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Report on Nanotechnology in Agrifood

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Executive Summary

The agrifood industry is the largest manufacturing sector in Europe. According to the European Technology Platform Food for Life "the agricultural sector employs over 11 million people (2.3% of the population of the enlarged EU)" and "the food and drink industry had a turnover of 810 billion euro in 2004, transforming over 70% of the EU's agricultural raw materials and employing over 4 million people, the majority within the SMEs sector."

There are a number of issues facing the industry:

- Shifting demands (and their articulation) from fork to farm: In the past the agrifood industry was driven by improvements to mass production and supply. However, increasing consumer interest and concerns over how and where food is produced and processed, means that this situation is becoming reversed as consumer requirements play a larger role (at least in the developed world). An increase in consumer choice through production of a variety of options, as well as catering for (an ever increasing number of) niche markets, means a more diverse and complex agrifood industry.
- Adaptive supply chains from farm to fork: There is a shift from stable supply chain[i] relations to more flexible and agile relationshipsm with shifts and reorientations based on the needs of the value chain. This means suppliers need to remain aware of the dynamics of the value chain and adapt meaning a constantly co-evolving situation between supply and value chains.
- Environmental sustainability and Agricultural management: As with all industries, agrifood needs to be environmentally sustainable. This encompasses new legislation affecting the number of pesticides which can be used; decreasing agricultural waste (or finding novel uses for it), for example Europe's fruit and vegetable industries generate about 30 million tonnes of waste a year[1]; and reducing the amount of waste at the end point (e.g. packaging).
- Decline in food scientists: With fewer students enrolling in food science programmes in universities, there could be a real shortage of trained personnel within the next decade. This would hamper development of new technologies and process innovations, at a time when there will be a greater pressure to deliver on the issues mentioned above namely environmental sustainability, more adaptive supply chains and shifting consumer demands.

Regarding nanotechnology, many different national and regional programmes dedicated to agrifood are already underway or under development. For example the EU finances a number of industrial collaborative projects through the Framework Programmes, and national programmes include Japan (CSTP Strategic S&T Priorities in Nanotech. & Materials)[2], US ("Nanoscale Science and Engineering for Agriculture and Food Systems", a part of the National Research Initiative (NRI)), Nano4Vitality in the Netherlands (€12M over 4 years).

Estimates vary for the number of companies involved in nanotechnology and agrifood global markets. For example, Cientifica estimates that 400 companies are applying nanotechnology to food at present, but points to difficulties in measuring the full scale of development because many companies regard their nanotech R&D products as sensitive, and the Helmut Kaiser Consultancy estimates that the global nanofood market will be worth 20.4 billion USD in 2010.

This report divides nanotechnology in agrifood into three subsectors: agricultural production; food processing and functional food; and food packaging and distribution.

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[i] Supply chain is taken as the provision of an element to a food product (such as wheat, barley, bioplastics for packaging ertc.) and value chain is the chain of developments from rw materials to end product in the grocers, on the shelves of supermarkets or for sale directly from source. Thus the value chain is a complex interlinking of many supply chains, requiring a great deal of management and coordination. ICT is playing a large role in this adaptive supply chain management but is beyond the scope of this report (for more information on advanced supply chain management see Ivanov Sokolov and Kaeschel (2009). A multi-structural framework for adaptive supply chain planning and operations control with structure dynamics considerations. Journal of Production, Manufacturing and Logistics)

Agricultural production: this section describes the processes to produce materials from plant cultivation and raising domesticated animals, including foodstuffs, fuel, and raw materials for other industries such as the pharmaceutical, textile, and construction industries. It covers novel sensors and diagnostic devices, delivery systems for pesticides and nutrients, and describes how nanomaterials are now being manufactured from agricultural waste and through biological processes.

Food processing and functional food: this section describes the processes and equipment involved in turning agricultural produce into consumer products. It also includes the mechanisms in place to ensure quality control, one of the key areas in industrialised food production. It covers mechanisms for quality control including sensors such as electronic tongue and noses; equipment coatings and filtration systems based on nanotechnology that could bring efficiency gains for food processing; and the manipulation of the nanostructure of foodstuffs to engineer novel sensations and to improve the nutritional quality of processed food. It also describes functional foods, and the growing field of nutraceuticals.

Food packaging and distribution: this section describes materials used to preserve and protect fresh and processed foods, and the procedures and systems in place to monitor supply chains and authenticate items. It covers nanocomposite materials used to improve the barrier and mechanical properties of plastics; new bionanocomposites that can be compostable and promise solutions to waste management issues and sustainability; active and smart packaging that currently provides visual indicators to a foods' freshness, and promises advanced innovationsthrough active intreractionof packaging with the internal environment and the food itself, through encapsulation technologies.

1. Nanotechnology in Agricultural Production

Keywords: sensor, diagnostic, nano-emulsion, cantilever, nano clay, precision agriculture, pesticide, nanocomposite, biogenesis.

1.1 Definition

Agricultural production for the purpose of this report is defined as the processes to produce materials from plant cultivation and raising domesticated animals. This material includes foodstuffs, fuel, and raw materials for other industries including the pharmaceutical, textile, and construction industries.

1.2 Short Description

Global agriculture today faces several issues: maximising land-use in different environments, sustainable use of resources (in particular fresh water) and ensuring that practices do not have an adverse impact on the environment (e.g. accumulation of pesticides and fertilisers). At the same time there are opportunities for agriculture to expand into new areas, for example the utility of what would previously have been regarded as agricultural waste which now can be used for industrial processes.

This report covers the application of nanotechnology developments in agricultural production. It is divided into five areas:

- sensors and diagnostic devices (to monitor environmental conditions, plant and animal health);
- disease and pest control (including the use of novel delivery systems for pesticides, and limiting the environmental impact of agrochemicals);
- water and nutrient control (including the use of novel delivery systems, and filtration and remediation systems to ensure access to clean water);
- genetic engineering of plants and livestock to improve productivity;

- agriculture as a means to produce nanomaterials (either harvesting natural nanomaterials from, generally, waste material, or using plants and microbes to manufacture nanomaterials).

This report will provide an overview of the state of research and development in each of the above areas, highlight additional research needs, review applications and perspectives, compare the current situation in the EU with other global regions and pick out key players.

Much of the first three sections relate to ‘precision farming’. This is the use of GPS, GIS and networks of sensors and actuators throughout an agricultural area that measure and report on (and in some case respond to) a number of different environmental, crop and pest variables. These effectively support the experience of the farmer by providing data and statistics that allow the farmer to make informed choices for intervention, including irrigation, fertilisation, pest control and even harvest. Although costly, this is becoming largely offset by the rising cost of food, the need for higher quality and increasing legislation.

1.3 State of R&D

1.3.1 Sensors and Diagnostic Devices

In agricultural production, sensors and diagnostic devices allow farmers to closely monitor environmental conditions, plant and animal health and growth. As part of precision farming they can facilitate targeted and early intervention, thus increasing productivity and decreasing the use of agrochemicals (e.g. antibiotics, pesticides, nutrients).

Sensors and diagnostic devices are used to measure a number of important variables for agriculture:

- physiological status of crops (such as growth rates, nutritional levels, crop maturity, disease status)
- physiological status of livestock (such as body temperature, respiration rate, blood biochemistry, disease status)
- presence and identification of pests or pathogens
- environmental variables (ambient temperature, levels of water and nutrients in soil)

They are also an essential element in the measuring of the environmental impact of the agricultural process itself, in particular the levels of pesticides and fertilisers in soil and run-off.

The technology already exists to measure each of these variables,however, the technology is not fully optimised for the user. For example, a measurement usually requires an individual to go physically to the location, obtain a sample and have this analysed at another location (usually an analytical lab). This process requires technical expertise, is labour-intensive and can take a number of days, by which time the opportunity for optimal intervention could be missed. By providing robust portable and/or remote in situ sensing and monitoring, backed up with analytical software, farmers can begin to make their own informed choices, in real-time, thus restricting the application of agrochemicals to and limiting the need to acquire technical support only when necessary.

A variety of different sensor and diagnostic systems based on nanotechnologies have potential application in the agricultural industry, these are described in the following sections and are summarised in table 1 below.

Technology	Description	Principle agents detected	Maturity
Uni-molecular sensors	Biomolecules enclosed by or attached to nanostructured materials such as liposomes, nanoparticles or carbon nanotubes. Detection is measured by electrochemical or optical readout.	Pesticides, gases.	Basic and applied research.

Bio-arrays	Biomolecules conjugated to substrates. Readout by chemical or electronic means.	Different chemical species and microbes.	Some mature, but application in the field still at the applied stage.
Solid-state sensors	Thin film or nanowire sensors. Readout by electronic means.	Gases.	Early-stage.
Optical and spectrographic sensors	CCD, lasers and spectrometers.	Plant growth, presence of various chemical species.	Some mature, but application in the field still at the applied stage.
Sensor networks	Individual sensor nodes that can be dispersed throughout an area, measure local variables and report to a central processing unit.	Potentially all desired variables.	Microsystems technology is mature. Nanotechnology developments still at basic and applied research level.

Table 1. Different sensor systems which could be used in agricultural production.

1.3.1.1 Uni-molecular Sensors

Bio-sensors utilise biomolecules to detect targets. However, the format of bio-sensors varies, from free molecules (molecular sensors) to those conjugated to a substrate such as nanoparticles, nanowires, nanotubes, and thin-films. Interaction of the target with the biosensor can be measured either directly or indirectly with readouts taking the form of changes in colour, fluorescence and electrical potential. In array technologies, multiple biomolecules are fixed to a substrate allowing multiple analytes to be measured simultaneously.

A number of different sensors, based on a nanotechnology platform and incorporating single biomolecular species have been studied, including acetylcholinesterase (AChE)[3,4m5], glucose oxidase[6,7], glucose dehydrogenase[8], tyrosinase[9,10]. For the agricultural and environmental industries it is the development of technologies based on AChE and tyrosinase which have gathered greatest interest. AChE is an enzyme that is involved in nerve signalling in many different species, and is inhibited by organophosphate and carbamate pesticides, and heavy metals. This inhibition can be measured by the failure of AChE to catalyse the conversion of substrate, or an analogue, that would normally result in a pH decrease. This pH decrease can be measured electrochemically, or by using a dye molecule that is sensitive to pH changes and exhibits a change in colour or fluorescence. Tyrosinase can catalyse the oxidation of phenolic compounds, which are present in many industrial wastewaters and are also used as pesticides.

Uni-molecular species can be either attached to an electrode or encapsulated in some form of matrix or other capsule, the nanostructured materials include liposomes[11], self-assembled monolayers[12], carbon nanotubes[13,14], nanoparticles[7,9,10]. Each provides increased sensitivity through the greater surface area of the nanoparticle; allowing either more of the biomolecule to be present, or greater access to the analyte. In the case of electronic detection the nanostructured material coated with biomolecule can either form the electrode itself or be used to coat the electrode (e.g. nanoparticles and self-assembled monolayers). While electrode based systems offer the convenience of an electrical readout, encapsulation affords greater stability (for example AChE is stable for at least 50 days at 4C when enclosed within liposomes)[15]. Whichever approach is used, sensitivity is better than that required to detect minimum legal safe limits, capable of detecting pesticide down to levels of 10^{-10} to 10^{-11} M [1,2]. While AChE sensors do not show specificity towards individual pesticides, they are cheap to manufacture and useful for an overall measurement, and therefore could be a tool for rapid assessment in the field, with follow-up as required in an analytical lab. However, to date there have been no field trials using such sensors with non-purified samples, a point which will need to be addressed.

1.3.1.2 Bio-arrays

Bio-arrays link several different biomolecules to a substrate in such a way that each is individually addressable. Arrays have been made using a number of different biomolecules, but have tended to concentrate on proteins (or parts of proteins) such as antibodies and enzymes, or DNA and RNA. These are quite mature technologies, having been developed and marketed by a number of companies for use in basic research, and diagnostic sciences (including forensics and medicine). To date they have largely been based on microsystem technologies and been used in laboratory settings, for measuring analyte concentrations in semi-purified (e.g. filtered and buffered) samples. Bio-arrays have the capability to simultaneously measure and quantify many different analytes (in some cases thousands). Such arrays are a mature technology manufactured by a number of different companies and used in fields as diverse as clinical diagnostics, environmental monitoring and bioscience research.

Nanotechnology is beginning to have an impact on bio-arrays. The advantages that it brings to such systems are: further miniaturisation, allowing more variables to be measured; greater sensitivity, thus requiring less sample material; faster detection rates, allowing read-out in real time; and novel detection methodologies (e.g. electronic, colourimetric, fluorometric, and mass changes).

There are a number of different formats for bio-arrays include planar forms, with biomolecules directly attached to the flat array surface; cantilevers, with biomolecules attached to a number of individual micro-sized levers (which resemble diving boards); and biomolecules attached to nanowires or nanotubes which in turn are attached to a planar surface, with each attachment point being a unique electronic address.

Array technologies can be used at different stages of the food chain such as: detecting the presence of pathogens in livestock or crops; measuring the levels of toxins or nutrients in soils; and monitoring the quality of processed food.

Cantilever arrays are perhaps one of the most interesting as they detect the presence of specific target molecules in a mixed environment based on mass displacement of the cantilever when the target binds a reporter molecule attached to the cantilever[16]. In addition, they can operate in gas or liquid phases, giving rise to the electronic 'nose' and 'tongue'. These topics will be discussed in greater detail in the report on food processing.

One interesting example comes from the FP6 funded Automated Water Analyser Computer Supported System (AWACCS) project which produced and field tested an optical bio-chip, that was capable of providing information on up to 32 different analytes by means of an integrated optical chip from water from a variety of different sources with only a pre-filtration step required. The attainable detection limits were at levels below the EU recommended safe limits, and the chip could be reused up to 500 times[17,18].

Further information on sensor arrays can be found in the report on diagnostics, within the medicine, health and nanobio technology sector.

1.3.1.3 Solid-state sensors

Solid state sensors have at their core a conducting or semiconducting material, which can bind target molecules and record this as a change in electronic property (conductance, capacitance, resistance). Materials that have been used include oxides of tin, indium, aluminium, zinc and many others, as well as composites of these materials[19].

Solid state sensors are primarily used to detect gases; for example, nitrous oxides, oxygen, carbon mono and dioxide. Although being largely used for the monitoring of combustion processes (e.g. automotive) and for environmental pollution, they have potential applications in agriculture, where the levels of the above gases give good indication of the growth status of the plant being monitored.

Further information on solid-state sensors for gas detection can be found in the security technology sector reports.

1.3.1.4 Optical and spectrographic sensors

Microsystems already exist which can monitor and analyse plant growth using cameras and sophisticated software, however these are expensive and can only provide trend analysis, with little real-time data. A useful system would monitor overall plant health and inform the farmer if growth is retarded, if physiological changes are evident, but not yet manifest on a visual level, and the best time to harvest.

Hyperspectral sensing (imaging spectrometry) was originally developed for mining and geology. It measures reflected radiance (UV to infrared) as a set of hundreds to thousands of contiguous spectral bands. From this data it is possible to distinguish between different mineral types. However, it has more recently been applied to vegetation and can be used to determine plant coverage and growth rates. Largely this technology depends on aerial or satellite imaging, however portable, ground-based sensors can also be used[20].

At present there do not appear to be any nanotechnology applications in this area. However, advances discussed in other technology sectors (electronics and security) could be applied here eventually providing for cost effective and sensitive detection and analysis.

1.3.1.5 Potential Applications

Sensor networks for crops

These are effectively the combination of different sensor technologies described above with a means to communicate this to a central processing unit. Ideally they would be distributed over the area to be monitored (e.g. a field) and provide sufficient real-time data or the farmer to be able to monitor any localised changes in the environment, crop or livestock. Such systems exist and are already in use for the high value crops, e.g. vineyards, however they are expensive and relatively bulky (being based on microsytems). Nanotechnology advances could have a real impact through decreased size, cost, durability and longevity through advances not just in sensor technologies, but in energy supply and durability of materials.

Monitoring livestock

By monitoring variables such as body temperature, heart and respiration rate, and eating and drinking frequency, farmers can evaluate livestock, compare with previous statistics and make informed decisions in case of deviation. Of all of these parameters, respiration rate has been shown to be a good indicator of animal stress[21]. However, conventional systems are ill-suited to the task of automated recording of such physiological data. Where monitoring livestock is not possible, then measuring local weather conditions can be used to infer impacts on respiration rate.

1.3.2 Disease and Pest Control in Crop Plants

Pesticides are used to kill organisms that are detrimental to agricultural production, including viruses, bacteria, fungi, parasites, weeds, and insects. They have been used for millennia (sulphur being the first recorded), however, modern pesticides place their own burdens on farming systems, for example accumulation in soils and ecosystems which can have unexpected and often deleterious effects, as was the case with DTT. This is not just historic; atrazine is widely used to control weeds, but is persistent in soil (with a half-life of anything between 41 and 231 days, dependent on depth of soil and water content[22]). It has a permissible limit of 3 ppb, but this is often exceeded locally and it can also migrate far leading to contamination of rivers and drinking water. The situation is further deteriorated when one considers that, depending on the environmental conditions and mode of application, as much as 90% of conventional pesticides are lost to the air during application, as run-off, or decompose; affecting both the environment and cost to the farmer[23]. There is therefore an urgent need to a) find alternatives to current pesticide deployment and b) find ways of rapidly and locally detecting levels of the pesticide and either removing or degrading it. Several systems based on nanotechnology are being developed for the purpose of detection (see section above) and degradation of pesticides (see environment report).

In the last few years there has been much activity by companies in the re-formulation of pesticides which are coming off patent, to protect market position. This is largely in the area of new adjuvants or delivery systems (as is the case with pharmaceuticals). For crop pesticides it is also driven by the need to resolve issues with current formulations including: use of organic solvents (many pesticides are poorly water soluble, and many of the organic solvents used in their formulations, such as benzene and toluene, are toxic); sensitivity to UV light (many have half-lives measured in hours or minutes, e.g. phoxim 40 minutes, avermectin 6 hours), bioavailability (crossing plant cell walls), deposition and drift (due to droplet size when spraying), foaming, rain-fastedness (sticking to leaves) and combining multiple pesticides into a single product.

Another issue is that of legislation. In the EU there is a drive to limit the numbers of pesticides available. Directive 91/414/EEC is the EU regulation covering the use of pesticides, and is essentially risk-based. However recent amendments could decrease the number of pesticides available to farmers (15% of the 300 accepted chemicals have been estimated by the UK government's Pesticides Safety Directorate), which various agrifood industry associations are concerned could affect yield and quality of produce[24].

The solutions are then to move towards measured release of small (but sufficient) amounts of pesticide over a period of time, in response to environmental stimuli (e.g. UV, moisture, temperature) or to target the pest more effectively.

This involves formulating the pesticide with a carrier, most of which are lipid or polymer based (nano-emulsions), however other systems including silica and nano clays are also being developed.

1.3.2.1 Nano-emulsions

Nano-emulsions are highly stable systems that show little coalescence of particles, nor sedimentation or creaming. They can consist of lipid or polymeric vesicles or particles, in the size range of 20-200 nm. They can have multiple phases, the simplest being oil-in-water. They are essentially similar to emulsions in that they require energy input to be made, and differ from micro-emulsions which form spontaneously when surfactants are added to a liquid medium (and are therefore technically not emulsions). Both nano- and micro-emulsions have particles within the same size range. The organic phase is non-toxic and can be made from food grade components. Nano-emulsions of solid particles can be dried, through evaporation of the outer phase, to leave particulates, which can then be suspended in another solution for application. Through encapsulation, the active ingredient is afforded some protection against atmospheric and environmental conditions, such as oxidation, and is released slowly.

Nano-emulsions can be produced by both high energy (mechanical process using rotators, ultrasound, or pressure homogenisers) and low energy (either spontaneous emulsification, due to solvent diffusion as a result of mixing or dilution; or by phase inversion temperature, a process which is controlled by specific surfactants, such as polyethoxylated surfactants, in response to temperature change) means[25]. In each process the active elements can be added during the synthesis stage (e.g. agrochemicals, nucleic acids) so that they are encapsulated by the nanoparticle or vesicle. High energy systems offer more control of size distribution and composition of the resultant nanoscale vesicles or particles, however complex and 'fragile' chemicals can be easily degraded during the process and they are not readily scaled up to the large volumes required by the manufacturing industry. In contrast, the phase inversion temperature system in particular, is readily scaled up to industrial levels. In addition, it affords the opportunity (with certain compositions) of effecting a phase inversion, e.g. oil-in-water to water-in-oil, during a transitional phase by changing the temperature, before the system is stabilised as a nano-emulsion.

In terms of agricultural applications, nano-emulsions can be used for hydrophilic and hydrophobic pesticides, but are largely being developed for those that are poorly water soluble. For example, pyrethroids such as γ-cyhalothrin and β-cypermethrin have been successfully formulated as lipid nano-emulsion, obviating the need for the organic solvents such as benzene and toluene normally required for its formulation[26,27,28], as have more ecologically friendly pesticides such as *Artemisia arborescens* L essential oil[29]. In one case the effects of such pesticides on aquatic life were studied and found to be reduced compared with conventional formulations, while not affecting efficacy[26].

In addition to exhibiting greater stability, nano-emulsions demonstrate increased coating of leaves and uptake through plant cell walls, as a result of low surface tension[27,30].

The main advantages to using nano-emulsions are therefore- solubilisation of hydrophobic pesticides (hence no need for toxic organic solvents), no precipitation or creaming (therefore no need for constant mixing), increased stability (protect against oxidation), improved uptake. However, it should be noted that manufacturing opportunities are limited, as the precise mechanisms by which nano-emulsions form and their properties controlled are still the subject of intense basic research.

1.3.2.2 Formulations using other nanostructured materials

Silica has been developed and commercialised for a number of years for medical applications[31], as it is known to be biocompatible and biodegradable. It can also be engineered as hollow nanoparticles with different pore diameters and shells of different thickness. This has led a number of research groups to investigate its potential as a drug delivery vehicle for medical and veterinary treatments, and more recently for pesticides, such as avermectin and validamycin, where it has been shown to afford protection against UV degradation and controlled release dependent on pore diameter and shell thickness[32,33]. Nano silica has been reported to provide insecticide activity on its own, through dessication of insects' cuticles. It has also been successfully applied as a thin film to boost cereal germination and decrease fungal growth[34].

Nano clays and layered double hydroxides are also being developed in this regard[35]. Both materials show good biocompatibility, low toxicity and the potential for controlled release. Chemicals can be loaded between layers of both materials (an arrangement that can be influenced by buffer conditions, in particular pH). In the case of hydrophobic chemicals, this arrangement prevents re-crystallisation, increases solubility, and therefore bioavailability.

For nano clays controlled release can be engineered through coating with different polymers, which manipulates electrostatic interactions between the chemical load and the clay particles[36]. In addition, nano clays can protect against UV-degradation of pesticides[37].

Layered double hydroxides have high affinity for anionic species and are dissolved in acidic conditions. A number of experimental studies have demonstrated their potential use in the deployment of agrochemicals such as fertilisers[38], plant growth promoters[39], and pesticides[40].

1.3.3 Disease and Pest Control in Domesticated Animals

Potential applications for controlling pests in domesticated animals based on nanotechnology developments, are broadly similar to those developed for human health, and include liposomes, polymeric nanoparticles, and nanoshells. However, these must take into consideration other factors such as species specific treatments and application methods, and the non-trivial aspect of cost (some species, such as chickens, have high numbers and a low profit margin). Many different economically important diseases are poorly controlled by existing technologies, for example nematode infestation, tuberculosis, foot and mouth disease, swine fever, avian influenza. This can be at the level of prevention, e.g. due to poor responses from existing (such as live attenuated strains or subunit vaccines) or inadequate therapeutic measures in diseased animals.

In most respects, the most convenient and inexpensive way to deliver treatment to domesticated animals is through feed or water. This is already the case for the use of antibiotics to combat bacterial infections (e.g. in poultry). For vaccination against disease however this is still largely delivered by injection, although there is much active research to develop efficacious aerosol vaccines that can be delivered to airways[41,42,43]. Nanotechnology may be applied to these measures, however at present there is little work reported in this area. Of the research that is underway, the use of conjugated nanoparticles is perhaps the most promising. These can be absorbed by the vaccinated animal's immune system leading to responses similar to that observed with the live pathogen. Although the research in this area, as far as animal health is concerned, is limited, there are published reports on foot and mouth disease[44,45] and swine fever[46]. Other systems that are being investigated include chitosan nanoparticles for fish oral vaccination[47], nasal vaccination against swine atrophic rhinitis[48], and as anti-bacterial agents in a number of settings.

Other preventive measures include the use of nano-clays to bind to mycotoxins on grain used in animal feed (these are non-toxic and have the additional benefit of aiding digestion)[49,50].

1.3.4 Water and Nutrient Control

Access to clean water is and will continue to be a global issue according to the WHO, which estimates that 20% of the world's population have inadequate access to clean drinking water and that by 2025 the increased demand on water supplies will mean that each person will have approximately 25% the volume that they would have had in 1960. Agriculture places considerable demand on fresh water and in turn, contributes significantly to pollution of groundwater through the use of pesticides and fertilisers.

In addition to contributing to decreased use of pesticides in the environment through improved delivery mechanisms, nanotechnology can enable better use (and re-use) of water, and active degradation of agrochemicals. This will be of particular importance for the continuing "greening" of different global regions (e.g. sub-Saharan Africa) to boost the levels of arable farmland available to developing countries.

1.3.4.1 Water use in agriculture

Considering the volumes of wastewater produced by farms on a continual basis, any technology for remediation and purification will need to be capable of dealing with large volumes and be cost effective. Clays, and more recently nano clays, are one such class of material. These have demonstrated ability to filter and bind to a variety of toxic substances including pesticides, either on their own or as part of a complex with other chemical species[51,52]. They are also relatively inexpensive, requiring little processing from the excavated clay.

Remediation of contaminated water can be achieved through photocatalytic breakdown. Using titanium dioxide nanoparticles (another relatively inexpensive material) a number of research groups have demonstrated degradation of a variety of agrochemicals by passing contaminated/waste water over filters coated with TiO2 nanoparticles and exposed to normal daylight conditions[53]. Field trials are currently underway in Canada to investigate the efficacy of large transparent and porous tubes containing TiO2 to photocatalyse the degradation of chemicals in ground water, by sinking these into bore-holes[54]. Requiring no external energy supply, these have potential to be used throughout the world.

1.3.4.2 Nutrients

Nanotechnology applications in enhancing nutrient uptake are largely restricted to crops, i.e. fertilisers (developments in the areas of functional foods and nutriceuticals are described in the report: "Nanotechnology in Food Processing").

In most cases fertilisers are applied directly to the soil. The critical factor is that the fertilisers remain available to the crop for a sustained period, not only to limit the number of applications (and therefore cost) but also the levels in run-off (e.g. the WHO recommends that nitrate levels are limited to 50 milligrams per litre). Promising applications are those that retain fertilisers (or water) in the soil. Included here are nano-clays which, as already discussed, are highly absorbent and capable of slow release of intercalated chemicals[55,56]. However, there are other alternatives to soil-based systems- for example one existing patent states that foliar delivery of nutrients to plants is 95% efficient, compared with 10% for soil[57].

1.3.5 Genetic Engineering of Plants and Livestock to Improve Productivity

Despite the controversy over genetically modified crops in the 1990's, as a result of advance in biotechnology, genetic engineering is still pursued to introduce new traits to crops and potentially livestock, whether these traits are naturally evolved in that species or are adopted from other species. In the case of crops the goal is to improve productivity, adapt the crop to different environments, or decrease dependence on agrochemicals. For livestock the focus is more on isolating successful traits from individual animals (e.g. growth rate, disease resistance) and introducing these into others (the ultimate approach being cloning).

Many of the delivery mechanisms discussed above and in the reports from the Medicine, Nanobio and Health technology sector are applied for these purposes and will not be described again here.

The genetic engineering of crop species has grown into a big business, in the 25 years since the first was produced. In 2007, 671 field release permits for 54 different organisms were issued in the US alone, with an estimated 102 million hectares of genetically engineered crops planted worldwide in 2006[58]. Traditionally, novel DNA was introduced using an attenuated strain of bacteria, which infects a variety of crop species, or by a 'gene-gun' which shot particles of gold coated with the desired DNA into cells. Recently however, mesoporous silica nanoparticles have been used. These have the advantage over traditional mediated DNA transfer, in that they can deliver several different elements at the same time (e.g. different DNA sequences, or other chemicals or proteins which can promote the correct expression of the novel DNA)[59].

1.3.6 Agriculture as a Means to produce Nanomaterials

Agriculture provides the opportunity for the production of nanomaterials through the use of engineered plants or microbes, and through the processing of waste products (such as stalks and other cellulose materials).

1.3.6.1 Synthesis of nanomaterials from plant materials

Most polymeric materials for packaging, casings, composite components have traditionally been manufactured from fossil-fuel derivatives. However, the increasing costs of oil and consumer demand for alternative sustainable methods which have a lower environmental footprint have led a number of organisations to explore "green" material production, that is from renewable or sustainable sources that do not generate large amounts of waste (particularly hazardous solvents). In recent years, agricultural waste products have drawn attention as alternatives to fossil-fuel derivatives.

Nanocomposites afford enhanced properties compared with micro or macro composite materials. This can include increased strength and impermeability, while not increasing weight. The use of nano-clays to enhance the properties of fossil-fuel derived polymers such as nylon has already been realised by companies such as Bayer, Nanocor, and Honeywell which manufacture shatter-proof beverage bottles and transparent packaging.

In turn, nanocomposites based on biomaterials are attracting more attention because of their novel properties, that they do not depend on fossil fuels and are renewable, and also because they generally require less energy to manufacture, use less harmful chemicals, have fewer waste products and can be compostable. Many processes are being developed now that make use of traditionally harvested materials, e.g. wood pulp, or agricultural waste products, such as straw, and soybean husks[60,61]. For example, electrospinning can be used to produce cellulose nanofibres, which when mixed with other chemicals can be used to create composite materials with specific properties[62].

1.3.6.2 Biogenesis of nanomaterials

Production of metal nanoparticles can place a burden on the environment through the use of organic solvents which are toxic in the environment. Green production methods look to alternatives that are environmentally benign and often based on plant extracts or biomolecules (such as glucose), for example gold, silver, nickel, cobalt and cobalt-nickel alloy nanoparticles have been synthesised from aqueous salts using reducing extracts from plants and algae[63,64]. Taking this a stage further, plants and microbes have been used as "factories" to synthesise nanoparticles of silver using biomineralisation processes. New work has focused on fungi, which synthesise particles outside the cells, facilitating recovery[65,66]. These appear to be stable over periods of weeks and show little aggregation. Other research is looking at manipulating the natural biological processes of different organisms to generate functional nanomaterials, for example diatoms[67].

1.4 Additional demand for research

Sensor systems for agricultural production based on nanotechnologies are still largely at the basic research level. To progress towards application status will require demonstration of an ability to operate in the field, and scale-up to manufacturing levels. It is most likely that such systems will be based on solid state materials, as these are most mature and have demonstrated application in other sectors.

Disease and pest control in crop plants using nano-emulsions has some maturity; however these technologies are largely proprietary, making it difficult for other companies to develop new delivery systems for other chemical entities. Other systems, especially those using natural compounds are very much at the basic research level, and so will require significant effort to scale-up including extensive large scale field tests.

The situation in domesticated animals largely follows on from advances in human health care, with the caveat that cost per unit is one of the main challenges to uptake.

Similarly for water and nutrient control, there are systems that have been developed and commercialised (based on nano-clay particles, see below), however cost will be a major consideration.

Genetic engineering of plants and animals has the potential to improve productivity. However, existing systems for genetic manipulation based on biotechnology are mature and have demonstrated success; so nanotechnology enabled systems will be viable alternatives only if they decrease time to development and cost

Agriculture has great potential to produce nanomaterials, both from waste products (such as straw) and by biogenesis (e.g. through micro-organisms). The production of nanocomposites from biomaterials is at the applied research stage, however issues of manufacturing scale-up still need to be resolved. The biogenesis of nanomaterials is at the basic research stage, and will require significant effort to scale-up to industrial process level

1.5 Applications and perspectives

In the area of sensor systems based on nanotechnology, solid state sensors and bioarrays based are the most developed. These are however largely used in other application fields, such as bioscience R&D, environmental monitoring, and internal combustion engine management systems.

There is substantial commercial activity within the area of delivery systems (in particular nano-emulsions). Several companies hold patents on nanotechnology applications in the area of delivery (including for pesticides) such as BASF, Proctor and Gamble, Henkel, Dow Chemical, Syngenta, of which BASF is the most prolific. Several recent patents for nanotechnology enabled delivery systems that have application for pesticides are held by Chinese institutions.

Slow release systems based on nano-clays are available from at least one company (based in the EU), and have been trialled in desert regions[68]. A second company (based in the US) manufactures drip flow herbicide systems, which potentially could be adapted for fertiliser use[69].

Existing biotechnology solutions for the genetic engineering of plants and animals have been developed for the last twenty years or more, and are therefore mature. With regards to nanotechnology applications, there are no commercial applications yet, but some patents. One example specifically for plants is that from Integrated Plant Genetics Inc. which has patented a silicon carbide nanoparticulate delivery system.

Nanocomposites based on renewable biomaterials have a definite place in packaging in the future. Pilot projects are actively being pursued by a number of different companies to realise this (e.g the SustainPack FP6 project which brought together leading packaging manufacturers and research organisations to investigate how nanotechnology could improve biodegradable fibre-based packaging[70]).

1.6 Current situation within the EU

Maximising output, minimising waste, and reducing the impact on the environment are key drivers for the agricultural industry. The agriculture sector as a whole employs over 11 million people within the EU (approximately 2.3% of the population). As such it represents a major opportunity for innovation to ensure that the EU progresses towards the Lisbon goals. At present there appears to be little direct application of nanotechnology within agricultural production. The exception is in the development of new delivery systems, in particular for pesticides. Technologies developed for other sectors are, however, most likely to see agricultural applications in the future, including sensor technologies. Applications utilising agricultural and forestry products (in particular those materials which would normally be classed as waste products) as the raw materials for new nano-composites are a promising area, both for the decreased reliance on non-renewable fossil fuel derivatives and the value-added technology.

2. Nanotechnology in Food Processing and Functional Food

Keywords: quality control, sensor, thin-film, electronic nose, electronic tongue, nanofilter, functional food, nutriceutical, nano-emulsion, liposome, solid lipid nanoparticle, micelle.

2.1 Definition

Food processing for the purpose of this report describes the processes and equipment involved in turning agricultural produce into consumer product, and the mechanisms in place to ensure quality control. It also describes functional foods, and the growing field of of nutraceuticals.

2.2 Short Description

The food processing industry transforms raw produce from agricultural and fishery industries, and manufactures packaged foodstuffs for consumers. In the main ood processing is ultimately driven by two factors: increasing output and decreasing waste.[71] Wuality control is also a vitally important aspect within the processing chain, from delivery and storage of raw materials, through various processing stages to the packaged foodstuffs that leave the factory for the retailer.

This is the central pillar of the agrifood industry, and although traditionally seen from the farm-to-fork perspective is now very much seen the other way round, with R&D and innovation driven by consumer needs. This requires a greater degree of responsiveness from the food manufacturing industry, sometimes to meet the needs of small sections of the population. There is growing acceptance of the need for a healthy and balanced diet creating a shift in consumer demand where traditionally consumers have grown accustomed to processed foods that are high in fat, salt, sugar and other flavour enhancers. In the EU this is emphasised in the vision document of the European Technology Platform ‘Food for Life’[72].

This report also describes the issue of bio-fouling, the implications this has for the food-processing industry and what nanotechnology enabled developments could be used to reduce the incidence.

The report is divided into the following three sections:

- quality control
- processing technology
- functional foods

2.3 State of R&D

2.3.1 Quality control

From the moment food enters the food processing chain it is monitored for a number of different aspects to ensure that it meets specific standards and continues to do so. The industry terminology for this process is Hazard Analysis and Critical Control Point (HACCP), which emphasises rapid and thorough analysis of raw foodstuffs before entering the process chain and in-line assessment of quality at key points, to ensure the quality of the final product. Key aspects are the detection and quantification of: agrochemicals (such as pesticides, fertilisers, antibiotics); other chemical contaminants (e.g. heavy metals); pathogens (in particular bacteria and fungi); and overall quality (measured by variables such as visual appearance, freshness).

2.3.1.1 Detecting chemical contaminants

Detection of chemical contaminants, such as pesticides, heavy metals, and antibiotics within food products is performed by gas or liquid chromatography followed by mass spectrometry, after extraction of a sample by suitable means. This is the industry standard, used by analytical agencies and departments worldwide, and developments as far as these systems are concerned focus mainly on decreasing the turn-around time while retaining sensitivity. This is a substantial business, with an estimated market of 55 million tests, worth 300 million euros, each year. Less than 5% of all tests are performed in-house and pesticides are estimated to account for 40% of this market[73].

Nanotechnology applications in this area have the potential for greater sensitivity and real-time detection, with lower sampling level; however they are very much at the basic research stage. Platforms include unimolecular sensors, sensor arrays, and solid-state systems (these are described in the reports 'Agricultural Production' and 'Packaging'). In contrast to other application areas (such as field monitoring), such systems do not need to be portable and can operate on standardised samples. However, they must accurately detect and quantify multiple analytes, if they are to replace the industry standard. Promising research includes electrochemical detection of various important chemical species (hydrazine, sulphite, nitrite) using composite electrodes containing gold nanoparticles[74] and immuno-detection using cantilever arrays conjugated to antibodies against specific pesticides[75].

2.3.1.2 Detecting biological contaminants

According to the European Food Safety Authority there were a total of 5,311 foodborne outbreaks, involving 47,251 people and resulting in 5,330 hospitalizations and 24 deaths in 23 Member States during 2005, the majority caused by *Salmonella* and *Campylobacter*[76]. Many of these illnesses are caused by bacterial enterotoxins, which are not easily removed from food, as they are often stable at temperatures used in normal cooking. To combat this, it is of critical importance to be able to detect food spoilage through bacterial, fungal or viral contamination at each stage in the food processing industry.

This is a major market, with an estimated 558 million tests performed each year, worth 1.45 billion euros. More than 90% are performed by service laboratories; however the use of rapid test kits is increasing. 70% of all tests are for *Salmonella* and *Listeria*[73].

At present such methods are largely based on classical immuno- (e.g. ELISA) or DNA (e.g. PCR) assays, which require some sample preparation and have a turnaround of a day or two. Although this is much quicker than other techniques (such as isolation and cultivation of microbes), there is still scope for greater sensitivity and faster detection times. The key drivers are lower detection limits, real-time detection, higher throughput, and discrimination between different species.

Most systems detect microbial components, rather than intact cells. Protein detection systems are favoured, as this increases the probability that the intact microbe is present and also screens for the presence of important bacterial enterotoxins and fungal mycotoxins (which can be present in the absence of viable microbes, and are responsible for significant illnesses). In general, such systems must be able to detect the presence of 10-100 infectious particles per ml. There are various biosensor platforms in development which are based on nanostructured materials, while there are large amounts of research on the development of electronic platforms (principally amperometric, but also voltametric and impedance) there are also efforts in the area of optical and mass change detection. In each case the nanostructured material is decorated with biomolecules capable of interacting specifically with the target analyte. This interaction is transduced by the nanomaterial into a quantifiable signal:

- electronic biosensors, based on protein conjugated nanowires[77,78], and carbon nanotubes[79]. These directly quantify the presence of specific analytes (e.g. proteins, nucleic acids, metabolites) which directly or indirectly indicate the presence of the microbe. As the output is an electrical signal, such platforms have the potential to be linked to other devices allowing data to be transmitted, shared and analysed further. By virtue of the nanoscale dimensions these demonstrate much faster electron transfer rates than microelectrodes, which manifests as higher sensitivity. CNTs have been combined variously with nanoparticles (e.g. gold or platinum nanoparticles or quantum dots) and polymer matrices to form composite materials with improved robustness and high porosity (facilitating entry of target biomolecules)[79]. Such composite electrodes exhibit even greater sensitivity.

- optical biosensors, with readout by a number of different techniques including surface plasmon resonance (SPR), fluorescence, colourimetric changes and based on a number of biomolecule-conjugated platforms including CNTs[80]; silica[81], gold[82,83], and latex[84] nanoparticles.

- mass-change biosensors, based on cantilever arrays, and piezoelectric devices[85,86]. Binding of analyte to the conjugated biomolecule results in changes in the resonant frequency of the nanomaterial, which is directly proportional to the amount of target bound, and can be read by, for example deflection of a laser beam.

Most of these technologies are still at the level of basic research; however Biophage Pharma Inc, in collaboration with NRC-Biotechnology Research Institute, has developed electronic biosensors capable of discriminating between different bacteria (in a process termed Electric Cell-Substrate Impedance Sensing, or ECIS). This is now at the pre-commercialisation stage and is expected to have applications for the detection of bacteria in water, food, and biological fluids[87].

2.3.1.3 Measuring quality with electronic noses and tongues

While it is important to detect and identify contaminants, it is equally important to manufacturers (particularly of high value foods) to measure the quality of their produce: primarily colour, smell, taste, and mouth-feel. Traditionally such quality control would have been performed by experienced individuals; however this is not always appropriate, especially for high volume foodstuffs. Developments over the last two decades based on semiconductor and polymer materials are going some way to automate the quality control procedures as far as taste and smell are concerned. These are commonly known as electronic tongues and noses[88]. The presence of specific chemicals within a sample (gas or liquid) can be quantified through changes in the electronic properties of the detector material as a result of binding that chemical species. By using different materials, or by doping the detection material, variable sensitivities to different chemicals can be engineered. These different detector materials are then arranged within the electronic nose or tongue; each constituting a separate electronic address. The detection profile (or fingerprint) from a sample can be used to determine the chemical composition and distinguish between different but related products.

Microtechnology-based systems are mature, for example commercially available electronic noses have been used to detect the presence of microbial contamination (indirectly, through the measurement of volatile metabolites)[89]. However, nanotechnology advances are expected to increase sensitivity and breadth of chemicals that can be measured, thereby giving greater discrimination between different chemical species over a wider range of concentrations. Recent work has demonstrated the potential for greater sensitivity, with electronic noses based on doped tin oxide thin films discriminating between two different red wines[90], and doped zinc oxide nanoparticulates discriminating between different vinegars[91,92].

2.3.2 Processing Technology

There are six events in food processing which together account for the greatest losses in productivity: breakdowns; set-up and adjustments resulting in downtime; small stops; reduced speeds; start-up rejects and production rejects. In-line quality control monitoring as discussed above can help resolve some of these issues, while advances in equipment coatings and new materials for waste management can help keep production in full flow.

2.3.2.1 Equipment coatings

Coatings for food processing equipment must be, first and foremost, non-hazardous to human health. Secondly they should minimise (or ideally prevent) biofilm formation which can lead to food spoilage and contamination, and finally they should be durable. Traditionally such equipment was manufactured from stainless steel as this is both durable and non-hazardous to human health. However, stainless steel is susceptible to pitting and scoring, which serve as focal points for microbial growth. As a result they require regular cleaning and disinfection, which at the very least means some production downtime, and can often require partial dismantling to allow access to internal spaces. The areas that are most prone to biofouling are heat exchangers. Bacteria that commonly contaminate food processing equipment include *Bacillus subtilis*, *Listeria monocytogenes*, *Staphylococcus aureus*, *Salmonella typhimurium* and *Escherichia coli*.

It has been known for a number of years that biofilms will grow in any nutrient rich medium and will strongly adhere to many different surfaces[93]. More recently it has been determined that the nanoscale structure of a surface can control the adhesion of biomolecules and by extension microbes[94,95,96]. Biofilms are a major concern to the food processing industry (as well as many other sectors, including medicine and marine industries) as bacteria within the biofilm are resistant to antibiotics and normal cleaning practices, but have the potential to 'break off' and contaminate foodstuffs.

Nanotechnology enabled processes can help resolve the issues of durability and biofilm prevention. This can be achieved through application of a coating or through the direct nanostructuring of the surface layers of the material. Both act to decrease the material's surface free energy thus decreasing the strength of microbial adherence. This can either help prevent adherence in the first instance or increase cleaning efficiency[97]. An established material that is widely used is Teflon (polytetrafluoroethylene), which has a low surface free energy, but poor abrasion resistance.

There are several methods for applying coatings to material surfaces:

- gas phase synthesis (e.g. chemical and physical vapour deposition, CVD and PVD, plasma and laser ablation). The material is vaporised by intense heat (e.g. laser) and then deposited on a substrate (usually under vacuum). This is generally expensive, difficult to scale-up and not suitable for temperature-sensitive materials (e.g. polymers, biomolecules).
- sol-gel processes. Reactants are mixed under defined temperatures and pressures to produce colloids of nanoparticles. Major issues include strictly defining particle size distribution (or porosity), preventing particle agglomeration, and the amount of waste material produced.
- electrospray and electrospinning. Reactants are passed through a fine nozzle, which is subject to a high voltage, causing the reactants to form charged droplets or fibres that are collected on a grounded collector. Such processes can be used to coat large surfaces.
- self-assembly. Reactants combine in a predefined manner to form a layer on the desired substrate.

Of these the most practical (in terms of cost, versatility and scale-up) is the sol-gel approach. Sol-gel techniques allow control of the porosity and nanoscale structure of the final coating (thus limiting microbial adherence) and can also incorporate anti-microbials (such as silver) and photo-catalytic materials (such as titanium dioxide). Both of these types of material help reduce biofilm growth.

For certain equipment parts, high durability is required. Diamond-like carbon (DLC) coatings (which are deposited by gas phase processes) show high durability and minimal biofouling. They are used in many different industries: for example, personal care (e.g. razor blades), car engine parts, medical device industry (e.g., implants such as stents and catheters). In food processing the applications are more likely in non-food contact areas, as there is experimental evidence that DLC coatings do not withstand the repeated cleaning cycles necessary in the food processing industry[98].

Other promising research in this area includes electroless plating with nickel and PTFE to produce a nanostructured surface on stainless steel[99], and the use of polymer coatings with and without antimicrobial nanoparticulates on a variety of surfaces, but which do not require high wear resistance[100,101].

2.3.2.2 Filtration

Filtration is an important process for several different foodstuffs, including milk, oils, wine, and beer, as well as for purifying bio-actives that are present at low concentration. In addition, it is estimated that the food industry uses more water per unit mass of product than any other industry[102], for example the dairy industry produces between 0.2 and 10 litres of effluent per litre of processed milk[103]. As a result, filtration technologies are becoming increasingly important in the drive to minimise and recycle as much of this waste-water as possible. In the dairy industry in particular, much of this waste also contains useful proteins (such as whey) but has a high mineral content. Nanofiltration technologies are seen as one solution to these issues. Nanofiltration systems employ multiple membrane layers where molecules and ions can be separated based on charge, size and water solubility. Most employ ceramic and polymer layers. They have demonstrated ability to separate and concentrate useful components from waste[104,105,106], however one issue that still needs to be addressed is bio-fouling, which is estimated to be the biggest contributor to decreased filtration efficiency[107] and to the loss of desirable proteins and peptides (through retention in the membrane)[108] .

2.3.3 Functional Foods

The importance of a well-balanced diet is well-known. Much effort has gone into persuading consumers in developed countries of the need to eat at least five portions from a variety of fruit and vegetables each day. The trouble is that fresh produce is not available to everyone, everywhere, all the time. Processing is the solution and has been used for millennia to preserve foods by for example, freezing, salting, drying, smoking, pickling, and more recently vacuum packing. However, nowadays, in the developed world at least, food processing equates with convenience. Consumption of processed foods is becoming more prominent, even where the tradition diet until recently had largely consisted of fresh produce, such as Mediterranean countries. Processed food, however, is often limited in its nutritional value and can contain high levels of fat, salt, sugar and artificial chemicals (such as preservatives and flavour enhancers).

While there is constant demand to be innovative in food products, there is also the need to be aware of changes in public attitude. It is estimated that in Europe 50% of all new products are withdrawn from the market within two years of launch[109]. According to the consultancy firm XTC, current trends are towards natural ingredients that promote health and well-being, while at the same time providing more sensory stimulation. In developed countries such considerations appear to be more important than convenience to consumers.

The situation differs in developing countries, where the problem is access to food that provides a balanced nutritional diet. Large numbers of the world’s population survive on just a few staples, maize being the most prominent, and as a result individuals can be both mal- and under-nourished. The use of processed food, with added nutritional value in such circumstances would be a great benefit. While many processed foods are supplemented (or fortified) with vitamins and minerals, there is much scope to enlarge this portfolio.

The agrifood industry then has the opportunity to produce more nutritional food that can also have a longer shelf-life and not require refrigeration, thus meeting demands from both developed and developing countries.

Although many nutrients can simply be added to processed food, via salts, or extracts of plant or animal origin; in some cases the nutrient is not so easily incorporated, as it can be poorly soluble in aqueous solution; sensitive to oxygen, light, temperature; or adversely affect the colour, smell or taste of the processed food. In other cases the nutrient binds so tightly to the food matrix that it is not readily available to be taken up by the digestive system during the limited period it is within the gastro-intestinal tract (GIT).

In such cases new approaches to packaging and delivering nutrients is required.

Table 1 provides an overview of several types of nutrients which would be useful to include in foodstuffs but are poorly suited for reasons of stability or sensory perception.

Nutrient	Sources	Benefits	Issues surrounding use
Carotenoids (e.g. lycopene)	Fruit and vegetables (e.g. carrots, tomatoes)	Decreased rate of cancer, cardiovascular disease and cataracts.	Hydrophobic. Susceptible to light, oxygen, and auto-oxidation. Solid at food storage and body temperature.
ω-3 fatty acids	Oily fish	Decreased rate of cardiovascular disease, immune disorders, and cancer, and increased mental acuity.	Hydrophobic. Extremely susceptible to oxidation.
Phytosterols	All plants (highest in cereals)	Decrease the uptake of cholesterol and as a result offer protection against cardiovascular disease.	Hydrophobic. Have a high melting point and tendency to form insoluble crystals, making their inclusion in aqueous solutions difficult.
Flavonoids (e.g. catechins)	Tea, cocoa, fruit, vegetables, herbs	Decreased rate of cardiovascular disease, and cancer.	Strong bitter taste.
Minerals (e.g. iron)		Components of many biomaterials including key metabolic processes.	Can react with other foodstuffs (e.g. iron oxidises oils), can affect taste and discolour food.

Table 1. Some important nutrients for which improved delivery systems would improve their utility.

2.3.3.1 Delivery mechanisms for nutrients

Delivery mechanisms must fulfil certain criteria: protect the nutrient from the external environment (such as oxygen, light, temperature, pH, water), not affect the sensory perception of the consumer and deliver the nutrient to the appropriate part of the gastro-intestinal tract (GIT) in a form that allows it to be absorbed and utilised by the body. A further consideration is that all such materials must be food-grade, Generally Accepted As Safe (GRAS) or listed by the appropriate regulatory authority.

There are a number of platforms available for this purpose, based on natural and synthetic materials. Many of these can be formulated as emulsions or nano-emulsions (see report “Nanotechnology and Agricultural Production” for a description of emulsions). This potentially allows for multiple phases, with different components included in a single system. Critical to this is the control of interfacial properties which control the stability of droplets (either water or oil) within the emulsion. In addition, such systems must be robust enough to withstand food processing conditions, and environmental changes during distribution and handling by the consumer. Finally, one of the main obstacles to using nano-emulsions for foodstuffs is the lack of food-grade surfactants[110].

In many respects, the boundaries between health and food have blurred over recent years, as the food industry has adopted or adapted many of the delivery systems developed within the pharmaceutical industry, where nanotechnology enabled drug delivery and diagnostic platforms have been developed to overcome issues of protection and selective delivery.

There are several different compounds, both biogenic and synthetic which are being developed for the purpose of delivering additional nutrients within food. Table 2 summarises the most promising of these.

Material	Description	Potential applications
Nano-emulsions	Made from a variety of lipids or other polymers, droplet size on order of 100 nm. Relatively stable systems.	Delivery of both hydrophobic and hydrophilic compounds. Possibility of multiple phases and hence simultaneous or sequential delivery of multiple compounds.
Solid Lipid Nanoparticles	Crystalline or semi-crystalline stabilised by a surfactant coating. Made by emulsion technologies. Stable system.	Delivery of hydrophobic materials.
Liposomes	Capsules consisting of lipid bi-layer with aqueous interior. Generally phospholipids, such as phosphatidyl choline.	Delivery of hydrophilic compounds.
Micelles	Droplets of surfactants (lipids or biopolymers) in a liquid	Delivery of hydrophobic compounds (normally).
Casein	Milk protein that self-assembles into micellar structures.	Delivery of minerals, proteins and vitamins.
Whey proteins	Largely ß-lactoglobulin and α-lactalbumin. Can form fibrils, hydrogels, and nanoparticles dependent on processing conditions. Resistant to stomach acid and enzymes.	Delivery of various hydrophilic compounds to the intestinal mucosa. Also can be used to provide nanoscale structure to food (i.e. affect mouth feel).
Chitosan	Carbohydrate isolated from crustaceans. Muco-adhesive, bio-compatible, non-toxic. Forms nanocapsules and hydrogels.	Delivery of different compounds to the oral (e.g. for taste) or to the intestinal mucosa, as part of a multi-component and layered system.
Silica	Bio-compatible and degradable. Can be made highly nanoporous.	Delivery of various hydrophilic nutrients to the stomach.

Table 2. Some promising nanostructured delivery systems for nutrients.

Nano-emulsions

These are generated by a variety of means including high pressure, sonication or through appropriate mixing conditions. They are stable, although will eventually separate into different phases. They consist of vesicles or particles (made from a variety of lipids and other polymers) suspended in solution. The system can be multi-phase; so oil or water phases can be encapsulated and the resultant vesicle encapsulated by still larger vesicles[111]. As a result they offer the opportunity to deliver multiple components in a single system. For example, oil in water in water (o/w/w) emulsions consist of oil droplets within an aqueous phase, which in turn is encapsulated in a lipid or biopolymer vesicle (stabilised by surfactants) that is suspended in an aqueous medium (which can differ from that in the interior). Decreased droplet size has been shown to correlate with increased uptake into epithelium[112].

Nano-emulsions do not affect optical clarity and so have received much interest from the beverage industry for inclusion of nutriceuticals.

Solid lipid nanoparticles

These can be generated from micro- or nano-emulsions. Solid lipid nanoparticles (SLN) offer greater stability than emulsions, and so can be used in other processed foodstuffs. During synthesis the desired hydrophobic nutrient is uniformly distributed throughout the solid lipid core. SLNs are stabilised by a layer of surfactant molecules, and multiple layers can be created, potentially allowing for the incorporation of different nutrients. As a result of their small size, they are rapidly absorbed into the intestinal wall, with consequent release of nutrient. Important aspects to consider are choice of lipid, melt temperature, surfactants and process control as all affect stability of the SLN and its load capacity[113].

Liposomes

These are hollow capsules, usually formulated from phospholipids (such as phosphatidyl choline) which can be in the form of single or multiple bilayers. In all cases they have an aqueous interior which has the same composition as the medium in which the liposome was made. They can be produced by a number of methods such as ultrasonication, freeze-drying, reverse-phase evaporation, detergent depletion, membrane extrusion, high pressure homogenisation[114]. They can be used deliver hydrophilic compounds, however as with nano-emulsions, they are not thermodynamically stable.

Liposomes have demonstrated an ability to protect labile compounds (such as vitamins) in foodstuffs from degradation[114]. However, they are highly unstable in low pH conditions and are therefore degraded rapidly within the stomach.

Micelles

These are droplets of aggregated surfactant, usually in aqueous liquid, such that hydrophobic chains are in the interior. This is a mature technology, which can be used to solubilise and deliver a wide variety of hydrophobic compounds, and has been commercialised by a number of different companies.

Casein

Casein is the major protein component of milk, and is a natural nano-carrier, responsible for delivering mineral nutrients such as calcium and phosphate to neonates. It naturally forms micelles (consisting of the four main caseins) which are quite stable to the different treatments used in food processing. Casein can self-assemble into nanoscale structures and encapsulate a variety of nutrients such as calcium, phosphates, other proteins and vitamins[115].

Whey proteins

Whey is the waste material from cheese, and is largely water, but contains some 20% of the original mass of milk protein, along with minerals and vitamins. With the advent of ultrafiltration systems, whey has become an important additive to many different foods, and is also used as a dietary supplement. The major protein component of whey is the globular protein β-lactoglobulin. When whey protein is heated it forms hydrogels, largely as a result of β-lactoglobulin. Nanoparticles of β-lactoglobulin can also be produced using a desolvation method[116].

Another component of whey, α-lactalbumin, has been shown to form nanotubes from enzymatically hydrolysed bulk protein in the presence of suitable cations, such as calcium. These nanotubes are stable when freeze-dried and under conditions similar to pasteurisation, suggesting wide potential applications in the food industry[117].

Chitosan

Chitosan is a de-acetylated derivative of chitin, which is the second most abundant polysaccharide (after cellulose) and is a component of the shells of shrimps, crabs and other crustaceans. Chitosan is more water-soluble and can form gel-like nanocapsules whose properties are dictated by the concentration and molecular weight of the chitosan and the type and concentration of cross-linking agents. These particles can be generated by a number of different mechanisms including emulsification, coacervation and precipitation[118]. It was originally developed for controlled release of drugs, however recently its applications within the food industry have received greater interest. This is primarily because of its muco-adhesiveness[119], which allows targeted uptake to either the mouth or intestinal epithelium.

Silicon

Silicon in the form of orthosilicic acid has been shown to be an essential trace element for human health. It has also demonstrated biocompatibility and biodegradability. Recent work has explored its use as a delivery vehicle for nutraceuticals[120]. Mesoporous silicon is stable in acidic pH and so passes through the stomach, it is however digested within the intestine[121]. It has been demonstrated that a variety of different nutrients can be loaded into nanoporous silicon such as vitamin E, omega oils, and lycopene[120].

Other systems

Many different polymers are being evaluated as carriers for nutraceuticals. These include globular proteins such as albumin; and filamentous proteins such as zein, collagen and gelatine. Other food-grade polymers have been successfully employed as nano-emulsions to encapsulate nutrients, such as poly(D,L-lactic acid) (PLA) and poly(D,L-lactic-coglycolic acid) (PLGA) which have been used for β-carotene[122]. Different technologies are being employed to create these nanostructured systems including supercritical fluids[123], hydrogels and emulsion gels (controlled by ionic concentrations and pH)[124].

2.3.3.2 Controlled and Targeted Release

While each of the systems described above has versatility in its own right, true controlled release can be achieved through the combination of systems. For example, multi-layered systems could have a layer to protect against stomach conditions (e.g. Β-lactalbumin), and a second to bind to and enter the intestinal epithelium (e.g. chitosan).

2.3.3.3 Food Structure- 'Mouth Feel'

Reducing fat, salt, and sugar in processed foods has become a major driver in recent years. In some cases the amount of flavour enhancers could be decreased by using nanotechnology, e.g. researchers at Leatherhead Food International are developing nanoparticulate sodium chloride which as a result of its larger surface area, gives the same salt taste, but at a fraction the amount[125]. However, replacement of taste enhancers does not always only affect taste, but also the texture (or 'mouth feel') of food. This is particularly true of low-fat foodstuffs, where the fat is generally replaced by a natural or synthetic polymer, e.g. guar gum or cellulose, to provide a similar mouth feel. However, these do not completely replace the sensation to the consumer and so there is a drive by many different companies to identify better alternatives.

Mouth feel is a complex interaction between chemicals within the food, the physical structure of the food (much of which is on the nanoscale) and the mouth. Engineering alternatives to the natural textures of food, is therefore a challenging task. Nanostructured components made from natural and synthetic polymers, could be one means by which the missing ingredients are more effectively replaced.

Whey proteins offer one alternative. Much research has gone into exploring ways in which these can be manipulated to form different structures based on solution chemistry and processing conditions[126]. For example, hydrolysates of whey proteins can self-assemble to form nanostructured systems, which can be incorporated in processed food. In addition to altering the structure of food, these can be used to encapsulate nutrients, as described above.

Other alternatives which are being explored include the use of nano-emulsion technologies for the reduction of fat content in foods. Various institutions including Wageningen University, the Food Research Institute (Norwich) and Leatherhead Foods International are researching water-in-oil-in-water nano-emulsions, which produce the same mouth feel as fat droplets within mayonnaise, but have a much lower fat content[125,127].

2.3.3.4 Edible Coatings

Edible coatings are used on several different foodstuffs, including fresh fruit and vegetables, and processed food. They are usually composed of lipids, carbohydrates or proteins and are designed to protect the food from environmental conditions such as oxidation, moisture, and handling. However, at present each material has its limitations. Nanostructured coatings in contrast could incorporate different food-grade additives in a matrix and be specifically designed to meet the conditions required. Such coatings could be engineered using conventional food coating processes (such as dipping or spraying)[128].

2.4 Additional demand for research

Quality control in the food processing industry ideally requires in-line monitoring so that contamination can be identified as quickly as possible, and production halted. This is a highly repetitive process, with sampling points a various stages of production. While nanotechnology enabled sensors have the potential to deliver on this- in terms of sensitivity and real-time response; these are not sufficiently mature. One of the major considerations for the detection of chemical and biological contaminants that will need to be addressed, before such systems become common-place, is the pre-treatment of samples to remove interfering components. In this regard a pre-filtration or lysis step, followed by an enriching system (such as functionalised magnetic nanoparticles[129]) could be used to remove other materials from the food sample prior to assaying for a specific contaminant. Different steps such as these could be incorporated into an integrated microfluidics device.

Novel coatings for food processing equipment and filters for handling of waste and purification of low concentration bioactives are expected to bring efficiency savings and improved products. However, coatings will need to demonstrate longevity, lower bio-film production and compatibility with different foodstuffs before they are adopted by the industry. This is most likely to require pilot plant production and rigorous testing. Ultrafiltration is an established technology for the separation of different food products and waste; nanofiltration in contrast has largely been employed within laboratory settings. It does offer the opportunity to discriminate between smaller molecular weight components, through engineering of the different membrane layers, however much fundamental research still needs to be undertaken before the fluid mechanics of these systems are fully understood and therefore controlled.

Functional foods offer huge potential both in terms of nutrition and in market value. The real advantages that nanotechnology offers is the inclusion of nutrients without affecting the sensory perception of the consumer, improving the uptake of nutrients by the body and/or the alteration of food structure to more effectively compensate for the removal of less nutritious components. However, much of this is still at the laboratory scale, with some (in particular nano-emulsions) still requiring fundamental research to fully define the relevant parameters controlling the system.

2.5 Applications and perspectives

Solid state sensors are the most likely to be developed first for use in food processing quality control, as these are sensitive, robust, easier and cheaper to manufacture. However, as stated above these will need to include some pre-filtration step to remove interfering components.

There are some applications of nanostructured coatings within the food processing industry: SPX Process Equipment, are applying DLC coatings in their Waukesha Cherry-Burrell pump range[130]; SuSoS AG manufacture nanostructured anti-microbial coatings using Teflon or PEG by a sol-gel process which has a life-span of up to 2 years[131]; Few Chemicals GmbH have developed a sol-gel coating using hybrid polymers which provides easy-to-clean and anti-corrosion for metals, and scratch resistance on glass, which have a life-span up to 5 years[132]; Sarastro GmbH produces anti-microbial, hygiene and anti-fingerprinting coatings based on sol-gel technologies with life-spans up to several years[133]; Other companies active in the field include Aquamarijn Micro Filtration bv (nanostructured filtration systems); ItN Nanovation (nanostructured filters and coatings); and NanoGate (nanostructured coatings).

Nanotechnology enabled delivery systems for nutrients may be a fairly young field, however there are already products on the market. For example, Salvona Technologies Inc. manufacture two solid nanoparticulate systems (made from undisclosed constituents, but including lipids and other biopolymers) for the delivery of nutriceuticals, NanoSal™ which consists of free solid nanoparticles and MultiSal™ which is microspheres containing solid nanoparticles; Encapsula NanoSciences produces liposomes for food manufacturers; BASF manufactures a nanoparticulate lycopene; and AquaNova which manufactures micellar delivery systems. In addition, there are several companies which hold patents for nanostructured delivery systems, including Proctor and Gamble (chitosan), Elan Pharma International Ltd (muco-adhesive nanoparticles), Kabi Pharmacia AB (solid lipid nanoparticles), DSM IP assets (isoflavone nanoparticles), BASF (multi-core nanoparticles, and colloidal systems), Snow Brand Milk Produce Co. (iron-whey nanoparticulates), Coletica (plant protein based nanoparticles), and Glycologic (carbohydrate based delivery system). A number of companies manufacture nanoscale minerals, which are promoted as having greater bio-availability (a regularly updated list is maintained on the Project on Emerging Nanotechnologies Consumer Inventory website[134]).

However, there are still many issues to overcome. For example BASF removed its nano-delivery system for CoQ10 (an important anti-oxidant) earlier in 2008 because "*consumers had not well received the boosted bioavailability and high absorption claims derived from its nanotechnology-driven encapsulation process.*"

2.6 Current situation within the EU

The EU has many different research groups active in these areas, as well as companies who are developing sensors, coatings and delivery systems, although there is as yet limited uptake in foodstuffs. Technical and manufacturing challenges aside; the other major issue is to ensure that all food contact materials (coatings, filters) and ingredients are safe for human health. Although there is no specific EU legislation governing the use of nanomaterials in food, it is likely, at present, that current legislation should be adequate: for example Article 14, Reg. (EC) 178 of 2002 states that "unsafe food" cannot be placed on the market. The Novel Food Regulation (EC) No 258/97, includes all foodstuffs or ingredients that have not been consumed to a significant degree before 1997. This could potentially be adapted to encompass nanotechnology, and has in fact already been cited by the Finnish government to prevent the importation of a liposomal nutriceutical[ii].

The EC has asked the European Food Safety Authority (EFSA) to "*provide a scientific opinion on potential risks arising from nanoscience and nanotechnologies on food and feed safety*". This has identified that there is a lack of information regarding: characterisation, formulation, and level of use of nanomaterials in food and feed. Among its recommendations are the generation of knowledge databases of nanomaterial usage in food and feed; potential environment, health and safety implications; and characterisation tools and methods[135]. The EFSA launched a public consultation on this opinion in October 2008[iii].

[ii] Lypo-spheric^{TM} Vitamin C claims to increase bioavailability of vitamin C through liposomal encapsulation, and was refused an import license in 2008 by Finland under the Novel Food Regulation.

[iii] http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902133445.htm

3. Nanotechnology in Food Packaging and Distribution

Keywords: packaging, nanoclay, exfoliated, biopolymer, smart packaging, active packaging, sensor, RFID, self-healing, supply chain.

3.1 Definition

Food packaging and distribution for the purpose of this report is defined as materials used to package fresh and processed foods, and the procedures and systems in place to monitor supply chains and authenticate items.

3.2 Short Description

Food packaging acts to enclose processed food in a stable environment and protect it from environmental changes (such as moisture, light, oxidation, and temperature), physical damage, and contamination by micro (and macro)-organisms. In addition it provides information to the consumer. By doing so it improves quality,extends the shelf-life of processed food and allows the consumer to assess whether the product is suitable. Food packaging also provides important ancillary functions: authentication of the foodstuff and product, evidence of tampering/breach of package integrity, and consumer convenience. Food can be packaged using a number of different materials, the most prominent of which are: plastics, paper and cardboard, metal, and glass.

Plastics are virtually ubiquitous in packaging, as single material films and containers, in combination with other plastics, or as coatings for other materials (such as paper card and metals). Global consumption of plastics has increased from some 5 million tonnes in the 1950s to nearly 100 million tonnes today[136]. Of this amount, approximately 44% is used for a relatively short period and then discarded. Plastics used for packaging purposes make up a significant portion of this, and food packaging materials in turn account for approximately 50% (by weight) of total packaging sales[137]. The packaging industry itself is worth about 2% of Gross National Product in developed countries[138]. A number of broad drivers in the packaging sector are shaping innovation in product and process development. Theseinclude decreasing material and energy usage, reducing packaging weight (termed light-weighting), increase food safety and quality (through improved performance in a variety of environmental conditions plus additional functionality), and recyclability or biodegradability (food packaging accounts for some two-thirds of total packaging waste).

These broad packaging drivers are linked to the drivers in the broader food manufacturing sector, which include the interest in decreased wastage (by improving shelf-life and giving visual indicators as to food’s freshness), and increasing consumer confidence and convenience in processed food. In conjunction with an effective packaging system, improvements in identification of items and stock control ensure that delivery is efficient and that foodstuffs are maintained in the appropriate conditions throughout the supply chain. This includes RFID tags for logging the movement of stock at all stages of the supply chain and other tags to provide covert or overt identification and authentication.

3.3 State of R&D

Nanocomposite materials offer improved functionality over traditional composites and polymers in terms of barrier properties, strength, elasticity and optical clarity. Nanocomposites can be functionalised to include other characteristics, for example, antimicrobial activities, visual indicators of food freshness, means of identification and possibilities which augment the ease of tracking. Another desirable property is sustainability. Most polymer composite materials are based on fossil fuel derivatives, however research into biopolymers (sourced from wood and crop waste) is offering biodegradable alternatives. The inherent drawbacks of pure biopolymers (dependent on type, can include poor barrier properties or poor mechanical properties) can be mitigated by the inclusing of nanotechnology to form nano-enabled biocomposites (bionanocomposites). Most nanocomposite materials employed, or being developed for use, in the food packaging industry contain nanoclay particulates, however other composites containing nanoparticles, nanotubes or nanofibres of metals, metal oxides, biopolymers[139],[140],[141] other carbon-based materials are also being developed.

Virtually all polymers used in food packaging are thermoplastic, rather than thermoset. As such they can be melted after use and re-moulded into another product. Issues arise, however, when different polymers are included in one product, requiring mechanical separation before re-use.

3.3.1 Barrier Packaging

Many fresh and processed foods are packaged in an inert or low oxygen atmosphere (by purging air with nitrogen or carbon dioxide); a procedure known as modified atmosphere packaging (MAP) that can increase shelf-life four-fold, by inhibiting microbial growth and consequently food spoilage. In most circumstances the packaging material used is polymer-based, however, these have limitations. While materials such as glass and metals are completely impermeable to gases, plastics in contrast are semi-permeable; which can affect food and drink quality undesirably over relatively short periods of time (e.g. carbon dioxide escape from carbonated drinks, oxygen ingress to packaged foods resulting in faster decay, and ethylene spread between fruits resulting in faster ripening).

Plastics, however, can be made more impermeable to gases through the addition of coatings (e.g. deposition of a thin film of alumina) or through the inclusion of nanoparticulates within the polymer matrix. These act as small, physical barriers to the progress of gas molecules across the polymer, and if present in sufficient numbers effectively reduce gas transport to negligible levels. It does this by complicating the path of gas as it transports through the material. Such “tortuous” paths characteristic of nanocomposites provide a significant advantage to polymer based packaging. Howeverm to achieve this level of barrier requires excellent dispersion of the nanoparticulate throughout the polymer matrix This dispersion is affected by three different chemistries: the polymer itself, the nanoscale filler, and the inter-facial materials (compatibilisers) used to help disperse the nanoscale filler evenly through the polymer.

3.3.1.1 Nanoclays

Clays consist of multiple layers of complex metallic ores (with the major constituents being aluminium and magnesium silicates). There are a number of different types, however those of particular interest to the packaging industry are smectite, kaolonite, montmorillonite, and hectorite. Structurally they are aggregates of stacked, ultrafine layered particles (or tactoids). Each layer (or platelet) within the tactoid is of the order of 1 nm thick and a few hundreds of nm in the other two dimensions. The ratio of the platelet length to its thickness is known as its *aspect ratio*. Clays, due to their relative abundance and low cost, have been used historically as materials for building, and containers for foodstuffs. However, a greater understanding of the nanoscale features of clays, and the ability to disperse the ultrafine layers within other materials has led to increased interest in their application in composite materials; to provide properties to lightweight polymers that would usually only be found in heavier or more expensive materials (such as glass or metals).

The key requirement for the generation of nanoclay composites is separation of the ultrafine layers, a process known as exfoliation. Depending on the degree of separation, the resultant composite is known as phase separated or immiscible (no exfoliation of clay platelets); intercalated (partial separation of clay platelets with polymer found between them, however some association between layers remains) and exfoliated (platelets are dispersed throughout the polymer matrix). Figure 1 illustrates this process. Immiscible composites are microcomposites, which may have improved mechanical properties, but not barrier properties. In contrast, intercalated and exfoliated composites are nanocomposites which exhibit properties described below. Generally speaking, the higher the degree of exfoliation, the greater the improvement in barrier and mechanical properties.

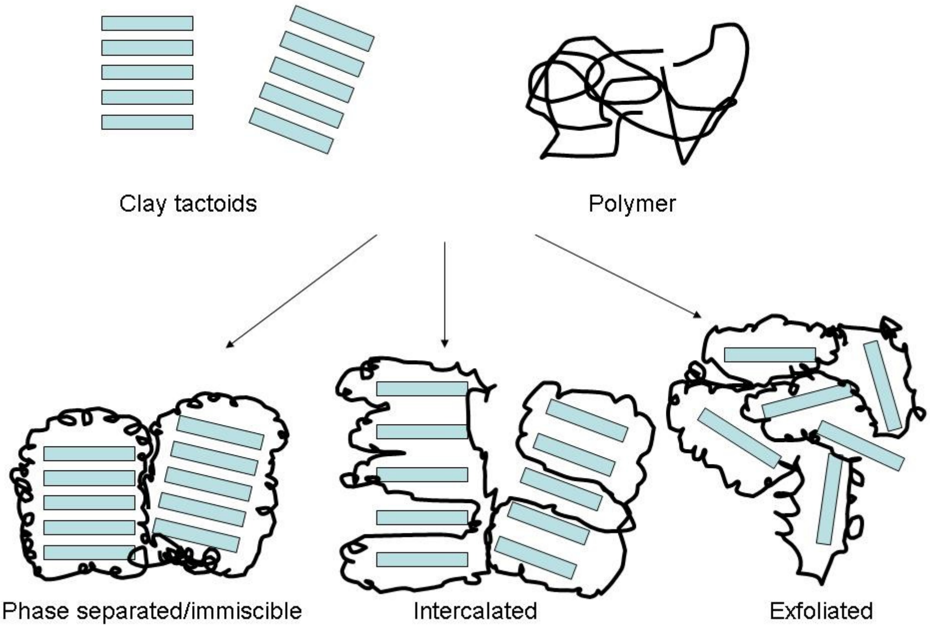

Figure 1 Creation of polymer clay composites. Without clay platelet separation a microcomposite is produced (phase separated/immiscible). Separation of the clay platelets leads to an intercalated nanocomposite, and full separation to an exfoliated nanocomposite. (Adapted from Rhing and Ng, 2007[142]).

The chemistries of the clay and polymer play a critical role in determining the degree of exfoliation. The nanoclay is usually treated with an organic compound (such as quaternary ammonium salts) which has a dual purpose. First it separates the platelets (up to two to three fold), and second it can act as a ‘compatibiliser’, by interacting with the non-polar regions of the polymer and favouring their intercalation between clay platelets. Both actions facilitate exfoliation, by promoting polymer entry to the space between platelets. Such clays are known as organo-clays (Cloisite®, manufactured by Southern Clay Products Inc, is an example of an organically modified montmorillonite[iv]).

[iv] Southern Clay Products Inc http://www.nanoclay.com/

Many different types of polymer have been used, including polypropylene, polyethylene, polyacrylamide, polycarbonate, polystyrene, and polyimide[143,144], and as will be discussed below, several natural biopolymers. However, it is polyamide-based nanoclay composites that have seen the greatest development with many now successfully commercialised (e.g. Durethan[v], Imperm[vi], and Aegis[vii]). Quaternary ammonium salts with different alkyl groups can be used for different polymers to assist in exfoliation, however in the case of highly organophilic polymers (such as polyethylene) additional compatabilisers such as polar monomers are added, to help stabilise the polymer platelet interaction.

Nanoclay polymer composites can be produced by a number of different methods:

- solution intercalation – the organo-clay is first swollen with solvent (e.g. water or an organic solvent) before mixing with polymer. The polymer diffuses between the nanoclay layers, displacing the solvent;
- in situ intercalative polymerisation – the organo-clay is swollen within a solution of monomer; so that polymerisation occurs between the clay layers;
- melt intercalation – (used for thermoplastic polymers) the organo-clay and polymer are mixed at a temperature above the softening point of the polymer.

Polymer clay mixes are also subjected to mechanical stress to help shear inter-platelet forces and allow the polymer to diffuse between layers. Of the above techniques, melt intercalation is favoured, as it is compatible with current industrial processes and reduces the requirement of solvent (and consequent waste). Other considerations for the production of polymer nanocomposites are the aspect ratio of the platelets (the higher this is the more difficult to exfoliate), the viscosity of the mix (higher amounts of nanoclay can improve exfoliation by increasing viscosity, but above a certain level this can lead to agglomeration and poorer composite properties)[145], and both the nature of the extruder (the device used to mix components and produce the final composite) and duration of the mixing process within it.

The degree of exfoliation and the aspect ratio of nanoplatelets within the polymer matrix correlate with altered properties of the nanocomposite compared with the pure polymer. These include:

- gas barrier properties – the nanoclay platelets act as physical barriers to the passage of gas, thus gas molecules must take a longer route through the polymer (the so-called ‘tortuous path’), resulting in lower gas transmission. The greater the degree of exfoliation, the greater the gas barrier properties.
- liquid barrier properties – the nanoclay platelets reduce moisture ingress to the polymer, which leads to polymer swelling, and can reduce the polymer’s mechanical and gas barrier properties.
- mechanical properties – the interaction between platelets and the polymer leads to increased tensile strength and elasticity. In addition, the glass transition temperature and thermal properties can be affected by the inclusion of nanoclays (e.g. improved fire resistance). These properties are dependent not only on the degree of exfoliation and concentration of nanoclay, but also the chemistries of the individual components.

Despite these benefits to the pure polymer, the addition of nanoclay in general does not significantly affect the optical clarity. In the case of some thermoset polymers, the nanoclay platelets can aid polymerisation.

While many nanocomposites are employed as free-standing packaging (such as bottles and films), they can also be applied as coatings to other materials, such as paperboard and metals. These can be for barrier purposes, or to impart greater strength. In some cases a coating can provide superhydrophobicity[146] (a property that can be exploited to minimise the amount of foodstuff retained by the packaging).

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[v] Bayer http://www.research.bayer.com/edition_15/15_polyamides.pdfx
[vi] Nanocor http://www.nanocor.com/Cases/case_imperm.asp
[vii] Honeywell http://www51.honeywell.com/sm/aegis/applications.html

There are a number of different technologies that can be used to coat other materials with nanocomposites including dip-coating, spin-coating, electrospinning, and ultrasonic spraying[143,147,148]. By using different materials in a layer-by layer assembly procedure, multiple layers can be built up, each with a different functionality (e.g. gas barrier, moisture barrier, or a 'smart' property- see below).

3.3.1.2 Other materials used for nanocomposites

A number of other nanomaterials can be added on their own, or in addition to nanoclays, to polymers to provide additional barrier or functional properties for food packaging purposes. These include metal and metal oxide nanoparticles, nanofibres[149] and nanotubes[150], and nanofibres. For example, DuPont are marketing a titanium dioxide nanoparticulate (Light Stabilizer 210) to block UV light and provide a longer shelf-life for food (this is currently before the US regulatory authorities for use in non-contact food packaging materials); and Rohm and Haas are marketing acrylic nanoparticles (Paraloid BPM-500) to increase the strength of polylactic acid, a biodegradable polymer.

3.3.2 Antimicrobial and Antimycotic Packaging

In addition to acting as a passive barrier, packaging can contribute to the control of microbial growth in foodstuffs that leads to spoiling. Most activities to combat this, have centred around nanoparticulates of silver, and zinc oxide, however there is also research into the antimicrobial effects of natural biological compounds[151].

Silver nanoparticles have been incorporated in a wide variety of consumer goods including clothing, electrical goods, kitchenware, and wound dressings[152]. Nanoparticulate silver releases ions more efficiently than bulk metal, and it is the silver ions that have a bactericidal due to the inhibition of a wide variety of biological processes within the bacteria[153]. As the levels of silver ions liberated are too low to have toxic effects in humans; it is likely that nanoparticulate silver will be included in further composite materials. However, there is some concern over the effects of large amounts of silver ions being discharged into the environment and accumulating in ecosystems, as silver ions are known to be toxic to aquatic life.

Zinc oxide exhibits antibacterial activity that increases with decreasing particle size[154]. This activity does not require the presence of UV light (unlike titanium dioxide) but is stimulated by visible light[155]. The exact mechanism(s) of action is still unknown. Zinc oxide nanoparticles have been incorporated in a number of different polymers including polypropylene[156]. In addition zinc oxide effectively absorbs UV light, without re-emitting as heat, and therefore improves the stability of polymer composites.

Chitosan is a biopolymer derived from chitin (a polysaccharide constituent of crustacean shells). It has seen much interest in recent years as a material for the encapsulation of nutriceuticals (see report 'Food Processing and Functional Food'). In addition, to its utility as a packaging material, it also exhibits antimicrobial properties[157]. This has led a number of groups to investigate its incorporation into different composite materials which could have applications in healthcare and food packaging, including using it as a 'green' reagent to reduce and stabilise silver ions[158], in combination with clays such as rectorite which could then be used in polymer composites[159,160].

3.3.3 Biodegradable Packaging

For many plastics recycling is made difficult as a result of the different components involved, which means that the item can not be processed in a single step, but needs to be dismantled and component plastics separated. One way to avoid this, but to still achieve sustainability, is to use biodegradable polymers from renewable sources. These are generally proteins or carbohydrates and can be derived from animal or plant origin. Lipid films can be created also, but these tend to be used to directly coat and protect foodstuffs (and are described in the report 'Food Processing and Functional Food'). When biopolymers (such as cellulose) are mixed with nanoclay particles, the resultant nanocomposites exhibit improved barrier properties compared with the pure polymer, and after their useful life can be composted and returned to the soil[136]. Other nanomaterials can be used including metal oxide nanoparticles, and carbon nanofibres and nanotubes.

In addition to melt extrusion, many biopolymers such as cellulose, collagen and zein (derived from corn) have been synthesised as nanofibres using electrospinning equipment. In some cases these have superior properties to the traditionally cast polymer, including increased heat resistance[161,162], and in addition, mats of such nanofibres possess a highly nanoporous structure and can be used as support matrixes for additional functionality.

Other biopolymers that have been combined with nanoclays include chitosan, starch, casein, whey, and gelatine[136]. The potential applications vary from stand alone barrier films to coatings on other polymers and paper based packaging, to direct coating of foodstuffs.

Such biodegradable nanocomposites could be of great use in other agrifood application areas, such as the plastics used in agriculture (polytunnels, wrapping for feed, wrapping for hay, etc) that are either disposed of into landfill or burned by farmers (estimated to be on the order of 6.5 million tonnes[136] per annum). Instead of incineration, they could be composted and returned to the soil.

The main considerations when using natural polymers, are that they often have poor mechanical strength, and are permeable to water. As with other nanocomposites, significant research still needs to be undertaken to determine how properties can be best enhanced for specific applications through the use of different nanoparticulates, plasticisers (some biopolymers, such as starch, are not thermoplastic) and melt conditions.

3.3.4 Active and Smart Packaging

Smart packaging responds to its environment either to regulate an external effect or to produce a visual readout of a change. It includes materials that can regulate the internal environment of packaged foodstuffs to maintain food quality (e.g. through the release or absorption of substances), sensors that provide an indication of the storage history of the product and whether it is still fresh, and materials which can repair minor damage (self-heal)[163,164].

3.3.4.1 Regulating the internal packaging environment

At its simplest, this can be controlling the temperature of the foodstuff. Manufacturers of chilled or fresh foods want to ensure that their produce reaches the consumer in good condition, however there are inevitable breaks in the cold chain, for example due to transfer between different transport systems. If these occur in high ambient temperatures, food quality can quickly deteriorate. Ideally, it would be useful to have a protective material, which is cheap, recyclable or re-usable and does not add significantly to package weight or volume. Traditional insulating materials (such as polystyrene) are bulky and inappropriate for this use, as they would add significantly to transport costs. In contrast, nanostructured foams, which are considerably thinner than conventional materials for the same thermal properties, could be an alternative, if available at low enough cost (at present these are used more for building insulation). An alternative system based on low cost materials, has been developed by researchers in New Zealand. This system based on nanoporous calcium silicate, is loaded with a phase change material (such as paraffin wax) that can mitigate the effects of an increase in external temperature over a short period of time (five hours), while having similar dimensions to bubble wrap[165].

Self-heating or cooling systems are an attractive option for consumers. Essentially the chemistry is simple. Exothermic reactions are used for self-heating (e.g. mixing water and calcium oxide) while evaporation of a refrigerant (e.g. water or carbon dioxide) is used for self-cooling. There are several examples of self-heating systems on the market, and at least one for self-cooling. It is unclear whether nanomaterials would offer significant improvements to self-heating efficiencies, however they may provide increased efficiencies for self-cooling, and there is at least one patent, based on fullerenes, for this purpose[166]. In the longer-term, completely different platforms such as combination thin-film photovoltaic and thermoelectric systems could be used (to harness solar power to drive the cooling effect of thermoelectric materials, in much the same way as solid-state coolers).

Gas scavenging or absorbing systems are also of interest for food packaging. There are several on the market using conventional technologies, such as the AGELESS system from Mistubishi Gas Chemical Co. which contains iron salts and vitamin C, and absorbs oxygen within a sealed package[viii]. Research using nanostructured materials may offer enhancements by: increasing the surface area of the active component (through nanoparticles, or loading of a nanoporous material such as silica, with active material). For example, preliminary work with polymer nanocomposites containing titanium dioxide, shows that these exhibit similar oxygen scavenging properties, in the presence of UV, as conventional iron and polymer based materials[167].

Other research themes have looked at the active release of compounds, to help maintain food quality. Mostly these are based on conventional technologies to release preserving compounds such as carbon dioxide or ethanol, however the last few years has seen the development of systems based on nanomaterials. Research patented from SouthWestern Research Institute provides a means for the release of antimicrobial agents (such as chlorine dioxide) inside packaging to inhibit microbial growth. This uses nanoscale capsules which release chlorine dioxide upon exposure to moisture[168] or nanoparticles of materials such as titanium dioxide to photo-catalyse the production of such gases from inert reactants[169]. This research is now developed by the Microactive Corporation.

3.3.4.2 Self-healing composites

Self-healing polymers have been the subject of intense research for over 20 years. These systems respond to stresses, fractures, tears, and punctures by mobilising polymers or monomers to repair existing bonds, or create new ones. In some case this requires input of energy (light or heat) in others it is driven solely by chemical reactions within the endogenous system, including self-catalysis by polymer components. For example, ionomers, which are polymers that contain polar and ionic side-groups, have shown the ability to re-close small punctures. One that is marketed as a self-healing polymer is based on poly(ethyleneco-methacrylic acid) (EMAA), React-A-Seal®. Although the precise mechanism is unknown, it is theorised that polymer chain movement as a result of elastic recovery, provides the kinetic energy to bring side-chains in contact and for re-establishing links with other side-chains.

Other research, particularly for thermoset polymers, has included catalysts and monomers (encapsulated by emulsions or fibres), which are released upon stress of the polymer matrix, and react to form new polymer. At the moment, this active area of research is focused on microparticles and fibres. Whether nanotechnology could offer increased efficiency, e.g. through nano-emulsions, or new application areas is unknown. Although such systems have been primarily developed for use in higher value added fields, such as structural composites for automotive and aeronautic components, this technology could have applications in food packaging.

Recent research has investigated the use of nanoparticles as the medium for repair of cracks within thermoplastic polymers. In contrast to other self-healing systems which rely on the re-formation of polymer bonds, this involves nanoparticle migration within a composite material to the site of damage, driven thermodynamically by repulsive interactions between the polymer matrix and the nanoparticle filler (the same constraints which make it difficult to evenly distribute nanoscale fillers throughout polymers in the first instance)[170,171].

3.3.4.3 Sensor technologies in packaging

Sensor technologies for packaging should provide a visible indicator to the supplier or consumer that foodstuffs are still fresh, or whether the packaging has been breached, kept at the appropriate temperatures throughout the supply chain, or has spoiled. Key factors in their use are cost, robustness, and compatibility with different packaging materials.

Oxygen sensors

[viii] Mistubishi Gas Chemical Co. http://www.mgc.co.jp/eng/products/abc/ageless/index.html

The ability to detect the presence of oxygen within packages of e.g. fresh meat, at the earliest stage would alert the consumer that the packaging has been compromised, even if there are no visual indications to suggest this. Such systems, for the purpose of food packaging, rely on changes in the colour of dyes in the presence or absence of oxygen. One commercialised, microtechnology product is ‘Ageless Eye’[ix] which is pink in the absence of oxygen and blue in its presence. Advances using nanoparticles are expected to produce more sensitive systems that respond faster and produce stronger colour changes. For example, researchers at the University of Strathclyde have produced a hydroxyethyl cellulose polymer film oxygen sensor, containing titanium dioxide nanoparticles and the blue dye, indigo-tetrasulphonate. Following incorporation in the packaging, the sensor is exposed to UV light, the dye is photobleached (a reaction catalysed by the titanium dioxide) and remains so until exposed to atmospheric oxygen levels, when it rapidly (within three minutes) returns to a deep blue colour (even in the dark)[172].

Stress and temperature sensors

While there is much research in the area of self-healing polymers, as described above, it is unlikely in the near future to be used in food-packaging. Packaging would therefore benefit from the presence of materials which would indicate that barrier properties have been compromised, through heat or mechanical stress. In some cases this can be achieved using oxygen sensor technologies, which indirectly indicate a break in the packaging.

New research using different nanomaterials may offer colour-assisted solutions. For example, photonic crystals have been shown to change colour dependent on structure, a property which can be exploited for strain sensors. Such structures have been successfully synthesised in flexible polymer composites by researchers at Southampton and Darmstadt Universities[173]. Other alternatives include diacetylenes, which have been shown to change colour in response to mechanical stress or temperature changes, a phenomenon which can be stabilised and enhanced through the nanostructuring of the polymers, for example by enclosing in a nanoporous silica support[174] or as nanocrystals of urethane-substituted polydiacetylenes[175].

Time temperature indicators (TTI’s) allow suppliers to confirm that processed foods requiring refrigeration have been kept at the appropriate temperatures throughout the supply chain. They fall into two categories: one relies on the migration of a dye through a porous material, which is temperature and time dependent , the other makes use of a chemical reaction (initiated when the label is applied to the packaging) which results in a colour change, the rate of which is temperature dependent. These have limitations in that they require multiple components (dyes, reactants, porous layers), which can affect accuracy under some circumstances, and so a single component system would be an improvement. Timestrip plc has developed a colloidal gold based system (iStrip)[176] which is red in colour at temperatures above freezing. Freezing leads to the irreversible agglomeration of the gold nanoparticles resulting in a clear solution, a useful indicator to detect the accidental freezing of chilled goods.

Biosensors

A great many platforms are being developed for the detection of biomolecules and microbes that are based on nanotechnology (see report on ‘Agricultural Production’), however most of these are incorporated within devices, and require the extraction of a sample to determine the presence of the target molecule. When considering such systems for food packaging, these are focused on detecting microbial growth. The challenge for such systems is that they must be capable of being integrated within the packaging, provide an easily distinguished response (most likely a colour change), and be cheap to manufacture. It is most likely that the presence of microbial contamination will be detected indirectly by measuring changes in gas composition within the package as a result of microbial growth, using gas sensor technologies described above.

[ix] Mistubishi Gas Chemical Co. http://www.mgc.co.jp/eng/products/abc/ageless/eye.html

Alternatively, systems based on caged biomolecules (e.g. fullerenes, liposomes, or nanoporous silica) that are linked to a colourimetric dye, could be developed for this purpose, as they provide stability for the detector molecule, could be incorporated in a permeable membrane within the main package, and do not require additional factors (e.g. pre-processing, power). One example of this comes from research at Tufts University where the potential of nanostructured silk as a platform for biosensors has been shown. The silk fibrils can be shaped into 'lenses' and modified with various biomolecules, which when bound to targets (such as microbial proteins) alter the shape of the silk lens resulting in a colour change. As the silk is biodegradable and edible, such sensors could be incorporated within packaging[177,178].

3.3.4.4 RFID tags and tracking

Radio Frequency Identification (RFID) tags have been in use for a number of years, but only for high value items such as clothing and electronics. They consist of two modules, one to process and store information, the second (an antenna) to transmit and receive information. A second device, the reader, is used to obtain information from the tag, and depending on the radio frequency used, this can be at distance of several tens of metres. RFID tags for the packaging industry are passive, they have no associated power source, and gain energy to transmit information from the incoming radio waves from the reader.

Their utility is that multiple items can be monitored at every stage in the supply chain without the need for line of sight; therefore increasing the speed and efficiency of distribution. This is a critical factor in modern supply chains where large amounts of raw materials may be coming from different global regions to be processed at one site, then distributed to consumers (in many different global regions). Eventually RFID tags are expected to replace barcodes[179].

RFID tags at present are largely based on silicon semiconductor technologies, however recent research could change this, allowing cheaper and easier production on a number of different materials.

Printable electronics (using conducting polymers, such as pentacene and oligothiophene, and metallic inks, including copper, silver and gold nanoparticles) are being developed by a number of institutes and companies around the globe[179,180]. While at present most are based on desktop ink-jet printing, other forms more suited to high production levels (as already used in the printing industry) could be developed.

In addition to printed systems, some research groups are exploring the use of carbon nanotubes as antenna[181,182]. However, this technology is not as highly developed as conductive inks based on metal nanoparticles.

Interestingly, there is some research into combining RFID tags with chemical sensing functions. One group has produced a prototype for ethylene sensing (for fruit ripeness)[183], while another has demonstrated the potential of this technology by constructing a moisture sensor[184]. While these are both microelectronic systems, the potential for nanotechnology to enhance such systems is clear.

3.3.4.5 Authentication

Many different systems are being developed including nanoscale bar-codes, quantum dots, and magnetic nanoparticles, however whether these are likely to be used widely within food packaging is unclear, and will be dependent on cost per unit and ease of use. It is more likely that RFID tags will serve a dual purpose of tracking and authenticating items. For a full description of anti-counterfeit and authentication technologies please see the security sector report 'Anti-counterfeiting, Authentication, and Positioning').

3.4 Additional Demand for Research

The underlying drivers in all packaging areas are reducing costs, while increasing sustainability and functionality.

Polymer nanocomposites represent an exciting field with applications in a number of different areas. However, there is still much to be learned regarding the parameters which affect the final structure and properties of the composite, and how to regulate these through processing conditions and chemistries of the polymer, nano-filler and additional materials such as plasticisers and compatibilisers. The drive towards greener and sustainable manufacturing means that biopolymers will be increasingly used. These have the advantage that in theory recycling is no longer necessary (and with that the difficulties that arise separating the mix of polymers usually present in one package)- such biopolymer nanocomposites can be composted but still if bionanocomposites are to become a major element in food packaging, composting and waste management is an issue to be dealt with (perhaps upstream). However, their barrier and mechanical properties are still inferior to fossil fuel derived polymers, which currently limits their use for some applications, and so further research will be required to improve this. However, certain biopolymers have the added functionality of being antimicrobial, thus bionanocomposites become even more attractive as the added value is multiplied.

Active packaging is an area where nanotechnology is expected to have a large impact. RFID tags, temperature and gas sensors based on nanomaterials are in developmentmand in some cases these have already been commercialised. Self-healing composites are unlikely to appear in food packaging materials in the foreseeable future due to the large cost, and the fact that such materials would need to be approved for food contact use or GRAS (generally accepted as safe). Biosensor technologies will need considerable development before they are robust enough to be included in food packaging material.

3.5 Applications and Perspectives

A number of companies already use polymer nanocomposite materials in their products (such as Miller and Hite). Compostable nanocomposites are also beginning to appear on the market, for example Innovia films has developed and patented a compostable nanoparticle coated packaging for foodstuffs with effective gas barrier properties, which uses nanoparticles of starch and a matrix of synthetic polymers[185]; the acrylic nanoparticle, Paraloid BPM-500, used by Rohm and Haas in its biopolymer, polylactic acid (PLA), allows wider applications of PLA. Other examples are NanoBioTer® from Nanobiomatters

Other barrier properties are important. Companies such as Nanograde GmbH market polymer composites containing nanoparticles of silver and calcium phosphate that demonstrate microbicidal activity. UV absorbers such as nanoparticulate zinc oxide, are likely to be used in materials other than polymer composites. According to John Parkes, director of quality at Rockware Glass, in *'15 or 20 years' time, all clear glass could be produced with a generic UV-blocking agent.'*[186]

Scavenging systems are also likely to benefit from nanotechnology. Multisorb Technologies Inc has patented technology using oxidisable sub-micron particles for use as oxygen scavengers in packaging[187].

With regards to printable electronics and RFID tags there are several companies developing and marketing these technologies. Companies such as Cima NanoTech and Novacentrix manufacture copper and silver nanoparticle based inks. These can be formulated in aqueous or organic suspensions and printed onto a variety of substrates. Other active players include Du Pont, HP, Samsung, and Hitachi.

There are, however, a number of non-technical issues to consider. These include regulatory and safety issues for materials used in food contact environments, and ethical issues arising from the use of RFID tags to track products, which in turn could contribute to tracking or storing information on consumers[188].

3.6 Current Situation within the EU

Several EU projects have been funded to look at packaging. For example, the SustainPack project (funded under FP6) looked at a number of drivers and market pulls for the fibre-based packaging industry, in particular sustainability and the impact that nanotechnology could have[189]; the GoodFood project (funded under FP6) looked at sensor technologies for food safety and quality assurance at different stages of the food production and supply chain[190]; Natural Antimicrobials for Innovative Safe Packaging (NAFISPACK) is an FP7 funded project that will look at antimicrobials in packaging and the risk of their migration into food[191].

As far as sustainability is concerned there is a long way to go. A study published by UK-based market analysts Applied Market Information (AMI) in early 2008, claims that the market for bioplastics remains small, this is compounded by the fact that there appears to be inadequate facilities for recycling or composting. According to AMI, "Less than one per cent of global polymers are currently classified as compostable bioplastics according to the European EN 13432 standard."[192]

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