field of medicine. There is an outstanding need to create approaches that accommodate the specific requirement of nanomedicine products beyond the European framework that exists for conventional products, so that they can be brought to market in a timely and safe manner.[103]

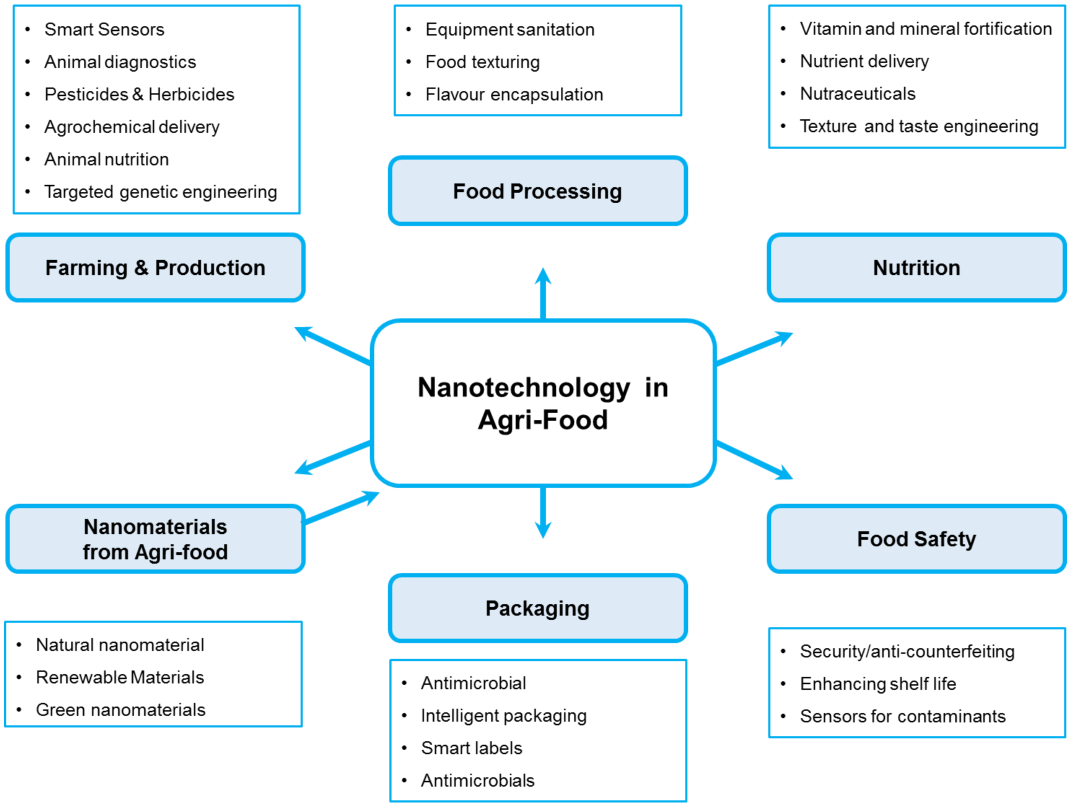
Nanomaterials and nanotechnology within the agri-food industry

The agri-food sector is Ireland's most important indigenous industry. Valued at €14.5 billion in 2019, it is a vital part of the Irish economy.[104] Globally, it was estimated by the World Bank that the added value of agriculture alone is over USD$3 trillion, and demand for food for is expected to rise by about 40% by 2050 as the global population grows.[105] Factors such as climate change, the drive to reduce greenhouse gas emissions and competing land uses, mean it will be ever more difficult to meet our food demands. This highlights the importance of innovation within the agri-food industry, which is seen as a priority at both Irish and European levels.[106]

With the requirements of sustainability and digitalisation in food markets, the increased use of technology within the agri-food sector is inevitable. The use of nanotechnology could provide many benefits to both agriculture and food processing. The use of nanotechnology in the agri-food sector is one of the fastest growing fields in nano-research. Research relating to nanotechnology covers almost every aspect of the broader agri-food industry, including irrigation/water filtration, farming, animal feed, aquaculture, and food processing and packaging.[107]

An overview of some of the applications of nanotechnology in the agri-food industry are shown in Figure 3. It considers the main areas in which nanotechnology and nanomaterials may be used in agri-food, but also that agri-food can be a primary source for nanomaterial production used elsewhere.

Figure 3. Applications of Nanotechnology in Agri-food Industry[108]



The potential advantages of nanotechnologies in farming include reduced environmental impact and improved productivity and food security. It is a topic of growing interest and over the last five years the number of studies on nanotechnology in agriculture has almost tripled.[109] However, much of the use of nanotechnology in agriculture is still at an early stage, and the transfer of such technologies to farm level applications remains limited.[110] For smarter agricultural systems, proposed uses of nanotechnology include the wireless monitoring of crop health, with passive unpowered sensors attached to plants to report on environmental conditions and plant health.[111] Another important use of nanotechnology in farming is the development and use of improved fertilizers and pesticides. Slow-release and controlled-release fertilisers have been designed using nanomaterials, so that nutrients stay in the soil for longer and are less affected by leaching, which reduces the overall fertilizer demand.[112] The use of such lower demand fertilizers could help in Ireland's ambitious planned reduction of agricultural greenhouse gases as part of the National Climate and Air Roadmap for climate neutral agriculture by 2050.[113] Nanoscale engineering of pesticides is being considered for similar reasons. Another way in which nanotechnology can be potentially used in crop production is in the genetic modification of plants[114], with a view to creating crops resilient against rapidly changing environmental conditions and to increase yields.[115] Animal welfare also has the potential to benefit from the use of nanotechnology through better sensors and diagnostic tools. Researchers at the Tyndall National Institute in collaboration with Teagasc are developing cost-efficient nanowire chip sensors, to provide on-site disease testing in cows within 15 minutes, this includes illnesses such as Liver fluke.[116]

Nanotechnology has uses at multiple stages of the food chain, from processing to packaging.[117] For food safety, applications include sensors to detect spoilage and antibacterial coatings to avoid contamination. However, there is growing interest in the nanoscience and technology of food, that is, the nanoscale design of food and food supplements, with possible applications that include super nutrients, the vitamin, food fillers, and control of food properties such as through stabilisers, preservatives and colour adjustment. The food industry has already been unconsciously using nanotechnology. Mayonnaise is an emulsion of tiny particles, a mixture of water and oil forced together. Rather than just accidental use, now food-scientists are developing techniques to precisely control these tiny droplets, to give foods specific tastes or textures.[118]

The agri-food industry could also become a supplier, as well as a user, of nanomaterials for nanotechnology applications. Some nanomaterials are naturally occurring in plant and animal products, including the constituents of milk, fibres in meat and fish, and the cellulose structure in plants.[119] For example, milk proteins have been used to form nano-delivery coatings to improve the transfer of vitamins and other nutritional supplements in foods.[120] Such functional foods, or nutraceuticals, are identified as being of research interest within the context of Irish priorities.[121]

Safety and environment

Despite the many opportunities and benefits nanotechnology can bring in agriculture and food production, its use is not without concern. Some of this hesitancy is due to perception and safety.[122] Nano-emulsions like in margarine and mayonnaise are generally considered to be safe, as they can be simply digested. The basic concern with adding nanoparticles to food is some are not easily digested, and it is important to understand where they end up if the body cannot break them down.[123] This is an important issue because some nanomaterials such as certain carbon nanotubes, can damage cells and DNA.[124] In Ireland the use of nanomaterials within food is regulated by EU standards. Very few novel nanomaterials that have made their way into human food, the most notable that have are titanium-dioxide and iron-oxide, which were already used extensively for food brightening and colouring.[125] However, use of titanium-dioxide (European food additive, E171) is no longer considered safe by the European Food Safety Authority (ESFA) when used as a food additive, due to concerns that it can accumulate in the body, and that its toxicity to genes could not be ruled out.[126] This change in status was the first time the 2018 EFSA Scientific Committee Guidance on Nanotechnology was applied to the safety assessment of food additives.[127] New engineered nanomaterials intended for food require a case by case risk assessment and authorisation by the EFSA before being placed on the market, and their use would have to be indicated on the list of ingredients.[128] The increased awareness of forms of nanomaterials has also led to greater understanding and the possibility of improved standards for existing food additives. For example, silicon dioxide is an approved and widely used anti-caking agent (European food additive, E551). Studies have shown this powdered food additive contains clusters of nanoparticles, and because of this they suggest that current EU specifications are insufficient to determine its safety as a food additive.[129]

However, most uses of nanomaterials relating to food are not intended for consumption, such as those used for active and intelligent food packaging. For example, both silver oxide and zinc oxide nanoparticles have been used in packaging to improve the shelf-life of apples.[130] These materials, which are not intended for ingestion but come into contact with food, are regulated differently from novel foods[131] that contain nanomaterials.[132]

Regarding farming applications, there is a trend towards more eco-friendly nanomaterials and technologies. This approach may minimise unwanted impacts like nanomaterial pollution and the unknown environmental end-point of new nanotechnology based agro-chemicals such as pesticides.[133] Greener products are therefore likely to become a key component of future nanotechnology in the agri-food sector and beyond.[134] The use of natural ingredients to produce nanomaterials, from renewable sources rather than petrochemicals, and designed to be environmentally benign, is being extensively explored. [135]

Future

Even with the rapid growth of nanotechnology, its adaptation for agriculture has been slower, interest is however increasing.[136] The use of nanomaterials in agricultural and food products are some of the most controversial aspects of the application of nanotechnology. The main reason, beyond public perception, is the limited regulation and legislation surrounding nanoproducts in food, which is slow to develop due to the complexity of nanomaterials. The approach to the regulation of nanotechnologies in food is largely reactive rather than proactive, and the risk arising from uncertainty or lack of regulations has been cited as an issue of concern.[137]

Despite the challenges, these technologies can potentially provide more ecologically friendly agrochemicals to help farmers to meet good production levels, and the sensors could offer smart ways to improve efficiency. The data provided by such sensors and the reduction in fertilizer use would be positive contributions to Ireland reaching its goal of climate neutral agriculture by 2050. The use of nanomaterials should be made on an educated basis, with environmentally sensible decisions to avoid longer-term problems, and there are opportunities for additional market diversity in novel agri-food products. There is a broad variety of possible technologies and there is scope for native innovation if the appropriate technologies beneficial to Irish interests are prioritised and regulation keeps pace.

Impacts of Nanotechnology

Nanotechnology and the Environment

The European Green Deal, and its Circular Economy Action Plan, set out the EU's ambitions and goals to make its economy.[138] They propose that Europe should be climate neutral by 2050 and that the materials used to sustain its economy continue to flow efficiently, being reused within it, and not contribute to waste. Reaching the targets set out in these plans will require both social and technological actions. It also requires that the development of new technologies must be done in an environmentally responsible way.

Nanotechnology offers opportunities for green growth through better materials for construction, renewable energy technologies and improved efficiency. There is also the opportunity to understand existing environmental issues, including micro- and nano-plastics, through nanoscience, which could help provide solutions to these problems through better choices of materials or engineering. Nanotechnology can also be used to respond to environmental pollution. For example, the use of filters with nanoscale fibres can be used to efficiently treat contaminated water and iron nanoparticles have been used to more rapidly treat the soil in sites contaminated by industrial chemicals.[139] However, many nanomaterials are new and developing an understanding the risks associated with their use requires continued support of fundamental research. If the use of nanotechnology is unmanaged it could cause harm and present environmental issues, particularly through waste, and this needs to be addressed to guarantee long-term sustainability.

Energy

Decarbonising the energy sector is a priority for Ireland, as is set out by the 2019 Climate Action Plan.[140] This will require both the production and consumption of energy to be cleaner and more efficient. Nanotechnology has the potential to enable innovative renewable energy production and can be used to improve energy efficiencies.[141] For example, solar and wind electricity generation are rapidly growing and already utilise nanotechnologies.

According to the International Energy Agency's World Energy Outlook report of 2020,[142] solar power is now the cheapest form of electricity.[143] The most common silicon-based solar cells already apply nanoscale processes used in the semiconductor industry. Nanotechnology improves the viability of solar power in several ways[144]:

- It can reduce the production cost of cells of by replacing expensive metals with cheaper composite nanomaterials;
- Improve environmental safety by replacing known toxic materials (such cadmium) with safer alternatives;
- Improve 'light management' by structuring the surface at the nanoscale to reduce reflections and increase the amount of light entering the cells; and
- Increase energy efficiency by minimising the thickness material layers in solar cells, allowing stacked light absorption layers.

In addition, continued advancements in solar cell technology is to be expected with the use of nanomaterials, such as improvements in efficiency or innovations like flexible solar cells.[145]

Nanotechnology can also improve the performance of wind turbines, from nanomaterials that reinforce the blades to more efficient lubricants to reduce wear.[146] The use of longer, stronger, and lighter-weight blades increases the amount of electricity that turbines can generate.

Energy captured from renewable sources needs to be efficiently stored for later demands. Hydrogen storage and batteries are common low carbon energy storage technologies. Batteries are seen as one of the key enablers of a low-carbon economy as part European Strategic Energy Technology Plan (SET Plan).[147] The European Battery Alliance (EBA) was launched by the EU to bring stakeholders in industry and the scientific community together to make Europe a global leader in sustainable battery production and use.[148]

The Irish government set the very ambitious goal of one million electric vehicles on Irish roads by 2030.[149] Lighter and stronger vehicle frames made with nanomaterials could help efficiency but better batteries are also required. Improved batteries, with higher energy storage densities, have already enabled many technologies such as smart phones and drones. However, for transport purposes further improvements would make electric vehicles more competitive with conventional engine vehicles. A class of ultra-thin nanomaterial called MXenes, used in battery electrodes, is one possibility offering better battery lifetimes. Irish researchers have shown such batteries could triple storage capacity compared to conventional materials, which would extend the distance electric vehicles could travel.[150]

The decarbonisation of energy intensive industry can also be aided through the use of nanotechnology. For example, the production of steel without the use of fossil fuels relies on hydrogen.[151] This can be produced by the splitting of water, but it requires large amounts of energy. Nanostructured materials are being developed to improve water splitting, and so provide an energy efficient and cost effective way to produce 'green' hydrogen from water, and to provide a safer way to store it.[152] Researchers in Ireland are developing porous nanomaterials called metal-organic frameworks, which can be used for hydrogen storage, but can also directly reduce greenhouse gases by taking carbon dioxide out of the atmosphere.[153]

Nanotechnology is also used to improve energy efficiency. For example, the miniaturisation of transistors to the nanoscale has been accompanied by a reduction in power consumption and the use of quantum dots can be used for efficient lighting.[154]

Materials

Nanoscience can help us understand the lifecycle of the products we use. When plastics degrade, they produce tiny fragments or microplastics. Environmental scientists have found microplastics are one of the most common types of marine pollution and can enter and accumulate in the food chain.[155] Little is known about the effects of eating microplastics. Researchers in Ireland have also shown that micro and nanoscale plastics are much more common than previously expected. Their research showed plastic baby bottles can be a source, resulting in infants ingesting millions of plastic particles per day.[156] The safe use of nanoparticle additives also needs to be considered for products known to wear with use, for example OECD studies have assessed the use of nanotechnology in more efficient tyres.[157] It is difficult to know how and where nanomaterials may be released into the environment due to the wide range of applications and pathways for release. The OECD has also identified, in a report on Nanomaterials in Waste Streams, the need for further research on waste containing nanomaterials.[158] It noted:

> *"It is anticipated that, as the production and number of nanomaterial applications increase, waste streams containing nanomaterials will also increase, and in addition to naturally occurring nanoparticles, engineered nanomaterials possibly might become more widespread in the environment, if insufficient knowledge about the fate and associated risks of nanomaterials released from waste treatment operations, as recycling, could result in inadequate management."*

It is also important to examine the environmental impact of the raw materials needed to produce devices and where they ultimately end up. Rare elements, such as gold and platinum, often have novel and transformative properties when used in nanotechnology, and these are commonly used in consumer electronics. For example, mobile phone can contain more than 30 chemical elements. This requirement for varied raw materials has implications for society, as the demand for some of these scarce elements has led to a trade in 'conflict elements', which has seen child labour being used in some mines.[159] One way of ensuring a more ethical supply of materials is recycling. For example, in 2017 Apple announced a goal of making its products from 100% recycled or renewable materials,[160] but such goals can be challenging due the diversity of materials used. However, the use of novel nanomaterials from more common elements, such as carbon, may replace the need for some of the scarcer metals.[161]

Understanding the place of technological innovation within the circular economy is important, not just in terms of materials but also in how products are consumed. Using additive manufacturing, nanomaterials can be printed to produce cheap disposable electronics, which could increase electronic waste. Nanotechnology could either help or frustrate the "right to repair" electronics, by inclusion of sensors to warn when components need replacement or preventing consumer access to components by deeper nanoscale integration.[162] The ability to repair electronics rather than replacing the entire device is an effective way to cut greenhouse gas emissions and electronic waste.

The gaps in knowledge surrounding the life cycle of nanomaterials is a recurring issue. This can only be resolved by longer-term planning. Academic researchers are not typically required to consider the life cycle of new materials when seeking funding to support their investigations.[163] Introducing such a measure at a national level could be a step to enable better future traceability and encourage sustainable practices.

Regulation of Nanotechnology and Nanomaterials

Regulation in nanotechnology is primarily driven by the practical risks associated with nanomaterials rather than ideas of uncontrolled nanoscale mechanisation.[164] Developing regulations based on risk is difficult as there is nothing inherently dangerous about nanosized materials, rather the hazards are circumstance specific. Nanomaterials existed long before our relatively recent ability to see, develop and intentionally use nanoscale materials. As noted, many nanoparticles occur naturally and as by-products of human activity[165], and our exposure to incidental background nanoparticles is much higher than the engineered particles being developed. However, with more new products containing nanomaterials the levels and variety of exposure are likely to increase, and it is important that their use is guided to safeguard human health and the environment. In addition, with increase scientific understanding, the regulation of existing products may need to be reviewed to account for their nanoscale features and by-products.[166]

The complex nature of nanotechnology reflects the difficulty in developing clear regulation around its use. Currently, the regulatory frameworks for nanomaterials within Ireland are mainly set at EU level. These regulations primarily focus on chemical substances rather than specifically on nanomaterials. However, more recently, additional guidance has been added to these regulations to address the specialised concerns when assessing nanomaterials.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals, EC 1907/2006[167]) is the over-arching European legislation applicable in Ireland on the manufacturing, importing, marketing and use of chemical substances.[168] Nanomaterials, while not referenced directly, are covered by the term "substance" in REACH. Under REACH, substances manufactured in quantities of one or more tonnes must be registered and supply chain information must be provided, which applies to nanomaterials as it does for any other substance. Changes in the REACH regulations, made in 2018, address nanomaterials specifically and provide clarifications and new provisions in the chemical safety assessment, registration information requirements and downstream user obligations.[169] As of 1 January 2020, explicit legal requirements under REACH apply for companies that manufacture or import nanomaterials or nanoforms. The European Chemicals Agency (ECHA) provides guidance for the characterisation and hazard assessment of nanomaterials.[170]

The implementation of these regulations is advised by the ECHA Nanomaterial Expert Group (NMEG). The NMEG aims to seek common ground among experts on scientific and technical issues relating to the implementation of REACH; Classification, Labelling and Packaging (CLP) regulation and the Biocidal Products Regulation (BPR) for nanomaterials. While the group draws on experts from across the EU, it is notable that Ireland does not currently have a representative, despite the importance of nanomaterials to its industries.[171]

Information on nanomaterials is also shared under the OECD Mutual Acceptance of Data (MAD) in the Assessment of Chemicals multilateral agreement of 1981 (OECD/LEGAL/0194).[172] The shared data from tests that follow OECD guidelines are accepted by all member states, and include information on:

- Physical and chemical properties;
- Environmental fate (degradation and accumulation); and
- Environmental and mammalian toxicology.

The sharing of chemical information reduces duplication, saving governments and industry around €309 million each year. However, these guidelines were not originally developed for nano-scale chemicals. The OECD has recognised manufactured nanomaterial may require additional testing and MAD is still being revised to assess nanomaterials.[173] Through the OECD Working Party on Manufactured Nanomaterials[174], more harmonised assessment of nanomaterials, allowing the design of safer products, is expected within the next few years.

The development of regulations for nanotechnology and nanomaterials, is at a decisive stage. The regulations are either new or not fully developed in many cases. Standard assessments for nanomaterials are not yet fully agreed and a need for clear guidance is recognised. A lack of clarity could delay applications in sectors where use has the potential to expand, such as in medicine and agri-food. To support innovation and future industry, while maintaining safe and sustainable practices, it is important that Irish nanotechnology stakeholders based in academia and industry are engaged with international efforts to develop suitable frameworks. This requires communication between legislators and stakeholders and supports to leverage their expertise.

Concluding overview

The use of nanotechnology is well established in some sectors and its applications are continuing to grow. In areas such as information and communication technologies, Ireland has seen economic returns on investments made in infrastructure and developing expertise. The capacity and knowledge built over the past decade needs to be sustained and managed to continue benefiting from the growing diversity of nanotechnology applications. Nanotechnology naturally crosses disciplines, meaning potential applications of nanotechnology are diverse. There are however a number of key areas in which nanotechnology can be expected to have a significant impact in Ireland:

- The use of nanotechnology could enable us to respond to environmental and climate change commitments.
- Nanotechnology will continue to define and underpin developments in information communication and digital technologies.
- There are opportunities for the expanded use of nanomaterials in sectors such as manufacturing, medicine and agri-food.

If Ireland is to retain its competitive advantages in these sectors, and take full advantage of new opportunities nanotechnology may bring, there is a need for forward planning which includes proactively dealing with the impact and life cycle of new materials to guarantee their environmental sustainability. This requires measures that create a robust environment for innovation and the cooperation of academia, industry and regulators. Measures that would help create this environment include:

- Secure support and steady development of centres of excellence that cover the whole innovation chain, from concept to market, and with strong links to industry. Such centres can retain expert knowledge and technical skills, rather than being lost by intermittent cycle-based funding. In addition, they could also be used to channel the much-needed engagement of researchers in the development of regulations and be a hub for research and development for small and medium enterprises.
- Publicly funded research can be used to guide development towards sustainability if awards to investigate and develop new materials and products consider the lifecycle, and place within the circular economy, of new materials and products at this point of first innovation.
- Continued investment in high quality educational programmes and support of academic research infrastructure to encourage broader long-term innovation. This would include the upskilling of the work force in industry as new technologies are introduced and would provide the skill bases needed for enterprise.
- Irish engagement with the creation of European and international standards for the use of nanomaterials and nanotechnology in industry and medicine.

The expanding use of nanotechnology will continue to shape the development of our economy, society and how we interact with the environment. Provided the long-term implications of its use are properly considered, it has the potential to enhance our quality of life by providing better healthcare and helping us meet the challenges of environmental sustainability.

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