Bioscience for Life?

Who decides what research is done in health and agriculture?

By Helen Wallace

March 2010

GeneWatch UK
60 Lightwood Road, Buxton, Derbyshire SK17 7BB
Phone: 01298 24300
Email: mail@genewatch.org Website: www.genewatch.org

Registered in England and Wales Company Number 3556885

GeneWatch UK

Acknowledgements

GeneWatch UK is grateful for funding from the Joseph Rowntree Charitable Trust for this report. The author would also like to thank David Armstrong, Timothy Caulfield, Anthony Jackson, Les Levidow, Paul Oldham, Alan Petersen, Geoff Tansey and Vivianne Willis-Mazzichi for their helpful comments on a draft of this report, and Kristina Staley for her input to the background research on the research councils. The content of the final report remains the responsibility of GeneWatch UK.

Declaration of interest

GeneWatch UK has received two research grants as part of the European Commission's DG Research 'Science in Society' Programme, i.e. from one of the funders discussed in this report. Both projects: PSx2 (Participatory Science and Scientific Participation) and FAAN (Facilitating Alternative Agro-Food Networks) are cited in Part 6 of this report.

Contents

Index of Boxes and Tables

Executive Summary

This report is an investigation of the shaping of science, innovation and the economy in the UK and Europe. Its starting point is that research funding decisions are *political* decisions, about how to best spend public money, which institutions to support and what incentives to provide to researchers in academia and industry.

Looking at the biological sciences, in the context of both health and agriculture, the report describes how the idea of the 'knowledge-based bio-economy' (KBBE) has become a key driver of research investment in Europe and world-wide. This vision of the future assumes the biosciences and biotechnology will be a major driver of economic growth and at the same time will deliver technical solutions to health, agricultural, social and environmental problems, within Europe and worldwide.

The development of the 'knowledge-based bio-economy'

In order to stimulate a new bio-economy significant financial and political investments have been made. Scientific institutions and funding systems have been re-structured and new systems of incentives for 'innovation' have been devised, with the aim of rewarding researchers who secure patents and venture capital and collaborate with the private sector to create 'spin-out' companies and commercialise new products, based on biological knowledge or biologically-based production systems.

These policies and investments have focused on how to exploit the commercial potential of the DNA molecule, which is found inside the cells of living organisms, including micro-organisms, plants, animals and humans.

Driven by the discovery of genetic engineering and the decision to sequence the human genome, the idea of a 'genetic revolution' in both health and agriculture has been widely promoted since the 1980s. Agriculture is supposed to be transformed by the ability to produce genetically modified (GM) plants, which are claimed to have higher yields and better nutritional properties, or which can be used as production systems for industrial chemicals, including pharmaceuticals and industrial-scale biofuels (agrofuels). A 'genetic revolution' in healthcare has also been promoted, in which knowledge of the human genome is supposed to lead to medicine becoming a more exact science, based on genetic information. In this vision of the future, each person's individual genome (their 'genetic make-up') is stored in electronic medical records, allowing the tailoring of medication and lifestyle advice to a person's genes and the 'prediction and prevention' of disease by treating the (presumed biological) causes, rather than the symptoms. This is sometimes known as 'personalised medicine' or as 'early health'.

Structural changes to R&D systems and policies, designed to exploit the potential of biotechnology and the human genome, began in the US under the Reagan administration. These changes were mirrored by the Thatcher and Major governments in the UK, and by the European Commission (EC), which identified biotechnology as a key driver for future growth. In Europe, investments in biotechnology research began in the early 1980s, and in 1987 the Single European Act explicitly gave the EC formal power in the fields of research and technology. A decade later, in 1996, the OECD (Organisation of Economic Co-operation and Development) began to promote the idea of the 'knowledge-based economy', in which the rich country members of the OECD were presumed to be able to compete with emerging economies such as India and China by patenting and trading 'intellectual property' rather than manufactured goods. Biotechnology was seen as a key 'technology platform' in the knowledge-based economy, and the idea of the 'knowledge-based bio-economy' (KBBE) was adopted as central to European growth. The 'vision' of GM crops as new production systems – allowing the creating of 'nutritionally-enhanced' crops and the production of industrial chemicals, including pharmaceuticals and agrofuels – has been supported by officials and policy makers in the European Commission and adopted as central to the KBBE.

In Britain, the New Labour Government, elected in 1997, invested heavily in the KBBE as the presumed basis of future of economic growth. The funders of New Labour known as the 'biotech barons', and other key supporters of biotechnology as an engine for growth, were appointed to task forces designed to identify the policies needed for future competitiveness. They promoted the idea of a 'genetic revolution' in both health and agriculture and advocated policies which strengthened protection for 'intellectual property' (IP), opposed regulation, and attempted to create the 'informed consumer' (presumed to be convinced of the benefits of GM crops, and to identify collection, storage and analysis of their DNA with major benefits to their health and to society). In the 1998 Comprehensive Spending Review the then Chancellor Gordon Brown announced "*the biggest ever Government-led public/private partnership for science*": this was the start of a major Government collaboration with the Wellcome Trust, designed to help Britain win the race to commercialise the fruits of the Human Genome Project.

The information contained in medical records stored in the NHS was identified as Britain's 'unique selling point' (USP) in the knowledge-based economy, and a plan to create a central database of electronic medical records ('the Spine') was adopted and funded. The UK Biobank research project was established as a pilot study to begin linking health data to DNA and to include information from people's genomes in their electronic medical records, with the aim of 'predicting and preventing' major diseases such as heart disease and type 2 diabetes.

The idea of a 'genetic revolution' in both health and agriculture was promoted at the highest levels in the British Government: for example, in the then Prime Minister Tony Blair's speech at the joint announcement with President Clinton of the completion of the first draft of the human genome in June 2000; and in Blair's major speech on science to the Royal Society in 2002.

The bio-economy: delivering on promises?

The benefits of the 'bioeconomy' to the UK and EU have been extremely limited:

- The net value of the bio-economy worldwide has been estimated to be zero or negative: with only two US medical biotech companies (Amgen and Genentech) and one US agricultural biotech company (Monsanto) making significant profits.
- Only two types of GM crops have been commercialised on any scale: insect-resistance and herbicide-tolerance. These crops are grown largely in North and South America for use in animal feed and (subsidised) industrial-scale biofuels (agrofuels).
- Concerns remain about environmental impacts, food safety, liability for contamination of non-GM crops and foods, and the extent of corporate control of seeds exercised through patents and licensing agreements.
- A number of new biotech drugs have been developed, but Britain's only blockbuster biopharmaceuticals were discovered in the 1980s.
- Most new biotech 'spin-out' companies from UK universities are never profitable and are a net drain on the economy: they employ only 1,000 people in total.
- Genetic tests of multiple genetic factors are poorly predictive of common diseases and most adverse drug reactions: none are sufficiently predictive or useful to meet medical screening criteria for use in the general population.

It is difficult to find exact figures on the cost to taxpayers of the political commitment to investing in a new bio-economy. The main costs identified are:

Time and money

In the UK alone, at least 60 Government policy initiatives and reports have been commissioned to support and develop the KBBE over the last 15 years, with many more initiatives focused on the broader context of the knowledge-based economy in general. Estimates of taxpayers' money spent or allocated include:

- £12 billion plus allocated to implementing the UK centralised system of electronic medical records known as the 'Spine', with the aim of implementing a 'genetic revolution' in healthcare;
- Euros 13.1 billion in national and regional government subsidies for biotechnology across the

15 old EU member states between 2002 and 2005, of which Euros 1.4 billion was spent by the UK. The breakdown across the EU was about 2.06 billion, 690 million, and 525 million Euros a year on health, agricultural and industrial biotechnology respectively. This level of spending continued but has not been documented subsequently.
An additional unspecified amount from the EU's DG Research.

Skills lost
Shortages in a wide range of skills in health and agriculture R&D have been identified as a result of an over-emphasis on the role of molecular biology: including: pharmacology, human and plant physiology, plant pathology and general botany, plant-soil interactions, weed science, and entomology/pest biology.

Opportunity costs
The UK and EU have failed to develop new competitive economies as a result of reliance on the idea that a new biotech economy would be developed. More practical solutions to existing problems have been neglected, as has much R&D that is not seen as contributing to the KBBE (such as agricultural extension services in England and Wales, which used to provide on-the-ground scientific support to farmers). Public sector plant breeding, which used to generate income as well as bringing significant international economic benefit and increases in food production, has been abandoned in favour of GM crop research, which has delivered zero return.

The evidence cited in this report suggests that the idea of the KBBE is failing in at least four ways:

It is not delivering, and cannot deliver, the promised revolutions in health, agriculture and sustainability. Indeed, in many situations, the false solutions that it offers may undermine alternative approaches and create significant opportunity costs.

It is not delivering, and cannot deliver, a 'race to the top' for Europe's economies.

By locking 'knowledge' into intellectual property, it fixes old ideas (such as the idea of genes as major risk factors for common diseases) and seeks to market them, distorting research priorities and promoting misinformation, rather than stimulating creativity.

The system of investment prioritises 'technologies of control', designed to monopolise markets and maximise profits.

Such technologies also increase dependency (for example, dependence on scientific risk assessment to determine which foods are safe and which human genetic variants are dangerous; and dependence on the performance of technologies such as seeds supplied by distant corporations, or databases managed by government institutions). In general, people are likely to be sceptical that technologies that reduce their control over their own lives are of benefit to them.

The uncritical promotion of (often barely credible) technical solutions for major social problems, combined with the loss of independent expertise to inform policy and regulation, is undermining democratic values and trust in institutions.

This does not mean that biotechnologies and the biosciences cannot contribute to health, agricultural or sustainability objectives, or to the economy. However, it does mean that it is necessary to re-think the whole idea of the 'knowledge-based bio-economy' (KBBE) and its role in the knowledge-based economy in general.

Structural problems with R&D investments

The key features of the knowledge-based bio-economy distort the market in ways that make research investment decisions unaccountable to either market forces or democratic processes. Problems include that:

'pre-competitive' subsidy, via research funding decisions, lacks accountability and transparency and hides political and commercial commitments to the bio-economy and to imaginary markets presumed to be created in the future;

public-private partnerships and public procurement policies shift investment risks and externalities onto the taxpayer, intermediaries such farmers, doctors and health services, and members of the public;

'light-touch' regulation fails to address market failures and protect health or the environment;
a 'cycle of hype' drives research investment decisions, which become disconnected from reality;
policy commitments are not debated but are instead 'sold' to the public as if they were the inevitable consequences of science and progress.

Both the UK Government and the European Union have adopted a 'vision-led' approach to research investment decisions in which a future world without hunger, or free from cancer and other disease, features prominently. Enthusiasts have portrayed implementing these visions as a 'race' to capture the economic and social benefits of genomics and biotechnology: policy analysis and responsiveness to external critiques are then considered luxuries that cannot be afforded. Thus, the technical, commercial and economic failure of the bio-economy has generally been attributed to unfavourable policies – particularly 'over-regulation' and weak IP protection – and public 'ignorance', rather than the underlying R&D strategy and its failure to appreciate the complexities of biology, society, markets, agriculture and the environment. This results in an agenda that is self-perpetuating, as there is no mechanism to re-appraise existing policies or to stop throwing good money after bad.

The long time-scales and substantial public investments involved in the bio-economy have led to political 'entrapment' in particular innovation strategies. As a result, significant amounts of taxpayers' money continue to be invested in failed or highly speculative approaches. For example, nitrogen-fixing and salt-tolerant GM crops were promised nearly 30 years ago: many scientists are sceptical that such products can be delivered and even enthusiasts predict that several decades more investment would be needed before any prospect of delivery. There is widespread recognition amongst geneticists that most diseases in most people, and many adverse drug reactions, are too complex and too dependent on environmental factors to be predictable by screening people's genes. Yet, significant investments of taxpayers' money continue to be made with a view to integrating scans of people's genomes into electronic medical records to 'predict and prevent' disease.

Alternative 'on-the-ground' approaches to improving health and farming have been side-lined, starved of funding, or even axed altogether, leading to significant opportunity costs due to the failure to implement existing knowledge and best practice in areas such as public health and farmland management.

Political entrapment also means that rejection by the market is treated as an obstacle that must be overcome, with more 'education' (of the public and/or medical professionals) and policies which seek to make adoption of the relevant technologies inevitable. In adopting this approach, policy makers undermine the knowledge and debate which they and society at large rely on to make informed decisions and to make realistic and informed appraisals of techno-scientific claims. They become dependent on a narrow circle of advisors who promote misleading 'visions' of how new technologies will deliver magic solutions to social and environmental problems. They also undermine public trust in scientific and political institutions, by creating unrealistic expectations and by hiding the real motivations for public statements and decisions.

The existing system of investment in research in health and agriculture has wasted billions in taxpayers' money and delivered nothing in terms of a viable new 'bio-economy'. It has also exacted a high price in human lives due to wasted opportunity costs by acting as a distraction from more immediate, lower-cost alternatives. This is partly because ensuring that existing treatments and a varied, balanced diet reach everybody would save a lot more lives than any possible technological developments; and partly because the system distorts the research agenda away from human needs as well as from the broader development of scientific knowledge and understanding. The problem is not that commercial interests should not play a role in funding and helping to drive (at least some) R&D investment, or that technology (including biotechnology) has no positive applications, but that the system of policies and incentives created to drive the 'knowledge-based bio-economy' is deeply flawed.

The main findings of this report are that:

Major investment decisions in R&D and in research infrastructure are being made by the EU and by the UK Government without due diligence – including scientific diligence – or cost-benefit analysis. 'Optimism bias' leading to significant underestimates of social, environmental and economic risks is rife. Yet the UK Treasury does not apply its rules for economic assessment or appraisal to major R&D investments, unlike other major infrastructure projects. A one-off assessment of the costs and benefits of highly uncertain future technologies is unlikely to help, but ongoing appraisals and analysis, combined with a greater awareness of the assumptions on which claims of progress have been based, would reduce the risk of throwing 'good money after bad'.

Expertise from a narrow range of commercial interests and perspectives seen as key to the KBBE has been integrated into the scientific institutions, government departments and research councils where research funding decisions are made. These advisors are likely to influence research strategies and choose research priorities from their own perspective, without being answerable to taxpayers or responsive to public concerns. This is taken to a new level by the European Technology Platforms, where research strategies in food, health and agriculture are being determined by the 'vision' of a small number of advisors to the relevant commercial sectors.

There has been a loss of expertise in important areas needed to achieve societal aims such as improved health and more sustainable agriculture. Whole areas of research and development, such as farmland management and public health, have been neglected. A lack of 'counter-expertise' also makes policy-makers and the public vulnerable to misleading claims about what can be delivered by genomics and biotechnology.

The financial, social and environmental risks of public-private partnerships are largely borne by the general public and the taxpayer, who are excluded from decision-making. For example, the 'Plants for the Future' EU Technology Platform was developed by the biotech industry to set the agenda for funding from DG Research. Its commitment to winning more public subsidy in order to develop new GM crops was never debated by voters or consulted on. The desire to build a genetic database of the whole British population underpinned the UK Government's decision to invest £12 billion in building a centralised system of electronic medical records. The Government has never been open about why it made this decision, nor did it assess the costs, supposed benefits, or risks to privacy.

A small number of enthusiasts for particular approaches dominate the decision-making processes for R&D investments. These individuals often have vested interests in promoting these approaches. They have led a 'vision-based' approach to policy-making, which involves promoting claims, rather than assessing their validity or their dependence on (often out-dated) assumptions about biology. Barely credible claims are often made that the development of genetics and genomics, including GM crops and large-scale genetic databases, will eliminate problems as diverse as hunger, cancer, crime, obesity and adverse drug reactions. Typically no independent analysis of these claims is made and critics are dismissed as 'anti-science' or 'anti-progress'.

Political commitments to particular approaches and the role of vested interests are often hidden and rarely open to proper public scrutiny. For example, the UK Government and the EU's DG Research have both endorsed a paradigm shift in medicine to personalised prevention based on genetic risk prediction. At various times, this approach has been supported by the tobacco, nuclear, chemical, food and pharmaceutical industries as a means to expand the market for medicines and functional foods and to avoid controls on unhealthy products and pollution, by promoting genetic explanations for cancer and obesity. There is no evidence that it is of benefit to health or likely to be cost-effective.

The research funding system encourages the patenting, promotion and marketing of scientific discoveries, even though most published research findings are later refuted by further research. This undermines the concept of the scientific method as a means of formulating and testing hypotheses with experimental evidence, and replaces it with a system that encourages exaggerated claims, including to policy makers and investors and to the public via the media.

Science and innovation has become increasingly disconnected from the users of research. This is most striking in food and farming research, where agricultural colleges, extension services for farmers, and traditional plant breeding have largely disappeared and research priorities are driven by what can be patented by commercial seed companies or 'add value' for food manufacturers.

There are likely to be significant opportunity costs as a result of poor investments made via the current research funding system. Billions of pounds and euros are being spent on ineffective or spurious solutions to major social, environmental, health and economic problems: including hunger and obesity.

The public is becoming increasingly alienated and disillusioned and is sceptical that research priorities are being set in the public interest or that they will deliver economic benefits. For example, the Science Horizons project found that it is widely assumed that policy-makers in government and big business are not candid with citizens and that technology is being developed by industry and/or government in order to make profits, rather than in response to societal needs.

Recommendations

There is an urgent need to re-assess what has been delivered by the major political and financial investments made in the bio-economy over the past three decades, and to review whether current funding structures, institutions and review mechanisms are fit-for-purpose to deliver genuine solutions to the problems that we face.

Review of the research funding system should lead to a major overhaul, including significant reforms to improve the scientific and technical advice available to the UK Government and to the European Union; reform the patents system; and re-structure funding institutions and systems of incentives for researchers. Objectives should include:

- More democratic decisions about research funding priorities and a more diverse research agenda;
- Greater accountability and scrutiny of major research investment decisions: including economic assessments and appraisals, scrutiny of scientific and technical assumptions, and active steps to prevent political 'entrapment' in research agendas based on false assumptions and misleading claims;
- A role for public engagement in setting research questions and priorities: including consideration of a variety of alternative approaches to addressing problems, and greater democratic accountability for science policy decisions;
- More public engagement in research itself, involving closer co-operation between universities, communities and civil society organisations;
- More funding for research which does not necessarily benefit large corporations but may deliver other benefits: including economic ones (for example, public health research, and research into improving agro-ecological farming methods);
- Funding for 'counter-expertise' and multi-disciplinary research which can identify long-term scientific uncertainties and regulatory gaps;
- Ensuring a thriving scientific culture that can analyse, critique and develop the theoretical concepts that often underlie decision-making, and which are key to developing new understandings;
- A commitment to take public opinions into account in decisions about science and innovation, including methods to ensure full consideration of the broader social, environmental and economic issues associated with adopting particular approaches and technologies.

Introduction

This report is an investigation of the shaping of science, innovation and the economy in the UK and Europe. Looking at the biological sciences in the context of both health and agriculture, it:

Describes the adoption of the idea of the 'knowledge-based economy' (KBE) as the key driver for future economic growth and competitiveness. How do policy commitments to the KBE in Britain and Europe influence research priorities? What is the role of the biosciences and biotechnology in the knowledge-based economy?

Considers whether and how universities and research institutes reinforce certain research trajectories. What encouragement is there for scientists to take a certain path and how do their aspirations affect the process? Are there mechanisms which reinforce central tendencies to follow a certain path and to exclude the public?

Describes how research priorities are set. The report considers the way in which the new European Framework 7 research program was established and how the Medical Research Council and Biotechnology and Biological Research Council set their priorities in the UK, including the role of government policies.

Documents the membership of science policy advisory committees and boards. To demonstrate who is having influence, and where and how conflicts of interest may arise, the report examines who is involved in formal consultations and the extent of any public engagement exercises.

The report examines the extent to which the research agenda is skewed towards attempting to create economic growth in particular commercial sectors, particularly those investing in research and development in the biosciences and biotechnology. It describes how two particular visions of how the biosciences will contribute to both growth and human welfare have been developed and promoted: the idea that everyone will have their own genome sequenced, leading to 'personalised medicine'; and the idea that genetically modified (GM) crops will be developed which improve nutrition, benefit the environment and create a new plant-based system for the manufacture of biofuels, chemicals and pharmaceuticals. It also considers whether the research funding system leads to important areas of research being neglected that could contribute to better health and more sustainable agriculture.

Finally, the report questions whether the current system of setting research priorities is sufficiently open, transparent and democratic. Ways of improving the system are suggested so that more people have a say about what research is done, with the aim of developing a research agenda that better reflects the needs of people and the environment.

1. Biosciences and the Knowledge-based Economy

1.1 Background - the politics of food, health and science

"*Knowledge is power*". Sir Francis Bacon, 1597.

The starting point of this report is that research funding decisions are *political* decisions, about how best to spend public money, which institutions to support and what incentives to provide to researchers in academia and industry. These decisions have economic consequences and potentially affect the lives of billions of people, because they influence what questions are asked and which approaches are adopted to tackle the problems that we face. Research funding decisions in food, health and agriculture can literally be life or death decisions and can also impact profoundly on the environment and the lives of future generations. Significant amounts of public and private money are invested in research and development (R&D), and poor investment decisions waste money and can have significant opportunity costs, if other approaches to solving a problem are neglected. Political decisions are influenced by a desire to solve political, social and environmental problems, but also by lobbying and vested interests, including the views and interests of corporations, scientific institutions, charities and patient groups.

For example, the 'war on cancer', declared by President Nixon in 1971, involved more than $25 billion in US Government research funding in an attempt to find a 'cure'. What research was funded, and the political response to the problem, were strongly influenced by commercial priorities: including those of the tobacco, asbestos, chemical and nuclear industries.[1] Fear of cancer became a powerful motivator for science funding for the Human Genome Project (HGP), but this also involved a political commitment to looking for causes *within* the human body (to the supposedly determining genetic code), rather than *outside*, at the consequences of everyday life and people's environments.[2]

More recently, concerns about the environmental, social and health impacts of industrial agriculture and mass food production have led to an intense debate about the future of food. There is an ongoing political battle between a new vision of agriculture, reliant on the industrial-scale application of biotechnology – including genetically-modified (GM) crops – and an alternative, less intensive, approach, with a focus on dietary diversity and ecologically sustainable farming.[3] These visions take very different political approaches to environmental sustainability, and to tackling problems such as the global food crisis and the current epidemic of obesity. In turn, this implies radically different research priorities.

The pharmaceutical industry is one of the most profitable industries in the world and spends significant amounts of money on research and development (R&D). Because commercial research priorities are driven by the market, significant biases arise in R&D investments: including the neglect of developing country diseases and the increasing medicalisation of ordinary life in order to expand markets. In the commercial sector, it is not surprising that profit is the major driver of health research, underpinned by the patent system. However, public sector funding is influenced by commercial research priorities and certain kinds of research attract little if any funding, either because results cannot be patented or they are of little scientific interest.[4]

Research funding decisions need to take into account what research is considered scientifically 'doable'. But they are not – and cannot be – made in some pure 'scientific' way. The subject of this report is how political decisions influence what research is done in the biosciences particularly in health and agriculture. Because the number of decisions is vast and often poorly documented, the approach used is to describe the developments of policies and processes, alongside one detailed case study.

Military research spending is outside the scope of this report, although there are significant areas of overlap with bioweapons research.[5] The use of biometrics for surveillance is also not discussed,[6]

although the report refers to the potential dual uses of DNA databases for both health and forensic purposes. Similarly, converging technologies (for example, between nanotechnology and biotechnology) and new approaches, such as synthetic biology, are not described in detail. Instead, the intention is to give the reader a clearer understanding of the processes by which research funding decisions are being made.

The focus is on how *public* money is spent, by the UK Government and the European Union, and the extent to which this is influenced by commercial research priorities and political commitments: in particular the commitment to the idea of a new 'bio-economy' as a driver for growth. The report considers the policies that determine what funding is available, the structures of scientific institutions, and the incentives that are provided to undertake particular types of research. Because research funding decisions are likely to have major impacts on the whole of society, it also asks to what extent people are being given a say about research priorities.

1.2 Visions of the future

This report focuses on how two particular visions of the future role of the biosciences and biotechnology in health and agriculture have been developed and promoted, and how these visions have shaped policies, institutions and decisions about research investments.

Driven by the decision to sequence the human genome and by the discovery of genetic engineering, the idea of a 'genetic revolution' in both health and agriculture has been widely promoted since the 1980s. Agriculture is supposed to be transformed by the ability to produce genetically modified (GM) plants, with higher yields and better nutritional properties, or which can be used as production systems for industrial chemicals, including pharmaceuticals and industrial-scale biofuels (agrofuels). A revolution in healthcare has also been promoted, in which knowledge of the human genome leads to medicine becoming a more exact science. In this vision of the future, each person's individual genome (their 'genetic make-up') is stored in electronic medical records, allowing the tailoring of medication and lifestyle advice to a person's genes and the 'prediction and prevention' of disease by treating the (presumed biological) causes, rather than the symptoms.

The first vision of the future is based on the idea that genetic engineering is an important tool to create new products based on living organisms (including plants, animals and micro-organisms, such as bacteria). The second vision of the future is based on the idea that genetic information can also be bought and sold, and that human genetic information can be used as a marketing tool for other 'personalised' products.

Both visions are focused on how to exploit the commercial potential of the molecule DNA which occurs in the cells of living organisms, including micro-organisms, plants, animals and humans.

The double-helix structure of DNA was first described by Watson and Crick in 1953, allowing scientists to begin to explain how the characteristics of different organisms might be inherited, and also how they might be changed when genes are damaged or mutated (either from birth or during life). Parts of the DNA molecule (called 'genes') contain a chemical code that contains instructions which enable the cell to make proteins: the building blocks of living organisms. Humans, and other organisms that reproduce sexually, obtain half their DNA from each parent, so family resemblances can partly be explained by the extent to which characteristics are inherited in genes. Identifying the role that different genes play in humans, animals and plants was initially laborious, but technology has allowed gene sequencing to become increasingly fast and cheap, so that the whole genomes (the 'genetic make-up') of any organism can now be sequenced.

This information can lead to new understanding about biological processes, including insights into human ageing and disease and how the different characteristics of plants and animals develop. It can also be used to seek to develop new products which arguably could improve human health or other aspects of people's lives and which are seen as being part of a new economy (known as the 'bio-economy'), based on the biosciences and biotechnology.

In plants, animals and micro-organisms, there has been a focus on the use of genetic-engineering (inserting new genes in a laboratory, usually from an unrelated organism) to create new genetically-modified organisms (GMOs), with altered characteristics. The technique of taking one piece of DNA and combining it with another is known as 'recombinant DNA' (or rDNA). This technique has been to create new biological production systems for biopharmaceuticals and industrial chemicals, using genetically-modified micro-organisms (GMMs) and also to attempt to create genetically-modified (GM) animals (such as sheep and goats, genetically-modified to produce useful chemicals in their milk) or plants modified to produce vaccines. Biopharmaceuticals are medicines based on chemicals that are normally made in the human body, which were previously difficult or impossible to make in a laboratory (an example is human insulin, made by inserting a piece of DNA into bacteria, which has now replaced the use of pig insulin for treating diabetes). Another idea has been to 'improve' the production of crops and livestock beyond what is possible with natural breeding, by creating GM crops and animals that are intended to be resistant to disease, or herbicides, or have higher yields or altered nutritional properties.

This idea has major implications for the future of food and agriculture because it allows the properties of foods to be altered, as well as pharmaceutical or industrial chemicals to be produced in crops. This vision of the future has not been universally accepted: the role of genetically-modified (GM) food has been particularly controversial, whilst the production of some chemicals in GM micro-organisms, including enzymes for washing powders and some new 'biopharmaceuticals', has generally been viewed more positively.

In humans, the focus has been more on the role of genetic information. In particular, enthusiasts have argued that in the future, everyone will have their own genome sequenced and that this will lead to a 'genetic revolution' in healthcare. Sometimes known as 'personalised medicine', or, more recently, as 'early health', the idea is that people will be given health advice and other products, including medicines, which will differ according to their genetic make-up.

This vision has major implications for healthcare systems in rich countries which it is argued will shift their focus to the 'prediction and prevention', rather than treatment, of disease. Enthusiasts claim that diseases will be prevented by treating people before they become ill and by 'personalising' products and advice. However, critics argue that genetic make-up is poorly predictive of most future diseases, which depend more on social and economic circumstances, and also of limited value in predicting many adverse drug reactions. There is also potential to erode privacy and lead to new forms of discrimination, since individuals and their relatives can be identified and tracked using their DNA, and categorised according to their genetic make-up (inherited or 'germline' genetic differences).

Less controversially, the early development of cancer might also be identified by looking at genetic mutations that arise as a result of genetic damage during a person's lifetime (known as 'somatic' mutations). Some drugs already exist that work for some types of cancer but not others, based on the genetic changes that occur in the cancer cells.

The first part of this report describes how interest from governments in capturing and exploiting the commercial value of genetic engineering and genetic information became a key part of the idea of a new type of economy – known as the 'knowledge-based economy'. Later, we consider how this has influenced the decisions that have been taken about investments in these areas.

1.3 The knowledge-based economy

> "*We talk of Britain's future as being a 'knowledge' economy by which we mean an economy where we do not compete on wages - how can we when China's wage costs are 5 per cent of ours - but on intelligence, on innovation, on creativity*". Former UK Prime Minister Tony Blair, 3rd November 2006.[7]

> "*Europe's economies will prosper or not depending how good we are at coming up with new ideas, new science; and particularly how good we are at technology transfer and innovation*." UK Science Minister Malcolm Wicks, 2007.[8]

The idea of the knowledge-based economy has become a key driver of research investment in Europe and world-wide. The 'knowledge' embedded in a product is seen as adding value to it and is protected by intellectual property rights, which give value to this knowledge and allow it to be traded rather than freely used. Within the European Union, the advocates of this approach argue that Europe, with its scientific institutions and capacity to produce 'knowledge', will be able to capitalise on this globally and sustain Europe's economy in the face of the threat from China, India and other developing countries that are rapidly industrialising and where manufacturing costs are low.

The term 'knowledge-based economy' (KBE) was first coined by the Organisation of Economic Co-operation and Development (OECD) in a 1996 report which argued that the OECD economies were increasingly based on knowledge and information.[9] The OECD is regarded as a club for the world's richest countries: twenty countries set up the OECD in 1960 including the US and the major European powers - and since then a further ten countries have joined.[10] The OECD's 1996 report discussed *"trends in the knowledge-based economy, the role of the science system and the development of knowledge-based indicators and statistics*".

1.3.1 The knowledge-based economy in Britain

> *"This is Britain's path to the future, lit by the brilliant light of science*". former Prime Minister Tony Blair, 2006.[11]

> *"We are redefining and we are restating our socialism in terms of the scientific revolution…The Britain that is going to be forged in the white heat of this revolution will be no place for restrictive practices or outdated methods on either side of industry*". Labour Party Leader Harold Wilson, 1st October 1963, in the run up to his election as Prime Minister.

For much of the post-war period in Britain, science was perceived as the engine of progress and the driving force for economic prosperity and innovation. However, the 1979 election of the Conservative government under Margaret Thatcher (who had trained and worked as a chemist before entering politics) marked a decline in public funding for science.[12] A series of official reports on science, technology and innovation in the mid-1980s argued that science policy needed to be re-orientated towards more commercial goals, with the aim of strengthening economic competitiveness and wealth creation. These proposals reflected the changes already made by President Reagan (elected in 1980) in universities in the United States.[13]

The 1993 White Paper 'Realising our Potential: a Strategy for Science, Engineering and Technology', published by the Conservative government under Prime Minister John Major, was the first major review of science policy for twenty years, and cemented the shift towards increasing commercialisation of university research. Britain was seen as being a world leader in fundamental science, but failing to capitalise on its potential applications, especially in comparison to the USA.

Building a new 'knowledge-based economy' subsequently became a central goal of the New Labour government elected in May 1997. The Third Way, the new approach to the economy advocated by Anthony Giddens and others, promised a new stage of capitalism that would deliver "*prosperity for all*" based on the new knowledge economy and supported by a culture of individual responsibility and enterprise.[14, 15] The new Prime Minister Tony Blair and his Chancellor Gordon Brown developed their policies on the knowledge economy as a key element of the Third Way, with an emphasis on 'partnership' between the public and private sectors.[16] A string of reviews, policy documents and changes in government structures and research funding systems followed, all of which emphasised the need for closer links between industry and universities (Box A).

Box A: UK science and technology policy timeline [17, 18]

1993: The 'Realising Our Potential' White Paper advocates closer links between universities and business. A new Council for Science and Technology is established.[19]

1994: Foresight panels set up to involve academics and industry to advise the Department of Trade and Industry (DTI) on research priorities. Research councils re-organised.

1995: Office of Science and Technology (OST) moved to the DTI.

1997: New Labour government elected.

1998: 'Our competitive future: building the knowledge-based economy' White Paper published by the DTI. Science spending boosted by £1.4 million over the following three years, in partnership with the Wellcome Trust.[20] Council for Science and Technology (CST) re-established, to involve industry leaders in providing scientific advice to Government. University Challenge Fund launched to provide £50 million of venture capital to universities.[21]

1999: The first in a series of reports of 'competitiveness indicators'.[22] Establishment of the first Science Enterprise Centres.[23] Joint Treasury and Arthur Andersen conference to promote the commercialisation of public sector intellectual property.[24] Baker report to Treasury on the commercialisation of research in the Government's Public Sector Research Establishments: 'Creating knowledge, creating wealth'.[25]

2000: DTI's 'Excellence and Opportunity' White Paper. The CST's 'Technology Matters' report.[27] The Treasury's 'Cross-cutting review of the knowledge economy'.[28]

2001: Launch of a new 'Science Research Investment Fund' for university research infrastructure,[29] with an additional £225 million from the Wellcome Trust for biosciences[26], and the 'Higher Education Innovation Fund' to support knowledge transfer.[30] The DTI White Paper 'Opportunity for all in a World of Change' announces University Innovation Centres, new Technology Institutes, and an additional £90 million to promote the commercial exploitation of research in genomics and e-science.[31] New Labour government re-elected. The Scottish Executive publishes a Science Strategy for Scotland.[32]

2002: Publication of Science Minister Lord Sainsbury's Cross-Cutting Review of Science and Research[33] and the Roberts Review of science and engineering skills.[34] Research Councils UK (RCUK) is launched to co-ordinate the work of the UK's seven Research Councils.[35] The Treasury's 'Investing in Innovation' report[36] is launched at the Wellcome Trust. National Audit Office (NAO) Report: 'Delivering the commercialisation of Public Sector Science'.[37]

2003: The Lambert Review of Business-University Collaboration,[38] which identifies a need to streamline and facilitate agreements over ownership of intellectual property in research collaborations, is published by the Treasury, along with a new DTI Innovation Report, 'Competing in the Global Economy'.[39] Launch of a new Skills Strategy.[40]

2004: The 'Science and Innovation Investment Framework 2004 2014' is published as part of the Treasury's 2004 Spending Review.[41] Launch of a Technology Strategy Board (TSB), led by business, with the aim of identifying and supporting new technologies, and re-launch of the CST with new terms of reference and new membership. Launch of a new 'Technology Strategy', inviting applications for Knowledge Transfer Networks and Collaborative R&D[42] and a 'National IP Crime Strategy' to crack down on illegal use of Intellectual Property (IP). Office of Government Commerce's 'Capturing Innovation' report.[43] Lambert Working Group on Intellectual Property set up.

2005: New Labour wins third election. Knowledge Transfer Networks (KTNs) established.[44]

2006: The Office for Science and Technology (OST) becomes the Office for Science and Innovation (OSI). The Northern Ireland Science-Industry Panel (MATRIX) is launched and the Welsh Assembly Government publishes its first Strategy for Science. The Scottish Executive publishes a progress report on its strategy, and appoints a Chief Scientific Advisor.[45, 46] Publication of 'next steps' for the Science and Innovation Framework, creating a single health research fund of at least £1bn a year and giving a wider remit to the TSB.[47] Publication of the Warry report to the DTI, on increasing the economic impact of the Research Councils,[48] and the Leith review of skills.[49] The Global Science and Innovation Forum (GSIF) publishes its strategy, arguing that the UK should use research and innovation to leverage global influence and meet development goals.[50] The Gowers review of intellectual property (IP) recommends stronger enforcement of IP.[51]

2007: Gordon Brown becomes Prime Minister and creates a new Department for Innovation, Universities and Skills (DIUS) – containing a new Government Office for Science to replace the OSI – and a Department for Business, Enterprise and Regulatory Reform (BERR). The third annual review of the ten-year framework is published. The Sainsbury Review of Science and Innovation leads to a new package of support for innovation.[52, 53] Chancellor Alastair

Darling announces that investment in science and university research will rise to £6.3 billion by 2010-11, following the Treasury's Comprehensive Spending Review, and provides funds to implement the recommendations of the Sainsbury and Cooksey reviews.[54, 55] Research Councils are required to set specific targets for the amount of R&D they conduct in partnership with the Technology Strategy Board (TSB), now at arms-length from Government. The new Scottish Government confirms plans to develop a new science strategy for Scotland.[56]

2008 BERR publishes the 2008 Enterprise Strategy.[57] DIUS publishes 'Innovation Nation', which advocates a role for Government in driving demand for innovation as well as supply.[58] DIUS issues a consultation on Science and Society.[59]

2009 Science Minister Lord Drayson,[60] Secretaries of State John Denham[61] (DIUS) and Lord Mandelson[62] (BERR), and the Prime Minister[63], all make speeches emphasising the role of science and innovation in rescuing the economy from recession. In June, a new Department for Business, Innovation and Skills (BIS), headed by Lord Mandelson, is created, which re-combines DIUS and BERR. Mandelson states that scientific research that will bring greater economic benefits to Britain will get more emphasis.[64]

2010 Research funding to English universities is frozen following the recession, whilst budgets for teaching and buildings are cut.[65]

The UK Government's stated ambition is "*for the UK to be a key knowledge hub in the global economy, with a reputation for not only outstanding scientific and technological discovery but also as a world leader in turning new knowledge into new products and services*".[41] In 1997/98 when the current Government came to power, the science budget was £1.3 billion: it more than doubled in real terms to £3.4 billion by 2007/8.[66] The Government's long-term objective for the UK economy is to increase the level of knowledge intensity in the UK as measured by the ratio of R&D across the economy to national gross domestic product (GDP), from its current level of around 1.9 per cent to 2.5 per cent by around 2014.

In addition to highlighting the need for economic stability in the short-term, the speeches of Gordon Brown as Chancellor (from 1997 to 2007) all claim that investing in science and innovation, via public-private partnerships with industry, is the route to securing the long-term future of Britain's economy. He stated, for example, that: "*Every economic and social reform we are making is creating a new Britain where from the foundation of these enduring values we harness modern technology for the benefit of all*";[67] and that: "*Increased wealth and prosperity for every country in the new century will depend on the essential foundations:*

> *Of economic stability that comes from a sound a disciplined monetary and fiscal policy; and*
>
> *Of enterprise in the new knowledge based economy*".[68]

As Prime Minister, during the recession, Brown stated that the economic importance of science would be even greater than before, and that the science budget would remain ring-fenced, arguing that: "*we* [should] *entrench investment in science as a national priority – maintaining our commitment to continue our path of raising investment in science across the board – targeting specifically the key sectors where we have a strong competitive advantage and bringing scientists and industry together in partnership to underpin a new extended science base in the UK*".[63]

Thus, since 1997, science and innovation have been seen as the keys to delivering economic growth and to improving people's quality of life. For example, the Department of Trade and Industry (DTI) 2000 policy states[26]: "*This White Paper sets out the way ahead…so that we ensure science and innovation combine to generate wealth, businesses and jobs for our citizens and help us attack disease, crime and environmental degradation*".

Rather than adopting a 'problem-led' approach – investigating a variety of possible approaches to solving a particular problem – investments in key technologies (particularly biotechnologies, see Section 1.3.1, and information technologies, including the 'database state'[69]) are expected to deliver a wide range of benefits: thus delivering solutions to problems as diverse as hunger, obesity, crime and cancer, as well as re-vitalising the economy.

Throughout the policy documents listed in Box A, the policies needed to deliver this vision are seen as those that 'modernise' Britain by designing institutions, funding mechanisms, education and regulation to create a 'culture of innovation'. Technical or scientific barriers to delivery are not discussed, although there are concerns about competition from overseas, and about the need to ensure that public concerns about new technologies do not derail the vision.

The dual purpose of delivering economic growth and improved quality of life is generally presumed to be unproblematic, provided Government does not try to 'pick winners' but instead creates the right climate for the commercialisation of new ideas. The science and innovation strategy is underpinned by various funding mechanisms and incentives, but throughout: "*Intellectual Property (IP) is an essential foundation to the UK's success in the knowledge economy*".[47]

Of the numerous policy documents listed in Box A, the 2002 National Audit Office (NAO) report[37] is the only one to refer to possible conflicts in priorities. Reporting the results of a survey, it states (paragraph 2.29) that some scientists are concerned about conflicts of interest and that "*that the confidentiality required for commercial work conflicts with the desire to share research findings openly and puts the impartiality of their advice at risk*". However, the report concludes that "*Conflicting priorities and conflicts of interest that may emerge from commercialisation can be managed*".

1.3.2 The knowledge-based economy in Europe

The European Union has also adopted a new strategy for science, technology and innovation, based on the idea of promoting a 'knowledge-based economy'. From the 1980s to the present, European innovation policy has involved: increased emphasis on stimulating university-industry linkages and on 'strategic' research in universities; the selection and support of generic technologies (particularly IT and biotechnologies); an emphasis on inter-company collaboration in pre-competitive research and the creation of new technology-based firms; and significant growth in the availability of venture capital.[70]

The European Community initially had no common framework for research policy, except for nuclear research under the EURATOM Treaty. In the 1970s the European Space Agency was launched and in 1971 the COST programme (European cooperation in the field of scientific research) was established to prepare and carry out pan-European applied research projects. The FAST programme (Forecasting and Assessment in the field of Science and Technology) was launched in 1978 to define the long-term priorities and objectives of the EC's technological policy. Under FAST, research institutes in the EC competed for grants to forecast developments in three main areas: work and employment, the information society, and the biosociety. The resulting thirty-six reports were used to create a FAST synthesis, which concluded that autonomous socioeconomic development in the EC would require "*a co-ordinated approach in order to derive maximum value from the scientific, technological and industrial potential of the Community countries*".[71]

The First Framework Programme (1984-1987) introduced the long-term planning of research activities at an EU level and the European Research Co-Ordination Agency (EUREKA) was launched in 1985 to promote 'market-driven' collaborative R&D involving industry and research institutes.[72]

In effect, funding supposedly 'pre-competitive' R&D became a key mechanism for providing European public subsidy to particular industrial sectors, beginning with the nuclear industry, but later expanding to other sectors.[72] Such subsidy became a means of seeking to improve industrial competitiveness with other countries – particularly the United States and Japan.

In 1987 the Single European Act explicitly gave the EC formal power in the fields of research and technology; and in 1993 the EU's White Paper 'Growth, competitiveness, and employment' stressed the importance of laying the foundations of the information society.[72] This signalled the beginning of a shift towards the idea of developing what later became known as the 'knowledge-based economy'. The European Commission's Green Paper on Innovation was launched in December 1995, and led

to the first 'Action Plan for Innovation in Europe'. Approved by the Commission at its meeting of 20 November 1996, the plan proposes three main lines of action for tackling Europe's "*innovation deficit*" (relative to the USA): promoting a genuine innovation culture; establishing a favourable legal, regulatory and financial environment for innovation; and gearing research more closely to innovation.[73] It argues that co-operation between public research, universities and enterprises must be intensified, and that the protection of intellectual property is "*at the heart*" of the innovation issue. A 1998 progress report reviews the priorities: protection of intellectual property; financing innovation; the regulatory framework and administrative simplification; education and training; gearing research towards innovation; and strengthened overall co-ordination.[74] Numerous innovation policy documents have been published by the Commission since, all advocating similar policies.[75]

In March 2000, European Union heads of state met in Lisbon and adopted the Lisbon Strategy, which aims to make the EU the "*most dynamic competitive knowledge-based economy in the world*". The strategy involves a programme of investment in the so-called 'knowledge triangle' – research, education and innovation. Like Britain, the Europe Union as a whole perceives itself as weak in translating the results of research into innovative products and services that can boost competitiveness.[76] As well as insufficient investment in research and development it has identified an 'innovation gap', which is seen as reflecting weaknesses in areas such as links between research and industry.[77]

The Lisbon Strategy placed innovation at the heart of the EU policy agenda and aimed to address the gap by means of a 'research push'. A subsequent summit adopted the 'Barcelona target', requiring R&D investment to rise from 1.9% to 3% of gross domestic product (GDP), for which two-thirds of the investments should come from the private sector.[78] Progress towards the Lisbon objective was reviewed by Industry and Research ministers in 2002 at a summit in S'Agaro, Spain.[79]

In 2005, the Commission asked a small group of four high-level experts, known as the 'Aho Group', to assess progress and make proposals to boost Europe's research and innovation performance.[80] The group's report, issued in January 2006, argues that there is a large gap between the political rhetoric about the knowledge society and the reality of budgetary and other priorities. It states: "*Europe and its citizens should realise that their way of life is under threat but also that the path to prosperity through research and innovation is open if large scale action is taken now by their leaders before it is too late*". The report calls for a Pact for Research and Innovation to be signed by political, business and social leaders and proposes a 4-pronged strategy focusing on the creation of innovation friendly markets (including 'light touch' regulation and an EU-wide patent system), strengthening R&D resources, increasing structural mobility and fostering a culture which celebrates innovation.[81]

Overall, the same themes emerge in European policy papers as are highlighted in Britain: the need to compete with emerging economies and 'narrow the gap' with the US, and the need to address the 'European Paradox', the perceived failure to turn an excellent science base into commercial products and economic growth.

The existence of a European-funded system of grants for research and pre-competitive development, soft (non-commercial) loans and tax incentives for R&D, allows companies to be subsidised either directly, or via links with universities. Companies, or whole sectors, such as biotechnology or nuclear power, can thus gain competitive advantage. However, although the system is intended to allow European companies to compete with public R&D investment in the USA without falling foul of competition law, it can also favour certain sectors over others without decisions on priorities necessarily being open to public scrutiny or democratic debate.

1.4 Role of biotechnology and the biosciences

Alongside computer-based information technologies, the 'knowledge-based bioeconomy' (KBBE), where products are derived from biological sources, is considered a key part of the knowledge-based economy.[82,83] Human genetic information is also seen as a commodity that can be patented and traded.

1.4.1 The knowledge-based bioeconomy in Britain

> "*Biosciences and biotechnology are a priority for the UK Government. The biosciences and the technology they generate will be one of the prime drivers of the 21st Century. They will impact on all our lives and provide tremendous opportunities and benefits to improve our quality of life through advances in healthcare and environmental protection and through their ability to generate the wealth we need to implement these advances*". Science Minister Lord Sainsbury, November 2001.[84]

Despite the Thatcher Government's lack of enthusiasm for public science funding, it sponsored two major initiatives aimed at preventing Britain from losing out in markets for new technologies: one in information technology (IT) and the other in biotechnology.[12] In 1980, Dr Alfred Spinks, the research director of ICI and a member of two research advisory boards, published a report recommending government investment in biotechnology research.[85] As a result, the Science and Engineering Research Council (SERC) set up a biotechnology directorate, and the other research councils (particularly the Agricultural and Food Research Council, AFRC) began to fund biotechnology and genetic engineering projects. The Spinks report also led to the establishment of Britain's first medical biotechnology company, Celltech (now owned by the Belgian chemical company UBC), half funded by the state and half by private investors.[86] Celltech was given the right of first refusal to exploit research funded by the Medical Research Council (MRC). A new Agricultural Genetics Company similarly obtained rights to research funded by the AFRC.

Starting in 1987, the Thatcher government began to eliminate public sector involvement in near-market research and to privatise government laboratories. In the late 1980s both the National Seed Development Organisation and a large part of the Plant Breeding Institute were sold to the multi-national food manufacturing company, Unilever.[87]

The international Human Genome Organisation (HuGO) was established in 1988, an initiative of Dr Sydney Brenner, then Director of the Medical Research Council's (MRC's) Laboratory of Molecular Biology (LMB) in Cambridge.[88] According to the Wellcome Trust, Brenner and Sir Walter Bodmer of the Imperial Cancer Research Fund (ICRF) initially had difficulty persuading influential bodies in the UK to "think big" about the human genome. But Dr Brenner (who subsequently won a Nobel prize) is credited with gaining the personal support of the then Prime Minister, Margaret Thatcher, for molecular genetics research funded by the MRC to the tune of £11 million over three years from 1989.[89] The Sanger Centre in Cambridge, financed by the Wellcome Trust, allowed the UK to play a major role in the HGP from 1992 (see Appendix A).[90]

The prospect of a new biotech-based economy won further support from John Major's government, and featured in attempts to push science policy closer to the needs of industry, particularly the 1995 reports of the Foresight programme. Subsequently, the support of the so-called "biotech barons" was a key element in winning power for the New Labour government in 1997 (see Appendix A). Investment in the biosciences, with a view to commercialising discoveries in both health and agriculture, became central to the development of the knowledge economy (Box B).

Box B: Bioscience policy timeline

1994: The Biotechnology and Biological Sciences Research Council (BBSRC) replaces the Agriculture and Food Research Council (AFRC).

1995: Biotechnology Means Business initiative launched by the Conservative government[91] (later continued by the New Labour government[92]). The fifteen Foresight panels publish their first reports[93,94], including those on health and life sciences[95] and agriculture[96], which emphasise the role of genetics and biotechnology.

1997: In the run up to the May election, the accountancy firm Arthur Andersen publishes its report 'UK biotech '97 - making the right moves'.[97] During the election campaign, New Labour is given financial and political support by leading biotech entrepreneurs and venture capitalists. In November, the New Labour government signs the European Directive on the Legal Protection of Biological Inventions, honouring its pre-election pledge to do so.[98,99] The

National Health Service (NHS) R&D Levy is established, following a review of NHS research by Professor Sir Anthony Culyer. [100]

1998: Treasury investment in science as part of the Comprehensive Spending Review includes a major new health biosciences public-private partnership with the Wellcome Trust. [101,102] A key area for science spending is identified as the need for a major expansion in molecular, biomolecular and biomedical research.[20] The Working Group on the Financing of High Technology Businesses, reports to the Treasury, claiming that genomics will deliver revolutionary changes in health and agriculture. [103]

1999: Review of the advisory and regulatory framework for biotechnology. [104] Lord Sainsbury's report on 'biotechnology clusters'. [105] DTI's 'Genome Valley' report claims high economic potential and strategic importance for biotechnology in the UK. [106] Medical Research Council Technology (MRCT) is created to combine the MRC's technology transfer activities, such as patenting and licensing. [107]

2000: Tony Blair and US President Bill Clinton announce the completed draft of the human genome, claiming that it will revolutionise medicine. [108] The NHS Plan, [109] and the DTI's Foresight Programme's report: Healthcare 2020, [110] endorse future 'genetic susceptibility' screening in the NHS. [111] The Department of Health publishes a report on R&D funding in the NHS. The LINK Applied Genomics programme is launched to support academic/industry collaboration.

2001: The House of Lords Science and Technology Committee recommends centralising electronic medical records to help researchers access data and build a national genetic database. [112] Blair gives a major speech on science to the Royal Society in London, advocating genetic screening and attacking critics of GM crops. [113] 'GM Nation?', a national debate on GM crops and food, is announced. [114] The report of the Pharmaceutical Industry Competitiveness Task Force (PICTF), [115] leads to the publication of annual 'Competitiveness and Performance Indicators'. [116] The Treasury's 'Investing in Innovation' report [117] is launched at the Wellcome Trust. The White Paper 'Opportunity for All in a World of Change' announces a new £25 million, 5 year programme on 'Harnessing Genomics'. [118]

2002: Blair approves the centralised system for electronic medical records known as the 'Spine'. [119] The first Wanless Report to the Treasury on the future of health and the NHS. [120] The Welsh Assembly Government publishes a strategic framework for health R&D. [121]

2003: The Department of Health publishes its White Paper 'Our inheritance our future: realising the potential of genetics in the NHS'. [122] Publication of the Bioscience Innovation and Growth Team (BIGT) report [123] and the Academy of Medical Sciences (AIMS) report 'Strengthening clinical research'. [124] Outcomes of 'GM Nation?' public debate and its reviews of economics and first report on science. [125] The results of the Farm Scale Evaluations (FSEs) of GM crops are also published. [126]

2004: Second report on GM science[125] and minister's statement on GM policy. [127] 'Sciencewise' is launched to help policy makers find out people's views on emerging areas of science & technology. [128] Government response to the BIGT report. [129] Report of the Healthcare Industries Task Force (HITF). [130] Establishment of the UK Clinical Research Collaboration (UKCRC), including NHS and industry partners. [131] Creation of joint MRC/NHS Health Research Delivery group. In the budget, NHS R&D funding is increased by £100 million per year, creating a single 'ring-fenced' health research fund of at least £1 billion per annum. The Research for Patient Benefit Working Party (RPBWP) is set up to develop proposals for implementing the recommendations in the BIGT and AIMS reports and set out the vision for UKCRC. [132] Department of Health report 'Choosing Health' [133] and the second Wanless Report for the Treasury. [134]

2005: The Agriculture and Environment Biotechnology Commission (AEBC) publishes its investigation of what shapes the agricultural research agenda [135] and Government responds. [136] Guidance to facilitate the conduct of commercially-funded research in the NHS is published, in collaboration with the pharmaceutical industry. [137] A report on strengthening UK clinical research is prepared for UKCRC by the consultants McKinsey. [138] In December, the Chancellor, Gordon Brown, and the Health Secretary, Patricia Hewitt announce a 'new deal for medical research'. [139]

2006: 'Best Research for Best Health: a new national health research strategy' is published by the Department of Health [140] and leads to the launch of the National Institute for Health Research (NIHR). [141] Publication of the Cooksey Review of UK Health Research, [142] which recommends a new structure for health research funding, including a new Office for Strategic Co-ordination of Health Research (OSCHR) and a joint MRC/NIHR Translational Medicine Funding Board. AMS report 'Personal data for public good'. [143] Blair makes a major speech on science to the Royal Society in Oxford.[11]

2007: OSCHR established. The BBSRC publishes its High-Level Food Research Strategy for 2007-2012. [144] Health minister Lord Darzi publishes the Interim Report of a new vision for the NHS, including a new Health Innovation Council, together with a fund of up to £100m to help the NHS develop and deploy hi-tech healthcare such as medical devices and diagnostics. [145,146] Ministerial Medical Technology Strategy Group (MMTSG) established, co-chaired by US company GE Healthcare. [147]

2008 Health minister Lord Darzi publishes the Final Report of his vision for the NHS. [148] OSCHR publishes its first report. [149] In December, executives from the UK's biotech sector send a dossier to the UK government proposing a national £1 billion biomedical public-private partnership with half coming from public funds and half from private investors. [150]

2009 Follow-up to the 2003 BIGT report.[151] Science Minister Lord Drayson advocates focusing its science spending more strategically on exploiting the information in NHS electronic medical records, linked to DNA and genomic information, in order to help rescue the economy from the recession.[60] New legislation is published, which includes proposals for sharing data in electronic medical records without consent, but this is withdrawn within weeks due to massive public opposition (see also Appendix A).[152] Lord Drayson seeks the extra £1 billion in the 2009 budget, but is unsuccessful.[153] A new Office for Life Sciences (OLS) is set up[154,155] and publishes its 'Life Sciences Blueprint'.[156] New NHS five-year plan published.[157] The Scottish Academic Health Sciences Collaboration (SAHSC)[158] and the Welsh National Institute of Social Care and Health Research (NISCHR) are set up.[159] House of Lords Science and Technology Committee's 'Genomic Medicine' report.[160] The Technology Strategy Board's Biosciences Strategy 2009-2012[161] and Medicines and Healthcare Strategy.[162] An NHS consultation reports on responses to proposals to use electronic medical record data (including genomic data) for research without consent.[163] At the Prime Minister's request, the Food Standards Agency sets up a steering group to develop a new public dialogue on 'Food: the use of genetic modification'.[164] Cross-departmental Human Genomics Strategy Group (HGSG) announced.[165]

2010 The OLS publishes 'Life Sciences 2010'.[166] AMS vision for UK medical sciences.[167]

A number of central themes emerge from these documents, which reflect the aims and limitations of the knowledge-based economy as a whole.[14]

Overall, the policy documents take a strongly 'vision-based' approach, in which significant future benefits are described and promoted, rather than evaluated. For example, the 1998 Treasury Working Group on the Financing of High Technology and the 1999 Department of Trade and Industry (DTI) report 'Genome Valley' both claim that genomics will revolutionise healthcare by allowing predictive human genetic profiling, and that the nutritional quality of crops will be improved using genetic modification (GM). There is no assessment of whether or not these claims will be delivered, the likely costs, or of the claimed benefits to health or the economy. The emphasis is on PR (most famously, the June 2000 launch of the draft Human Genome by Clinton and Blair), and on 'educating' the public (and doctors) to accept the new technologies, rather than on a critical assessment of these claims.

Bioscience research, like the knowledge-based economy in general, is seen as serving the dual purpose of creating wealth and improving quality of life – particularly improving health outcomes in the NHS, but also contributing to sustainability and a better environment. For example, the "vision" outlined in the 2006 report 'Best Research for Best Health' is *"to improve the health and wealth of the nation through research*". In the process of developing this policy agenda, both wealth and

knowledge become narrowly defined. Wealth means economic benefits for those investing in research and development in the biosciences and biotechnology (particularly venture capitalists), and knowledge is knowledge about biological processes and technologies (including genetic information and genetically modified organisms) that can be patented and traded in the new knowledge economy.

Despite this narrow focus, the benefits for the economy as a whole are claimed to be substantive. The UK Department of Trade and Industry's Genome Valley report[106] cites figures from a 1997 EuropaBio report, which claims that the value of EU products using biotechnology was already 40 billion European Currency Units (Ecus) in 1995 (Ecus were succeeded by, and equivalent in value to Euros, since 1st January 1999). By 2005 the value of biotechnology products was expected to reach between 25 billion and 250 billion Euros, with a base case scenario of 150 billion Euros, assuming steady progress. The three key external business factors which the industry trade body EuropaBio identified in its scenarios were: market conditions (whether consumer attitudes were favourable or not); whether effective protection of Intellectual Property (IP) exists; and the framework of regulatory controls. The Genome Valley report concluded that the most likely scenario was that the value of biotechnology products would reach 100 billion Euros by 2005, and that 1 million jobs throughout Europe would be based on biotechnology.

Although concerns about consumer attitudes and the regulatory framework are highlighted, no doubts are expressed in the policy documents about the ability of science and technology to achieve the twin goals of wealth-creation and improved quality of life, or about possible conflicts in the priorities, institutions or incentives needed to achieve these aims. Technical and scientific solutions to social and economic problems, particularly the 'genetic revolution' in healthcare and agriculture, are presumed to exist and to provide a 'win-win' option, often claimed to be cheaper and more efficient for the public sector at the same time as achieving industry growth.

Throughout the policy documents, there is a strong commitment to 'partnership' between the public and private sectors, in which the aims of the two sectors (for example, the pharmaceutical industry and the NHS), and of different types of business (for example, organic and industrial agriculture), are assumed to coincide, or at least be able to 'co-exist'. There is little if any discussion of potential conflicts, or debate about the financial risks or externalities which fall on members of the public or other business sectors. Decisions about what systems and infrastructures to create, and what research to fund, are therefore 'industry-led' on the assumption that this serves the public interest. To achieve this, expertise from a narrow range of industries seen as key to the knowledge-based bio-economy has been integrated into the scientific institutions, government departments and research councils where research funding decisions are made (see Section 3).[168]

The documents also reflect an ongoing concern that Britain will lose the 'race' to commercialise bioscience research, due to failures on the part of government or industry (particularly failure to invest sufficiently in R&D, or to create a 'culture of innovation' in the NHS) or lack of public support and understanding. In a chapter entitled "*What does industry want from Government?*" the Genome Valley report identifies:

> Long-term government support for the science base in bioscience.
>
> A "*balanced regulatory regime*" in the UK, EU and internationally which "*encourages industry while at the same time ensuring public and environmental safety*".
>
> A fiscal regime which encourages investment in the sector and provides "*attractive incentives*" to those who risk their own capital.
>
> A "*discriminating and informed NHS*" which considers fully the "*potential benefits of novel treatments*" and helps to pull through commercial opportunities while taking into account evidence of clinical and cost effectiveness. A willingness for Government Departments and industry to "*work together to consider how clinical, purchasing and prescribing practices might evolve as a result of scientific progress*".
>
> Availability of NHS information for research purposes "*within an appropriate ethical framework*".

Changes in school curricula to encourage young people to study biological sciences and to make them "*informed consumers*"; provision of modern biological research equipment into schools and especially into Universities to prepare the generation who will "*reap the benefits of the biotechnology revolution*". Better targeted courses to meet the future skills needs of industry. More competitions to encourage entrepreneurship among degree and postgraduate students.

Strengthened technology transfer machinery and better quality teams to "*manage publicly-funded research for the economic benefit of the UK*".

Britain is seen as playing a leading role in bioscience research, especially the human genome project and stem cell research, but remaining weak on commercialisation. Its trump card is seen as the vast resource of information that may be provided for genetic and other research by patients in the NHS. As described in Appendix A, the idea of building a national genetic database, or biobank, linking DNA with information in electronic medical records, has been developed and promoted by the Government on the grounds that medical data and biological samples stored in the NHS are Britain's 'unique-selling point' (USP) in the knowledge-based economy.

Following growing public opposition to growing GM crops and eating GM food in Britain – which started with the commercialisation of GM crops in 1994 and had become headline news by 1997 – policy documents reflect a strong underlying fear that the public will reject all the claimed benefits of biotechnology and thus undermine the entire strategy. Questioning the 'knowledge-based bio-economy' approach, especially the role of biotechnology, is often dismissed as irrational ('anti-science', 'anti-progress', or 'scaremongering'). For example, in 1999, Sir George Poste – an advocate of creating a national DNA database linked to electronic medical records in the NHS (see Appendix A) - urged ministers to ignore "*scaremongering by anti-technology lobbies"* and *"above all, to recognise that the dramatic pace of change renders many traditional approaches to technology transfer and policy review obsolete*".[169] Thus, Prime Minister Tony Blair's major 2002 speech on science attacked critics of GM crops as using "*emotion to drive out reason*", at the same time as making the contentious claim that gene sequencing would in future allow doctors to "*pinpoint flawed genes and gene products and predict what diseases you are likely to develop years in advance of any symptoms - and how to help you avoid them*".[113]

There is some willingness to make concessions to address public 'fears', but only in the face of public protest. This includes, for example, delaying (although not abandoning) the commercial growing of GM crops and recognising the need to tackle privacy concerns regarding the use of patient data and samples in health research (whilst ensuring that companies nevertheless get access to the data). However, criticism of the underlying scientific or economic approach – or the merits of the underlying strategies for health and agriculture – is seen as off-limits to the public.[170,171] Implementing the 'genetic revolution' in health or agriculture is never abandoned but simply repackaged and resold, on the assumption that the right PR strategy will convince the public. For example, in 2008, ministers again began preparing to open the way for genetically modified crops to be grown in Britain on the grounds they could help combat the global food crisis.[172] Meetings with the biotech industry led to plans for a new 'public dialogue' on GM crops, to be led by the Food Standards Agency (FSA), and due to be launched in 2010.

The bioscience policy documents listed in Box B also demonstrate a commitment to 'light touch' regulation, on the grounds that this will stimulate innovation and avoid undue delay in the supposed 'race' to commercialise products. This is accompanied by a frequent failure to seek independent evidence of the claimed benefits of the overall approach or of specific technologies or policies (for example, during the development of the 2003 White Paper on genetics in the NHS). A small circle of the same advisors, with close links to specific industrial sectors, has influenced virtually all the policy reviews of bioscience research, often recommending the establishment of new committees to which they get appointed (see Section 4).

The exception to the general trend towards more 'industry-led' research agendas is some recognition of the need to engage the public more in decisions about science and technology. This is reflected in

the 2004 launch of the 'Sciencewise' programme and the 2005 report 'What Shapes the Research Agenda?'[135] published by the Agriculture and Environment Biotechnology Commission (AEBC), a Government Advisory Committee (now disbanded) which had a broad membership (including natural and social scientists, people from the biotechnology industry, environmental campaigners and lawyers), and was set up in response to public concerns about GM crops and foods. The report recommends more 'upstream' public engagement in the research agenda, at the strategic level. This idea, and the extent to which it has been adopted, is considered further in Section 6 of this report.

The approach to the biosciences and biotechnology differs somewhat in Scotland, Wales and Northern Ireland. Most significantly, the devolved administrations have taken a more precautionary approach to GM crops, and have adopted GM-free policies.[173] Attitudes to privacy, consent and the role of public services also differ. At Westminster, a major controversy was sparked in 2009 by plans to adopt data-sharing legislation covering information contained in people's personal electronic medical records, which would have allowed access to this data by private companies without consent. However, the Scottish Government withheld legislative consent for the plans as a result of public concerns.[174] The industry-driven Office of Life Sciences (OLS) set up in 2009 by the UK Government's Department of Business, Innovation and Skills, also differs in emphasis from the new the Scottish Academic Health Sciences Collaboration (SAHSC) and the Welsh National Institute of Social Care and Health Research (NISCHR), both of which place more emphasis on the needs of health and public services, and less on the role of science and industry in generating a new biotech economy.

1.4.2 The knowledge-based bioeconomy in Europe

The EU sees biotechnology as "*at the forefront of those frontier technologies which are helping to take the European Union towards its long-term strategic goal established by the Lisbon European Council in March 2000*".[175]

Biotechnology was first identified as a key component of European economic competitiveness in 1979, in the EC FAST programme's report 'Biosociety'. The European Commission's support for biotechnology research began in 1982 under the First Framework Programme (FP1) with the EUR 15 million Biomolecular Engineering Programme (BEP), and has since continued with increasing funding and industry involvement (see Section 3.3).

These developments mirrored those in the US, where a 1981 report of the Office of Technology Assessment (OTA) covered the options for Federal support of biotechnology R&D; methods and applications of genetic engineering; risks, patents, regulation and options for public involvement in decision-making.[176]

In 1988, the Commission published the first draft of its Directive on patenting in biotechnology (led by the 1980 ruling of the US Supreme Court, in the landmark case of Diamond v. Chakrabarty, see Section 2.2.3). The controversial draft Directive was rejected by the European Parliament in March 1995, following widespread opposition to 'patents on life', but was finally adopted in 1998 (see Section 2.2.3).

The European Commission approved a 2-year human genome effort in 1990.[177] In 1991, the Commission issued the 'Bangemann Communication', which states that:
"*Biotechnology is a key technology for the future competitive development of the Community*".[178] Key recommendations of the Bangemann Communication are[179]:

(i) public funding of biotechnology research and development (R&D), training and the information infrastructure;
(ii) harmonisation of the legal and regulatory framework;
(iii) the creation of a bioethics advisory committee;
(iv) the creation of Community legislation on intellectual property rights.

In September 2001, the European Commission launched a consultation exercise in order to develop a strategy on life sciences and biotechnology.[180] The Strategy, including a roadmap up to 2010, was adopted in 2002.[181] According to the Commission the publication of the Strategy reflected the importance attached to life sciences by the European Council in reaching the Lisbon goal.[182]

The strategy reaffirms Europe's commitment to biotechnology as an engine for growth, and to strong patent protection. It states that: "*A main objective must be to ensure that the EU maintains competitiveness vis-à-vis major industrialised countries such as the United States and Japan*" (page 25) and its Action Plan includes support for biotechnology research via its Framework Six (FP6) research programme (see Section 3.3).

The introduction to the Strategy expresses concerns (page 8) that "*Europe seems to be hesitating*" and refers to the "*intense public debate*" on genetically modified (GM) crops, claiming that uncertainty about social acceptance has "*stifled our competitive position, weakened our research capability and could limit our policy options in the longer term*".

However, the Life Sciences Strategy is upbeat about the potential of biotechnology. In relation to health, it states (page 10):
"*Biotechnology already enables cheaper, safer and more ethical production of a growing number of traditional as well as new drugs and medical services . . . Biotechnology is behind the paradigm shift in disease management towards both personalised and preventive medicine based on genetic predisposition, targeted screening, diagnosis, and innovative drug treatments. Pharmacogenomics, which applies information about the human genome to drug design, discovery and development, will further support this radical change. Stem cell research and xenotransplantation offer the prospect of replacement tissues and organs to treat degenerative diseases and injury resulting from strokes, Alzheimer's and Parkinson's diseases, burns and spinal-cord injuries*".

In relation to food and agriculture, the Strategy states (page 11):
"*In the agro-food area, biotechnology has the potential to deliver improved food quality and environmental benefits through agronomically improved crops. . . . Food and feed quality may be linked to disease prevention and reduced health risks. Foods with enhanced qualities ('functional foods') are likely to become increasingly important as part of lifestyle and nutritional benefits . . . Considerable reductions in pesticide use have been recorded in crops with modified resistance. The enhancement of natural resistance to disease or stress in plants and animals can lead to reduced use of chemical pesticides, fertilisers and drugs, and increased use of conservation tillage and hence more sustainable agricultural practices, reducing soil erosion and benefiting the environment. Life sciences and biotechnology are likely to be one of the important tools in fighting hunger and malnutrition and feeding an increasing human population on the currently cultivated land area, with reduced environmental impact*."

The EC's Strategy also highlights biotechnology's potential to *"improve non-food uses of crops*" as sources of industrial feedstocks or new materials such as biodegradable plastics and states that "*under the appropriate economic and fiscal conditions*", biomass could contribute to alternative energy with biofuels such as biodiesel and bioethanol.

The Strategy does not refer to any evidence which contests these claims of benefit. Nor does it recognise obvious sources of potential conflict, such as that between the use of land for growing food or growing biofuels.

In addition to its claims about benefits to health and the environment, the Strategy report predicts major economic benefits:
"*Some estimates suggest that by the year 2005 the European biotechnology market could be worth over EUR 100 billion. By the end of the decade, global markets, including sectors where life sciences and biotechnology constitute a major portion of the new technology applied, could amount to over EUR 2 000 billion*".

The Strategy Action Plan includes a commitment to establish a 'Competitiveness in Biotechnology Advisory Group' (CBAG). This was set up in 2003 (see Box C). In its 2004 report, the CBAG refers to biotechnology as: "*the backbone of a knowledge-based economy, a vital driver of Europe's competitiveness*".[183] Its 2006 report[184] recommends that the Commission develops "*a major campaign to make the revolution of Life Sciences and Biotechnology visible to all major stakeholders, including the broader public, still-hesitant decision makers and investors, to increase awareness and acceptance*".

Box C: The Competitiveness in Biotechnology Advisory Group (CBAG)

The role of the Competitiveness in Biotech Advisory Group (CBAG) is to develop recommendations on how the Commission can support the biotech industry.[185] In 2006, members included companies involved in GM crops, such as Monsanto, Syngenta, and BASF Plant Sciences, plus the Dutch food ingredients company DSM and medical biotechnology companies such as Genzyme Europe.[186] The pharmaceutical company GlaxoSmithKline (GSK) was represented by Dr Peter Goodfellow (see Appendix A).

More recently, the 2006 Aho Report to the European Commission identified a number of 'pervasive technologies' which they highlight as requiring both R&D support and early action to "*anticipate and smooth the path to their commercialisation and application*". These are: information and communication technologies (ICT); biotechnologies including genomics; nanotechnologies; and cognitive and neuro-sciences (and their interaction with social science and humanities).

In April 2007, the European Commission published a mid-term review of the Life Sciences Strategy (known as 'Bio4EU'[187]) and proposed refocusing it on five "biotech-specific priorities"[188]:

(1) Promote research and market development for life sciences and biotechnology applications and the Knowledge Based Bio-Economy (KBBE).
(2) Foster competitiveness, knowledge transfer and innovation from the science base to industry.
(3) Encourage informed societal debates on the benefits and risk of life sciences and biotechnology.
(4) Ensure a sustainable contribution of modern biotechnology to agriculture.
(5) Improve the implementation of the legislation and its impact on competitiveness.

A new vision paper – known as the Cologne paper – was also developed for the EC in 2007 by a group of experts, including representatives of Bayer, AstraZeneca, BASF and Nestlé. It promises a future which includes 'personalised medicine' and 'personalised nutrition'; and 'high performance crops' which will serve as factories for enzymes, amino acids, pharmaceuticals, polymers and fibres and for the production of biofuels, biopolymers and chemicals, leading to "*agriculture thriving without subsidies*". The paper argues that the European Commission and member states should together improve the co-ordination of policies concerning the KBBE, including funding schemes for 'multiple company consortia' to build small-scale industrial plants to process biofuels and other chemicals from plants (biorefineries).[189]

The European Union also has a website on the Knowledge-Based Bioeconomy (KBBE), which states[190]:

"*The KBBE will play an important role in a global economy, where knowledge is the best way to increase productivity and competitiveness and improve our quality of life, while protecting our environment and social model. It is a sector estimated to be worth more than €1.5 trillion per year. KBBE addresses the following needs:*

growing demand for safer, healthier, higher quality food;

sustainable use and production of renewable bio-resources;

increasing risk of epizootic and zoonotic diseases [diseases causing epidemics in animals, and diseases shared by animals and humans] *and food related disorders;*

sustainability and security of agricultural, aquaculture and fisheries production;

increasing demand for high quality food, taking into account animal welfare and rural and coastal contexts and response to specific dietary needs of consumers".

Just as in the UK, bioscience research, like the knowledge economy in general, is seen as serving the dual purpose of creating wealth and improving quality of life for the European Union as a whole. Again, wealth is narrowly defined as economic benefits to those emerging or existing industries which trade in particular types of (patentable) 'knowledge' about biological processes or new genetic technologies. No doubts are expressed about the ability of the science and technology to deliver; potential downsides are not considered; and the possibility of conflicts between this narrow definition of wealth and knowledge-creation and other objectives, such as sustainability and improved health outcomes, is ignored. The main threats to delivering the claimed benefits are seen as potential public opposition, or social unease, and/or the failure of policy-makers to commit sufficient funds or create the right regulatory environment (particularly a failure to implement strong protection of intellectual property). Hence, there is a strong emphasis on promoting public "*awareness and acceptance*" of the claimed benefits of the Commission's strategy, and on convincing "*still hesitant*" investors and decision-makers.

The 'vision-based' approach seen in the UK is reflected in the EU's Life Sciences Strategy and also in new documents produced more recently as part of the adoption of the European Technology Platforms, such as 'Food for Life' and 'Plants for the Future' (See Section 3.3).

1.5 Summary of the knowledge-based economy

The idea of the 'knowledge-based economy' (KBE) has become a key driver of research investment in Europe and worldwide. The Organisation for Economic Co-operation and Development (OECD) has developed and promoted the 'knowledge-based economy' as a means for the rich countries which are its members to compete with much lower manufacturing costs in India and China, without resorting to protectionism in manufactured goods. The UK Government and the EU have both adopted this idea as central to the future of the economy.

In the knowledge-based economy, science and innovation are seen as the key to securing future economic growth. Thus, scientific research and development has received major public subsidies, directed at achieving innovation in particular sectors and technologies. In Britain and Europe, a central objective for policy-makers has been to avoid an 'innovation gap' developing with the United States, as Europe is seen as good at doing science but poor at exploiting it for commercial gain.

The rich country members of the OECD have developed their policies on the knowledge-based economy partly to capture the value and economic growth expected to emerge from investment in the biosciences and biotechnologies. The biosciences – particularly human and plant genomics – are thus seen as central to the knowledge-based economy, and as key to developing a new 'knowledge-based bio-economy'.

Significant investment of taxpayers' money has been accompanied by a 'vision-based' approach to policy making. This involves describing and promoting visions of the future in which heath, sustainability, food supplies and security have been significantly improved by these investments, and political problems such as the rising costs of health care, growing inequalities and over-dependency on oil have been solved by new technologies.

In Britain, in particular, a 'genetic revolution' in healthcare, involving a shift away from treatment to 'prediction and prevention' of disease, is described as both improving health and saving money for the National Health Service as it struggles to cope with an ageing, and increasingly overweight, population. Access to human genetic information, obtained from patients in the National Health Service (NHS), is seen as Britain's 'unique selling point' (USP) to attract the biotech and pharmaceutical industries.

In the EU, the idea of the 'knowledge-based bioeconomy' (KBBE) – involving plant-based production of a wide range of products, including novel foods and industrial chemicals – has been adopted as a key driver of future competitiveness. The creation of a new generation of genetically-modified (GM) plants, containing altered levels of nutrients or resistant to drought, is intended to both prevent and treat diseases associated with over-eating and to tackle hunger and malnutrition across the globe. Future GM plants designed to produce pharmaceuticals and industrial chemicals, and produce industrial scale biofuels (agrofuels) for cars, are supposed to lead to a more sustainable agricultural economy, involving both rural re-generation and reduced dependency on oil.

The UK's 1999 Genome Valley report, and the EC's 2002 Strategy report on life sciences and biotechnology, predict major economic benefits, based on industry figures, stating that by the year 2005 the European biotechnology market could be worth over EUR 100 billion and that, by 2010, global markets could amount to over EUR 2 000 billion.

The extent to which these promises are realistic and whether they are being delivered is considered later, in Section 5.

The main threats to delivering the predicted economic benefit have been identified by industry as consumer rejection; hesitation on the part of investors and/or decision-makers; lack of sufficient protection for intellectual property (IP); and over-regulation. Thus, the key features of the policies developed to underpin the knowledge-based bio-economy are:

- Protectionism in 'knowledge' rather than manufactured goods - via patents and intellectual property rights (IPRs), which confer monopoly rights on 'inventors' and patent applicants;
- Pre-competitive government subsidy of particular 'science-based' business strategies, via public investment in R&D, plus tax incentives for venture capital investors;
- The use of public-private partnerships to share the risk of investments, and public procurement to stimulate demand;
- Restructuring of education and universities to provide employees and researchers with the required technical and business skills, and to create the "*informed consumer*";
- A commitment to 'light touch' regulation of new technologies, on the grounds that government intervention will stifle innovation.

The next section of this report first considers how research funding decisions are influenced by these policies and by the strong political commitment to the knowledge-based bio-economy made by the UK Government and the European Union.

2. Incentives, Assessment and Entrapment in the Knowledge-based Economy

> *"What makes fields such as genomics interesting…is that they combine two forms of value together: the medical and scientific value of "discovery science," and the institutional and commercial value of products, services and property rights*". Eugene Thacker, The Global Genome, 2006 (p94).[191]

> *"'Knowledge' is now regarded not as a public good but instead as 'intellectual property' that is produced, accumulated, traded like other goods and services in the so-called Knowledge Society*". Professor Peter Scott, Vice-Chancellor, Kingston University, UK, 2003.[192]

The central idea behind the knowledge-based economy is that knowledge can be patented and claimed as 'intellectual property' that is valued and traded. This knowledge can also be used to add value to existing or new products. When the Organisation for Economic Co-operation and Development (OECD) developed the idea of the knowledge-based economy it also developed means of measuring how good economies were at producing 'knowledge', by counting patent claims and scientific publications. This idea fits neatly with the idea that DNA contains instructions that can be decoded piece by piece and then patented by the scientist who has discovered the relevant gene 'for' a human or animal disease or useful trait (such as drought-tolerance in plants). The company or institution that funded the research can apply for the patent, and both the 'applicant' and the 'inventor' can then be financially rewarded for their investment and their work. In theory, trading this knowledge, or for investing further to develop products based on the discovery, brings income for researchers and investors, growth and further investment in research, thus stimulating the knowledge-based bio-economy.

In the 1990s, scientists and institutions began to be rewarded for producing 'knowledge' in this way, and for forming new public-private partnerships with industry, facilitating 'knowledge-transfer', and obtaining venture capital investment in small and medium sized enterprises (SMEs) spun-out from universities. Education also began to be restructured to provide the necessary technical and business skills, and to create the "*informed consumer*" who would recognise the benefits of the 'genomic revolution' in health and agriculture and consume or use the new products that were expected to be created.

This section describes the main ways in which research is now assessed, and how incentives are provided to researchers to build partnerships with business and boost the knowledge-based economy.

2.1 Measuring the knowledge-based economy

> "*In the last two decades, concepts have appeared that have influenced and even defined entire science and technology policies in Western countries…In all these policy developments, the OECD, acting as a think tank for its member countries, has been an important promoter of these concepts, turning them into buzzwords*." Benoît Godin, 2006.[193]

The OECD's 1996 report on the knowledge-based economy underpins the shift in science and technology policies documented in Part 1 of this report.[9] It discusses some of the difficulties in measuring and pricing knowledge but also establishes a system by which governments can seek to measure their success in the new knowledge-based economy. Box D shows some of the measures discussed in the report.

Box D: Measures of the knowledge-based economy

Knowledge inputs

Expenditures on research and development (R&D).
Employment of engineers and technical personnel.
Patents.
International balances of payments for technology.

Knowledge stocks and flows

Total knowledge stock accounting for depreciation (such as expired patents).
Flows of knowledge, via technology diffusion (introduction of technology, licensing of patents, use of technologies by businesses and households).
Citation analysis of scientific publications and patents.

Knowledge outputs

R&D intensity (ratio of R&D expenditures to gross output).
Rates of return (financial and social).

Knowledge networks

The distribution of knowledge among universities, public sector institutions and industry (e.g. via outsourcing of industry R&D to universities).
The distribution of knowledge within markets, between suppliers and users.
Institutional capacities to transfer knowledge (e.g. via joint industry-university research projects and publications).
Private sector capabilities in knowledge transfer (e.g. research co-operation within the enterprise sector and internationally).

Measuring knowledge and learning

Social rates of return: education expenditure and attainment, and its impact on growth.
Private rates of return: human skills and training, and its impact on a firm's performance.

The OECD publishes a Science, Technology and Innovation (STI) Scoreboard every other year, which includes a growing number of measures of the knowledge-based economy.

The OECD's measures are now widely used to measure the development of the knowledge-based economy. For example, in its 2007 analysis, the EC's Biopolis project used fourteen indicators to measure the performance of the national biotechnology system of innovation in Europe: [194]

1. Biotech publications per Million Capita (pMC)
2. Biotech publications per biotech public R&D expenditure
3. Biotech patents per biotech publication
4. Biotech publications as share of total number of publications
5. Citations to biotech publications
6. Graduates in life sciences per Million Capita (pMC)
7. Biotech patent applications pMC
8. Biotech companies pMC
9. Biotech start-ups pMC
10. Biotech Initial Public Offerings (IPOs) pMC
11. Venture Capital per Capita (pC)
12. Biotech acceptance index
13. Number of biomedicines
14. Number of field trials.

Only one of these indicators (numbers of biomedicines) is likely to represent actual marketable products.

In this Section, we consider the implications of using public investment in R&D, patents, scientific publications, and increased research co-operation between universities and industry as measures of success in the knowledge-based economy. We ask how these measures:

influence the research agenda and funding priorities;

affect what 'knowledge' is produced and valued and who gains access to it;

impact on science communication and public trust in science;

drive expectations of what science and technology will deliver in the future.

2.2 Patents

> *"Genes are the currency of the future"*: George Poste, then research director of SmithKline Beecham, 1993.[195]

> *"Conceivably…the knowledge economy could be the ultimate commodification, as forms of good hitherto seen primarily as non-economic resources (culture, talent, knowledge, social relations) become forms of capital*." Professor Jenny Andersson, Uppsala University, 2007.[14]

> *"An increasing number of claims per patent, an increasing patent-to-R&D ratio, increasing delays in patent applications, and an increasing use of divisionals, all point to a strategic use of patents which is directed more toward preventing others from innovating, rather than to reap the rewards for innovation*". Report of workshop on EU patent policy, 2007.[196]

> *"The current system, 'Old IP,' rests on the belief that if some intellectual property (IP) is good, more must be better. But such thinking has proved counterproductive to industry, which in health fields has seen declining levels of innovation despite increasing stakes in intellectual property. The era of Old IP has also proved counterproductive to the world's poor who await advances in health and agriculture long available to the global elite*". The International Expert Group on Biotechnology, Innovation and Intellectual Property, 2008.[197]

> *"Arguably, the current threshold of inventiveness for existing patents is also too low. The inventive steps required to qualify for patents should be considerable, and the resulting patents must be well defined, so as to minimise litigation and maximise the scope for subsequent innovators*". The Cutler Report: Review of the National Innovation System (Australia), 2008.[198]

The OECD argues that patents "*since they represent ideas themselves*" are the closest direct indicators of knowledge formation. However, it is more accurate to say that patents indicate a demand for monopoly over an 'invention'.

Patents give the patent-holder monopoly rights to commercial exploitation of an invention for 20 years or more. In theory, patents act as a reward for invention that is supposed to stimulate investment, creativity and economic growth. The patent-holder is required to disclose the details of the invention, so that others can build on it by undertaking further research and development, but ownership of the patent prevents others from simply copying the invention – if they do so they are considered to have stolen the patent-holder's 'intellectual property' (IP).

The OECD treats patents as a positive measure of knowledge creation.[199] However, the role of patents in the economy in general and the knowledge-based economy in particular, is controversial. The system is defended by some as providing essential rewards for innovation, but criticised by others for not delivering benefits to the economy or meeting human needs.[200,197] For example, the Nobel Laureates Sir John Sulston and Joseph Stiglitz warned in 2008 that medical research is hindered by patent law, arguing that it is increasingly being manipulated by industry to thwart rivals, block research or to direct it away from humanitarian goals towards those that maximise profits.[201]

The Food Ethics Council describes concerns that[202]:

> Intellectual Property (IP) protection is based on an individualistic model of invention and creativity, rewarding a small number of individual 'inventors' in what is usually a collective process.
>
> A proliferation of biologically-based patents, including patents on DNA sequences, is threatening to grid-lock research in some areas.
>
> IP creates a market for knowledge that may not meet many of society's needs.
>
> IP selectively rewards certain types of knowledge (knowledge that can be patented).

Patents are intended to stimulate investment, by rewarding the investor with a temporary monopoly over their invention. However, because patents grant monopoly rights (really 'privileges', rather than rights), they can also restrict access by people in poorer countries to vital medicines, and other new technologies. Patents also do little to stimulate innovation in the absence of a profitable market for the products, as is often the case, for example, with medicines for diseases that disproportionately affect people in developing countries.[203]

Patents are primarily used to protect inventions from imitation and to secure markets, however companies increasingly have other motivations for patenting, including: blocking competitors; increasing the company's reputation and value; using patents as a means of exchanging value with partners, licensees and investors; and as a means to control internal performance and motivations.[204] A 2007 EU patents policy workshop identified increasing strategic use of patents: directed more toward preventing others from innovating, rather than encouraging innovation. The workshop also highlighted the difficulties in weeding 'bad' applications: those that have little economic value but nevertheless create a backlog at the patent office and difficulties for competitors.[196] In 2006, patent examiners at the European Patent Office went on strike amidst concerns about the pressure to grant increasing numbers of patents without a thorough assessment of the claims made in them.[205]

The International Expert Group on Biotechnology, Innovation and Intellectual Property argues that the existing system of intellectual property which underpins the knowledge-based economy has been based on two faulty assumptions made nearly three decades ago: that since some intellectual property (IP) is good, more must be better; and that IP is about controlling knowledge rather than sharing it.[197] The report argues that the system therefore has multiple flaws:

> It fails to recognise that knowledge leads best to new products and services if shared.
>
> It wrongly assumes that companies obtain IP to protect their inventions from being copied rather than to trade or enhance their reputations.
>
> It wrongly presumes that if a company has a patent right it could actually use it to prevent others from copying the invention.
>
> It exaggerates the importance of patents in driving innovation.
>
> It fails to address the reality of public health and public health care systems.

Below, we consider how the patent system has developed and expanded to underpin the knowledge-based bio-economy, and how this influences research funding decisions in the biosciences. Significant changes in the patent system have been made in an attempt to drive the 'knowledge-based bio-economy'. However, the role of patents is not straightforward and is often difficult to disentangle from the other factors influencing R&D investments and innovation.

2.2.1 Patents and universities

> "[The pursuit of IP] *is in my view a distraction from other areas that bring more income into universities,* [such as] *meeting the needs of business*". David Sweeney, Director for Research, Enterprise and Skills at the Higher Education Funding Council for England (HEFCE), 2009.[206]

Since the 1980s, there has been a major shift in the role of patents in university research. In Britain in 1985, the Thatcher government officially abolished the British Technology Group's first right of refusal on patents generated by publicly funded research, paralleling the 1980 adoption of the Baye-Dohl Act

in the US, and allowing universities to own and commercialise patents arising from in-house inventions. This decision, combined with the increased involvement of private firms in molecular biology, growing acceptance of intellectual property as a result of academic research, and increased attention to commercialising such intellectual property, has changed the role of university scientists significantly.[207]

Renault, of the US not-for-profit consultancy RTI International, describes the "*emerging ethos of academic capitalism*" in the US as emphasising "*intellectual property rights and the public good attained through the commercialization of results*", in stark contrast to the traditional academic ethos, which emphasised "*disinterestedness, universalism, organized skepticism and communism of intellectual property*".[208] She notes that patents, based on science not validated by other academics, are becoming part of the equation that measures prestige, and therefore career advancement and funding. However, the norm of academic capitalism is not universally embraced and individual professors' beliefs about the appropriate role of universities in commercialising technology are the single most important predictor of whether they make patent applications or seek to create spin-out companies.

Guena and Nesta note that little is known about the changes taking place in public research as a result of increased patenting by European universities, and assessment of the effects is difficult because patents are just one of a set of new technology transfer activities developed over the last 10 to 20 years.[209] Suggested positive impacts may include:

Increased financial resources (as a result of increased licensing and royalties).

Increased contract research funding for further developments into a final product.

Creation of spin-out companies that are partially owned by the university.

Faster exploitation of new inventions.

However, there is generally a lack of strong evidence for these positive outcomes, and no conclusive evidence regarding whether patenting is an efficient device for transferring technologies and know-how. Genuinely useful inventions are inherently rare and the value of inventions is difficult or impossible to forecast, suggesting that only a few universities are likely to win, while the majority may eventually get poorer through the expensive daily conduct of their technology transfer and patenting offices. There is also a failure amongst policy makers to consider possible negative impacts of university patenting, such as:

Negative impacts upon the culture of open science, in the form of increased secrecy (reduced willingness to share data with colleagues), delays in publication, increased costs of accessing research material or tools, etc.

Diverting research resources (researchers' time and equipment) from research questions that may not to be suited to the development of patents.

Threats to future scientific investigation from the existence of patents on previous research.

The Director for Research, Enterprise and Skills at HEFCE has argued that an "obsession" with generating income from intellectual property (IP) is distracting universities from the real issues when engaging with business. David Sweeney has pointed out that even the Massachusetts Institute of Technology, the world's most business-engaged university, earns only about 3% of its income from IP. At the same 2009 conference, others argued that industry is having too much influence over university teaching and research, and that universities are losing sight of their wider role in society.[206]

There is a recognised tension between the academic need to publish and the commercial requirement for secrecy, in order to be 'first to file' patents on inventions. The core principle of Europe's Paris Convention (1883) for the Protection of Industrial Property is the first-to-file system: that is, the person that receives the patent is the first to file an application, regardless of whether he/she is the original inventor. Public disclosure, in a scientific publication or discussion with colleagues prevents a subsequent patent application because the invention is no longer regarded as new (it does not meet the requirement of 'novelty'). Unlike the US system, the European patent system does not allow a 'grace period' in which the inventor is allowed some months after publication to file the application.[210] This impacts on the open system of publication that has traditionally

underpinned the dissemination of scientific knowledge, because researchers cannot disclose findings without their funders losing the patent, and thus they may be required to delay publication. In the UK, the Lambert model agreements[211] for use by university researchers and their commercial sponsors, include *"a protocol that allows the sponsor an element of control over the content of, and the timescale for, publication (e.g., in order to give the sponsor an opportunity to secure patent protection)."*

2.2.2 Expansion of the patent system

The advent of the knowledge-based economy has led to a major expansion of the patent system, intended to underpin the trade in 'knowledge' and extract commercial value from it.

Two changes have attracted particular criticism: the globalisation of intellectual property rules under the World Trade Organisation's (WTO) agreement on Trade Related Intellectual Property Rights (TRIPS)[200,212] and the extension of the patenting regime to cover gene sequences, micro-organisms, cells, plants and animals created through genetic modification ('patents on life')[213,214]. Although imposed under the 'free trade' system of the WTO, these expansions of the patent system in effect create tariffs on 'knowledge' (supposedly the province of the rich OECD countries and their 'knowledge-based' economies), rather than on manufactured goods (increasingly produced by cheaper labour in poorer countries). They also privilege certain type of 'knowledge' over others (knowledge that can be patented and traded in the knowledge-based economy).

The TRIPS agreement represents the single greatest expansion of intellectual property protection in history.[215] It has forced poorer countries to accept rules initiated by the US pharmaceutical company Pfizer and lobbyists in the US Advisory Committee on Trade Negotiations.[200] Developed countries are expected to be the major beneficiaries of TRIPS – the benefit to the US is estimated at $19 billion a year – with developing countries the net losers.[240] The implications of the TRIPS agreement for access to medicines in poorer countries (especially treatment for HIV/AIDS) have been particularly controversial, because generic (off-patent medicines) are much cheaper than patented ones and are increasingly produced in middle-income countries in Asia and South America. In addition, because the market demand for diagnostics, vaccines and medicines needed to address health problems mainly affecting developing countries is small and uncertain, the incentive effect of intellectual property rights may be limited or non-existent.[216]

However, the implications of broadening patent protection in other ways may be very different from the impacts of patents on useful medicines. For, example, patents on human gene sequences have included many claims of limited practical use and poor reliability (as discussed below). One of their main effects – rather than restricting access to useful treatments like HIV drugs – was to help create the 'biotech bubble' that burst in the late 1990s. Patents on GM plants have had different effects again, being one factor that has contributed to the consolidation of the seed industry as the relevant intellectual property (IP) became concentrated in the hands of a small number of multinational companies. In both cases, the granting of 'patents on life' was part of a system which drove investment in particular types of research and development, that otherwise might have attracted less resources.

2.2.3 Patents on life

The process of granting 'patents on life' began with the 1980 ruling of the US Supreme Court, in the landmark case of Diamond v. Chakrabarty, that genetically engineered micro-organisms are patentable; followed by decisions by the US Patent and Trademark Office (USPTO) in 1985 and 1987 that plants and animals are also patentable. It was these decisions, and the international agreements that followed, that drove corporate investment in biotechnology, because it allowed the new developments in bioscience and biotechnology to be controlled, privatised and traded.[217]

In 1988, a Committee of Experts on Biotechnological Inventions and Industrial Property established by the World Intellectual Property Organisation (WIPO) proposed that biotechnological products and

processes should be patentable, provided the usual conditions for patenting were met.[179] The EC published the first draft of its controversial Directive on patenting in biotechnology the same year. Ten years later, in 1998, despite considerable opposition within Europe to the idea of 'patents on life', EC Directive 98/44/EC on the 'Legal Protection of Biotechnological Inventions' was adopted (see also Appendix A).

In the US, a patent must be novel (not previously made public), non-obvious (to someone 'skilled in the art') and useful. In Europe, the invention must be novel, must constitute an inventive step and must demonstrate industrial applicability. These three requirements are broadly equivalent, although there are some important differences between the two different systems. In both systems, genetic sequences are argued to be novel (i.e. 'inventions' rather than discoveries) because they are patented in an isolated and purified form. They are then treated in the patent system just like any other chemical compound. However, the classification of genes or other biological entities (such as proteins, cells, plants or animals) as 'inventions', rather than discoveries, is controversial.

Debates have raged about whether discoveries about nature, such as gene sequences, should be patentable in principle; whether innovation is stimulated or stifled by 'patents on life'; and how benefits should be shared in situations where biological material or knowledge from a particular area underpins the claimed 'invention'. These debates have focused on how the monopolistic rights granted in 'patents on life' restrict scientists' or patients' access to new biological discoveries or their applications[218] and whether they disproportionately reward companies which claim patents based on the results of shared scientific discovery or indigenous knowledge ('biopiracy')[219]. Although a 'research exemption' allows the use of patented gene sequences and other protected products and processes, the activities allowed under the exemption are narrow in scope and poorly defined, leading to concerns that in practice patents may restrict research.[220] Whilst some researchers argue that there is no evidence that research has been harmed,[221] others claim that the extension of patents to cover scientific information, such as a natural correlation between a biomarker and risk of a disease, is a threat to science.[222]

A 2008 report from the UK Intellectual Property Office shows that the numbers of patents for inventions in the general field of biotechnology, which includes genomics and genomic medicine, represent a significant portion of the overall numbers of patents applied for in the last 20 years.[223] From 1985 to 2000, the numbers of biotechnological patents increased significantly, however there has been a decline since 2000. The downturn is most noticable in relation to patents for new human genes, probably because it is unlikely that there are significant numbers of human genes still to be identified: there has instead been an increased emphasis on the diagnostic uses of genetic information. There has also been a tightening of the rules for granting patents on genes in the US. Raw sequence data from the Human Genome Project was made public and not patented following the much-publicised race between the HGC and private sequencing, led by the US entrepreneur Craig Venter. However, human genes can still be patented once a 'use', or industrial application, has been identified. The courts' interpretation of a valid use has, however, become more restricted: one recent court case confirmed that patents based on speculative uses (many of which were granted in the past) will not be considered valid in the future.[224]

The effect that patents have on research priorities has been much less widely discussed than their impacts on access to medicines or to research data. Treating knowledge as property raises questions not only about who gains access to this knowledge and who benefits from its use and sale, but also about how patentable knowledge (including 'genetic information') is defined and may become prioritised above other types of research.

To meet the 'industrial applicability' requirement (equivalent to showing 'utility' in the US), the EU Biotechnology Directive requires a gene patent 'to specify which protein or part of a protein is produced or what function it [the gene] performs'. As Calvert notes[225], patenting fits nicely into the simplified model of biology known as the 'central dogma' because this involves an assumption that if the function of the gene is discovered, then there will necessarily be a link to a protein, and that this protein will result in a trait (such as increased risk of a disease). In this sense there is a parallel between the central dogma and the patenting requirements. However, it has become increasingly

problematic to define a gene separately from its genomic context and the simple idea of a single gene 'for' a given trait or disease has largely been abandoned by researchers: making the idea of patenting a gene 'for' cancer, for example, increasingly questionable.

Nevertheless, the idea that genes can be patented has been central to generating investment in the 'knowledge-based bio-economy'. The discovery of a new link between a human gene and a disease thus forms the basis of many patent applications. The main claimed uses of DNA patents filed between 1996 and 1999 were as research tools (27% of DNA patents) and as genetic tests or diagnostics (18%): although many such patents had no immediate therapeutic value.[226] The UK Intellectual Property Office reports that the numbers of patents for mere detection of common genetic variations (the simplest of which are known as SNPs, or single nucleotide polymorphisms) has been in decline since 1998. However, the focus of activity has switched towards diagnostic methods based on the discoveries of correlations of SNPs and haplotypes (haploid genotypes: a combination of genetic variants at different places on the same chromosome, that may be inherited together) with diseases, particularly cancer. UK companies which are particularly active in this area are AstraZeneca, GlaxoSmithKline, ICI, and the University of Oxford's technology transfer company, Isis Innovation, as well as Imperial College Innovations Limited and University of Cambridge Technology. The Medical Research Council (MRC), UK Government and the charity Cancer Research UK have also applied for patents in these areas. Two UK hospital trusts, Tayside Universities Hospitals and St James & Seacroft University Hospitals, have recently begun to file patents in the area of gene expression profiles and SNP/haplotypes respectively.[223]

Numbers of patent applications and income from intellectual property have become measures of both university and industry success which underpin policy-makers' attempts to shift towards a knowledge-based economy. It can therefore be argued that scientific knowledge that can be made the subject of a patent application is being favoured above the acquisition of other knowledge.

Because patents are claimed before publication, and hence prior to peer review and to replication of the discovery by other scientists, the shift from patenting inventions to patenting discoveries has important implications for what counts as scientific knowledge. Most statistical associations between genes and diseases later turn out to be wrong (they are refuted by later research) – as do most discoveries in science.[227] The statistician Ioannidis sums the situation up: "*We should now recognise that most of the biomedical information that is likely to be found, discussed, and disseminated will be false…Any single study in the molecular era, no matter how well-designed, well-conducted, well-analysed, and well-presented is probably more likely to be refuted than validated*".[228] Therefore 'knowledge' that is patented – the key measure of the knowledge-based economy – does not represent a scientific consensus about what has been established, or meet traditional definitions of knowledge as established by the 'scientific method'.

Measuring knowledge in this way allows much 'knowledge' to be patented that is simply wrong, in the sense that it has not been scientifically validated and is likely to be refuted by further studies in the future. It is thus not only *access* to biological discoveries that is controlled and shaped by the patent system, but what constitutes scientific knowledge itself.[229] Although it is clearly not the only factor driving research agendas, the commodification and prioritization of 'genetic information' (and misinformation) via patent claims therefore plays a key role in the 'geneticisation' of both health and agriculture: including the focus on genes as the explanation for ill-health and the promotion of GM crops and animals as new production systems.

Patenting in the biosciences is now ubiquitous and patent applications are often not declared in scientific papers, raising additional issues about conflicts-of-interest and transparency.[230,231] Scientists who are named as inventors on patents will in some cases have a direct financial interest in the promoting the claims of 'industrial applicability' made in the patent. In other cases, the patent may not confer a direct financial reward, but defending the claims made in it may still be important for the scientist's career and future funding.

2.2.4 GM plants and patenting

> "*The interplay between technology (biotechnology and genetic engineering) and intellectual property rights (patents and PBRs* [Plant Breeders' Rights]*) through the commodification of germplasm has secured for corporate agri-business the much needed control over the self-propagating power of seeds*". Chidi Oguamanam, Dalhousie Law School, Halifax.[232]

> "*The relative importance and 'power standing' of seed companies has risen inexorably in recent years, not least as public sector funding of breeding programmes has declined and private investment has increased*." David Hughes, Royal Agricultural College.[233]

> "*What clearly differentiates the current biotechnological revolution from the preceding green revolution is that in a system of global competition, agricultural technology will probably be used as a strategic tool in a commercial war*". PB Joly, INRA (France).[234]

Following the 1980 'Chakrabarty' decision in the USA (Section 2.2.3) the US Board of Patent Appeals and Interferences issued the 'Ex Parte Hibbard' opinion in 1985.[235] Hibbard, a scientist with Molecular Genetics, had applied for a patent on the tissue culture, seeds, and whole plant of a maize line selected from that tissue culture. The patent was initially rejected on the grounds that plant variety protections were sufficient, but Hibbard won on appeal. This decision opened the door to a wide variety of utility patents on plants and their component structures: the US patent office granted more than 1,800 patents over the next 15 years, covering various aspects of plant germplasm (the genetic resources stored in seeds).

Europe followed suit when it adopted its new patenting directive in 1998 (see Section 2.2.3).

Since the TRIPS agreement (see Section 2.2.2), all countries in the World Trade Organisation (WTO) must provide some form of IP protection for plant varieties. The complex system of global negotiations and agreements that govern these decisions about the future of agriculture and food include: the UPOV (Union Internationale pour la Protection des Obtentions Végétale) Convention (which covers plant breeders' rights); TRIPS; the World Intellectual Property Organization (WIPO); the Convention on Biodiversity (CBD); and the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA).[236]

There has been particular concern about 'biopiracy': attempts by western scientists to patent plants that have long been in use for food, medicinal or other purposes elsewhere, such as neem in India.[237]

However, the most striking feature of patent activity in relation to agriculture is growing trends towards genetic engineering for plants. Between 1990 and 2000, Oldham and Cutter identified approximately 15,064 publications in this area in the global patent data, increasing to 29,684 by 2004 and 32,667 by 2005.[238] The reason is that patenting gives commercial companies increased control over the global market for seeds. Under European patent law there is an exemption for "essentially biological processes for the production of plants or animals", which means that most non-GM plants cannot be patented, although this exemption is currently being tested as companies seek to expand patenting beyond GM to include conventional breeding.[239]

Many of the relevant patents are concentrated in the hands of the six global seed companies, Monsanto, Dow, DuPont, BASF, Bayer and Syngenta (see Section 5.2). However, UK spin-out companies such as the John Innes Centre Innovations Ltd (the technology transfer company of the BBSRC's John Innes Centre, see Section 3.2.1) are also active in this area.[223] According to the UK Intellectual Property Office, the most cited patent with a UK inventor and/or applicant in the field of genes and regulatory sequences is patent no. WO90/08830 (ICI/Bright et al.), a method of plant genetic modification.[223]

Before the development of high-yield crops based on hybrid seeds, agricultural research was undertaken mostly in the public sector. Private investment in plant breeding was not attractive

because it was hard for companies to claim ownership of plants and seeds because they were self-propagating. However, because seeds from hybrid crops do not give reliable yields if they are replanted, farmers became dependent on plant-breeding enterprises for hybrid seeds and also for the chemicals used to boost agricultural production. The Green Revolution encouraged the use of agro-chemicals, such as synthetic fertilisers, pesticides and herbicides, and the growth of a small number of high-yielding hybrid crops, providing a strong foothold for agri-business to dominate production in both developed and developing countries.[232]

Oguamanam argues that the development of GM crops and animals has involved a further shift "*from classic property, such as a farmer's ownership of his or her crops or farm animals, to proprietary claims over component genetic information through intellectual property rights*".[232] Patents give much wider monopoly rights than the more traditional plant breeders' rights, where plant varieties can be used by others to produce new varieties. The patenting of GM crops has therefore helped drive agricultural research further into the private domain changing the research priorities from public good to market potential, with particularly serious implications for poor farmers in developing countries.

The advent of patents on plants has also contributed to the takeovers and mergers which have led to consolidation of the seed industry and placed increasing control over seeds in the hands of a small number of companies.[240] In addition, other research into agricultural systems for crop or animal production has received minimal funding, as the knowledge cannot be privatised through patenting.

Monsanto's most profitable strategy has been to package its own-brand herbicide with herbicide resistant GM plants, extending the marketable life of its most profitable product (the herbicide 'RoundUp'). This strategy is now being adopted by other companies (see Section 5.2).

Joly notes that the privatization of agricultural research and development is related to economic policies and to "*the promises associated with the biotechnology revolution, and specifically the 'molecularisation' of life sciences, which prompted major changes in research and development (from the experimental field to the research laboratory, increasingly disciplinary and reductionist research and development, concentration of research in a small number of institutions), and the patentability of life forms*…".[234] Beyond the fundamental reorganisation of research and development, implications include: further standardisation of farming practices and products; increased dependency of farming systems on patented technology, commodity markets and privatisation of information; and further erosion of genetic diversity.

2.2.5 Patents, medical biotechnology and the human genome

> "*A strong focus on monetizing intellectual property has impeded flows of information, led to fragmentation, and created a proliferation of new firms*". Pisano, 2006.[241]

The decision to allow the patenting of life, including human genes, is closely linked to the business models adopted by biotechnology companies. Gary Pisano of Harvard Business School explains how three interrelated forces drive the business of (medical) biotechnology[241]:
(1) the transfer of technology from universities to the private sector through the spawning of new firms;
(2) capital markets, including both venture capital and public equity;
(3) the market for know-how in which younger companies trade intellectual property (IP) for funding through various forms of alliance with more established enterprises.

Together these forces comprise a system for "*monetizing intellectual property*".[241] Thus, biotechnology became a business when the knowledge emerging from scientific research became IP that was valued and could be bought and sold. The US biotech company Genentech's decision to enter a collaborative development and licensing agreement with Eli Lilly (to develop and produce human insulin from genetically-engineered bacteria) in 1979 is described by Pisano as a "*watershed event*", because it showed venture capitalists that IP could be bought and sold independently of the final product. According to Pisano, the majority of publicly held biotech companies remain R&D firms and

only 20% of them have any products on the market or are earning royalties based on products commercialised by partners.

First-generation biotech firms, like Genentech, developed replacement versions of hormones such as insulin and growth factor, which had already been on the market prior to the development of modern biotechnology. These products were commercially successful and allowed mass production of useful products that were previously difficult to supply (although some researchers have questioned why human insulin was introduced without proof of being superior to animal insulin[242]). Second-generation firms focused on new biopharmaceuticals, such as the highly successful erythropoietin developed by Amgen (marketed as Epogen, or EPO), and less successful proteins such as interferons. Overall, patent activity in relation to biotechnology is dominated by patents that refer to microorganisms or enzymes, including some claims to the whole genomes of organisms.[238] Patents have also been claimed for cell lines and cloned or genetically modified animals.

Third-generation biotech firms have focused on the applications of genomics and bioinformatics – the fruits of the Human Genome Project. These firms have suffered from (i) the increasing recognition of biological complexity for example, the number of human genes was much smaller than expected, meaning there are very few single-gene diseases (see Appendix A) and (ii) the bursting of the "biotech bubble" that developed in the late 1990s. More recently, the pioneering gene testing company DeCode Genetics – which has claimed patents on many genes as a result of its research in Iceland – filed for bankruptcy.[243]

Some gene testing companies now oppose gene patenting, partly because they wish to by-pass the multiple licences that full genome-sequencing would require if each gene is patented by a different company or research institute.[244,245,246] Generally, these companies have invested in gene sequencing technology or genetic testing services, rather than gene discovery. Often they rely on publicly-funded genetic association studies to generate the information that they sell or interpret: investors in these studies will therefore not recoup investment in the way the patent system supposedly intended. The emphasis on making 'genetic information' freely available addresses concerns about patents restricting access to genetic test results. However, it neglects broader issues, such as whether 'genetic information' is really reliable and whether whole genome sequencing is really good for health (see Part 5).

Whilst there is concern is that access to genuinely useful genetic tests may be restricted or blocked if genes are patented, this has not happened extensively in Europe.[247] The role of gene patenting in driving the 'biotech bubble', and biasing the research agenda towards the genetic 'prediction and prevention' of disease, thus appears to be more significant (although impossible to disentangle from the policy commitments and other factors driving this approach).

For pharmaceutical companies, as well as for public health, it is arguable that gene patenting has given undue emphasis to the wrong kind of research. By discovering (possible) links between genes and diseases, genomics has identified a massive number of potential new drug targets and/or diagnostic or predictive tests which can be patented. However, this has not led to the expected bonanza of new drugs or useful tests. One issue is that most of these new drug targets have not been validated: meaning that the link between the gene and the disease has not been confirmed. The hard scientific work of validating genetic and biological information is not encouraged by the patent system, which requires patents to be filed as soon as possible. Because it involves no scientific test of what constitutes reliable evidence or information, the patent system also allows real links between genes and diseases to be swamped by false leads and misinformation, as described in Section 2.2.3.

The patent thickets that result from different companies and institutions patenting multiple pieces of information (which they claim to be 'inventions') may also act as a block to more useful research and development, although it is difficult to demonstrate concrete evidence for this. For example, the not-for-profit Malaria Vaccine Initiative attempted to map the intellectual property it might need to license to develop a malaria vaccine for poor people. The map was extremely complex and involved multiple, overlapping patents held by many different inventors, some with conflicting claims.[248] Negotiating

through these patent thickets can be difficult and expensive and may delay and discourage research and innovation, as well as adding to costs.[249] In 2002, New Scientist published a graph of the number of patent lawyers per billion dollars of spending on R&D in the US.[250] The number had nearly doubled over 15 years.

2.3 Public investment in biotech research and development

Subsidising research and development (R&D) is one of the main mechanisms for national governments and the European Union to drive research trajectories in particular directions. Expenditure on R&D is one of the OECD's measures of the knowledge-based economy, and subsidising biotech R&D – often using public-private partnerships - has thus become one of the means by which countries seek to win the race to develop a new bio-economy.

A major assessment of national public policies that stimulate research in biotechnology was published as part of the European Commission's 'Biopolis' project in March 2007.[194] The report includes:

1. Plant biotechnology
2. Animal biotechnology
3. Environmental biotechnology
4. Health biotechnology (human and animal health; including drugs, diagnostics, vaccines, cell therapy, embryonic stem cells, tissue engineering and other therapies)
5. Food biotechnology
6. Industrial biotechnology (production of intermediates for number of end industries, including chemical biotechnology)
7. Basic biotechnologies (in case basic R&D and/or technology are subject of a programme that cannot already be awarded to an application area)
8. Non-technical areas of biotechnology.

According to the Biopolis report, in the period 2002-2005, the total public funding of biotechnology for the 15 old EU member states, amounted to an estimated 13.1 billion Euros, including national and regional non-policy directed and policy directed funding of biotechnology (Table 4.1).[194] The UK share of this investment amounted to 1.4 billion Euros: only Germany and France invested more. Of this UK share, approximately 1 billion was 'policy directed', including Euros 87.9m for plant; 94.1m for animal; 100.8m for environmental; 341m for health; 36.4m for food; and 25.8m for industrial biotech (Table 4.4 of UK national report).[251]

Health-related biotech received by far the largest share of this investment, followed by agricultural biotech and finally industrial biotech, although the latter's share of funding is now growing. According to the Biopolis report (page 20), public financial support for agricultural biotech in the 15 old EU countries was nevertheless about one third of the budget for health biotech, and industrial biotech received about 16% of the total funds. This suggests that the split was roughly 8.25 billion Euros for health-related biotech, 2.75 billion Euros for agricultural biotech, and 2.1 billion Euros for industrial biotechnology, over these four years (or: 2.06 billion, 690 million, and 525 million Euros/year respectively).

Some major investments are missing from the Biopolis report, because of the way the figures are categorised and calculated. In particular, the evidence in Appendix A shows how the UK Government's desire to win the race to commercialise the human genome was a key driver in the decision to build a centralised database of electronic medical records (known as the 'Spine'), increasing costs to over £12 billion, compared to the original estimate of £1 billion for a de-centralised system.

The Biopolis report does not include private investment. In 2004, Europe had 2163 dedicated (medical) biotech companies, which spent in total €7.6 billion in R&D; however, the total spent on biotechnology by other companies, particularly the pharmaceutical industry, is unknown.[252]

Although the focus of this report is on public funding for research, it is likely that the policies and systems set up to encourage investment in the knowledge-based bio-economy would also have influenced the investments made by venture capitalists and by industry in general. In particular, venture capitalists have been encouraged to invest in biotech companies spun out from universities (see Section 2.5.2) and a number of major infrastructure investments have been made as public-private partnerships. For example, the UK Biobank genetic research project has been set up at an initial cost of £61.5 million as a 'resource' to allow the pharmaceutical industry and other commercial companies to conduct research on 'genetic susceptibility' to common diseases and adverse drug reactions, using biological samples from half a million people, linked to medical records (see Appendix A). The initial resource is being established using joint funding from the UK Medical Research Council (MRC) and the Wellcome Trust medical research charity, but industry will pay fees to use the data in the future. UK Biobank is dependent for its success on the much larger sum of public money being invested in electronic medical records.

The total funding cited in the Biopolis report also does not include investment by the European Commission itself, for example the money allocated to the Framework Programmes by DG Research (see Section 3.3). This includes funds being allocated to establish and link biobanks across Europe.

It is very difficult to obtain accurate figures on public investment in plant biotechnology to date in Europe because data are not recorded in a form that is amenable to such analysis. However, in 2003, the Prime Minister's Strategy Unit reported that estimates of global GM crop R&D were about $4.4 billion a year (£2.7 billion), composed of roughly three-quarters private and one-quarter public sector research.[253] According to the same report, Syngenta – the only multinational agricultural biotechnology company with a major research station in the UK – spent about £120 million in the UK on R&D and the main public sector sponsor of GM crop development, the Biotechnology and Biological Sciences Research Council (BBSRC), invested about £55 million a year on agricultural biotechnology research, of which nearly £18 million was in GM crop research. A 2007 press report suggested that in the UK, the Government still spent £50m a year on research into agricultural biotechnology.[254] The proportion spent on GM crops is therefore presumably still about £18 million a year. For comparison, public spending on organic agriculture research was about £1.6m in 2006.

In 2004 the European Commission estimated that the then 15 European Union countries spent around €80 million annually on research in plant biotechnology, and that European firms invested about €400 million annually.[255] However, this estimate of public funding would appear to be an underestimate compared to the figures in the Biopolis report (cited above), which suggest that the total funding for agricultural biotechnology in these countries averaged at more like Euros 690 million a year from 2002-2005. This includes national and regional funding, using both non-policy directed and policy directed instruments. The German chemical company BASF stated in 2009 that it had invested over €1bn into GM crop research over the past decade, or 100 million Euros a year.[256] If we assume that the other EU-based company investing in agricultural biotechnology, Germany's Bayer, invested a similar amount (it is currently investing 150m Euros a year, see Section 5.2), this would suggest that public subsidy for R&D into GM crops across the EU may have actually exceeded private investment.

A much smaller amount of public money, $5 million (€4 million), was spent annually on biosafety research in the 12 years to 2001.[257]

Based on the funding allocated to individual research projects in the European Framework Programme, Friends of the Earth Europe has estimated that, in addition to the national spending identified in the Biopolis report, around €353 million of EU public funds had been spent on science to underpin the R&D efforts of agricultural biotech companies since 1982.[508]

As part of the European Commission's Framework 7 (FP7) 'Plants for the Future' Technology Platform (Section 1.3.2), the agricultural biotech industry has claimed that it requires an investment of more than 45 billion Euros for R&D over the next ten years. If the ratio of public to private investment is the same as was estimated by the EC in 2004, about 7.5 billion Euros ($10 billion) would be public

money – equivalent to the total global value of the existing industry.[258] However, the figures from the Biopolis report suggest that the ratio of public to private investment may be even higher.

In Britain, the Royal Society has called for the UK Government to invest £2 billion in agricultural R&D over the next ten years, some which would be spent on biotechnology and the development of new GM crops.[259]

2.4 Scientific publication and research assessment

One of the OECD's key measures of the knowledge-based economy is numbers of publications in scientific journals, and citations of these papers.

Unlike patents, which are supposed to be a measure of industrial applicability, citations measure the impact of the authors' work on other researchers, or the manuscript's contribution to a scientific field.

Also unlike patents, journal publications are subject to scientific peer review. Peer review has strengths and weaknesses: it is based on assessment by a scientist's peers of the value of their work. The recommendation of peer reviewers is a strong predictor of whether work is ultimately published and agreement between reviewers signals that there is reasonable consensus on what constitutes scientific knowledge. However, the system also allows a small elite group of researchers within each speciality to be fundamentally in control of what is published in scientific journals.[260]

The role of journal citations in research assessment is changing, as is the nature of scientific publications. This section considers how journal publications inform research funding decisions and how commercial influences are changing publications.

2.4.1 Research Assessment: a changing role for peer review

In the UK, research is evaluated by the Research Assessment Exercise (RAE), which was first conducted in 1986[261]. The RAE is a peer review process, based on the judgement of experts. The focus is on details of journal publications and other forms of assessable output which research departments have produced during the publication period. The RAE will be replaced by a new Research Excellence Framework (REF) from 2010.

The RAE determines most of the research budget allocated to universities via the Higher Education Funding Council for England (HEFCE), the Scottish Funding Council (SFC), the Higher Education Funding Council for Wales (HEFCW) and the Department for Employment and Learning, Northern Ireland (DEL). These bodies provide public funding for staff and most infrastructure and equipment, whilst the Research Councils, European Union, government departments, industry and charities usually fund specific research projects (see Section 3). The total government research funding distributed by HEFCE in 2009 was £1.5 billion, distributed according to a 'quality weighting' based on the outcomes of the RAE.[262,263] HEFCE also provides additional support for research that universities and colleges carry out on behalf of charities: this funding amounted to approximately £194 million in 2009-10.

The 2008 assessment involved over 1000 panel members appointed by the funding bodies, chosen for their "*standing in the academic and wider research community, their extensive research experience, and their understanding of the needs of research users and commissioners of research from both the public and commercial sectors*".[264] The outcomes will be used to substantially inform allocations of research grants for a five-year period.

The UK government announced in its 2006 Budget that the RAE was to be reformed following the 2008 assessment, a key concern being that too much emphasis on publication of findings in prestigious journals had led to a lack of incentives across all research disciplines to translate basic research findings into marketable products. In explaining its reasons for reform, the Government

noted: *"…the nations that will thrive in the global knowledge economy will be those which produce the highest-quality research with relevance to the wider economy*"; and stated: "*in theory, the RAE is supposed to reward excellent user-focused research in the same way it rewards excellent curiosity-driven research, but it is not at all clear that this has occurred in practice*".[47]

However, like the patent system, a shift from peer review-based systems is likely to change what counts as 'knowledge' and 'good' science. For example, using research income from commercial companies as a measure of success may bias both research priorities and findings (see Section 2.3.2).

In a submission paper to the 2006 consultation on the future of the RAE, Universities UK (UUK), an umbrella group representing vice-chancellors, expressed concerns that the government's preferred option – based entirely on research income and excluding peer review – would be "*unlikely to be fit for purpose*".[265] The journal Nature also warned that citations of research papers are a poor measure of research quality, and that, although peer review is far from problem-free, it must play a central role.[266]

The new approach to the RAE – to be known in future as the Research Excellence Framework (REF) – for science, engineering, technology and medicine will now be based on a mix of quantitative indicators of research quality and outputs (including journal publications, external research income and postgraduate student information), with a role for expert advisors in determining the use of these indicators. For other disciplines there will be a 'light-touch' peer review-based assessment process. [267]

2.4.2 Publication and commercial interests

Scientists gain prestige from seeing their work published, and obtaining publications in prestigious journals is essential to advancing their careers. However, the evaluation of evidence is never totally objective or completely independent of scientists' convictions or theoretical ideas.[268]

There is no doubt that a shift has been taking place in academic research funding and that this may have significant implications for what is published. For example, in 2006, the British Medical Journal published a systematic analysis of articles published in the area of clinical medicine between 1994 and 2003.[269] The authors found that the proportion of most frequently cited articles funded by industry increased over time and was equal to the proportion funded by government or public sources by 2001. Sixty-five of the seventy-seven most cited randomised controlled trials of medicines received funding from industry, and the proportion also increased significantly over time. Eighteen of the thirty-two most cited trials published after 1999 were funded by industry alone. They conclude that, although academic affiliations remain prominent among the authors of the most frequently cited medical research, such research is increasingly funded by industry, often exclusively so, and academics may be "*losing control of the clinical research agenda*".

North American researchers have highlighted concerns about the impact of industry funding on representations of research results[270,271] and several studies have concluded that industry-funded medical trials are more likely to be associated with statistically significant pro-industry findings in journal publications.[272,273,274,275,276] A 2003 analysis also found that industry sponsored studies in the field of cancer treatment and care were nearly twice as likely to reach positive conclusions about costs than studies sponsored by non-profit organisations.[277] Similarly, a survey of research on the nutritional value of drinks found that studies funded entirely by food and drink companies were approximately eight times more likely to produce results favourable to their funders, compared with studies which had no industry funding.[278,279]

In medical journals, ghost-writing has become a major problem and hundreds of articles claiming to be written by academics or doctors have been penned by ghostwriters in the pay of drug companies.[280,281,282,283] Although some medical journals have tightened up their rules on conflict of interests, issues include: the publication of commercial supplements sponsored by drug companies, with inferior scientific quality controls; financial incentives to publish industry trials as a result of journal income generated from companies buying expensive reprints of the paper; and the effects of revenue from drug advertising in medical journals on editorial decisions.[284]

A 2005 study concluded that publication bias (where some findings are more likely to get published than others) and other forms of bias and statistical problems, mean that most research findings are false.[227] Amongst other factors, the author concludes: "*The greater the financial and other interests and prejudices in a scientific field, the less likely the research findings are to be true*". For example, Ramsey and Scoggins found that less than one in five studies in cancer that are registered with the National Institutes of Health's online registry have been published in peer-reviewed journals.[285,286] Among published studies, 64.5% reported the results as positive findings, whereas, for industry-sponsored trials, 75% gave positive results.

Publication bias can be a problem for investors as well as for other users of research. Pisano argues that the role of sponsoring drug companies in decisions about whether or not to publish in academic journals "…*creates a bias in which only favourable results are published. In order for the information to be useful for investors, both positive and negative findings need to be made available early in the* [drug] *development process, not just after approval.*"[241]

Publication bias also impacts negatively on healthcare. The UK House of Commons Health Committee of MPs concluded in 2005 that: "*The Department of Health has for too long optimistically assumed that the interests of health and of the* [pharmaceutical] *industry are as one.*" and noted that: "*The suppression of negative clinical trial findings leads to a body of evidence that does not reflect the true risk:benefit profile of the medicine in question*".[287]

In a 2005 survey of British universities and government laboratories, more than one in ten scientists claimed that they had been asked to tailor their research conclusions by a commercial funder.[288] Of the 358 union members who responded to the survey by the Association of University Teachers and the public service union Prospect, 7.9% reported they had been asked to tailor their conclusions to suit a funder's preferred outcome, 1.2% had been asked to do so to obtain future contracts and 1.7% in order to discourage publication. The survey does not say whether the scientists succumbed to pressure, or, if so, what practical impacts this might have had. However, in a similar US survey, more than 200 scientists employed by the U.S. Fish and Wildlife Service claimed they had been directed to alter official findings to lessen protections for plants and animals. The survey of the agency's scientific staff of 1,400 had a 30% response rate and was conducted jointly by the Union of Concerned Scientists and Public Employees for Environmental Responsibility.[289]

2.5 Universities and industry-university collaboration

"*The universities will be at the heart of this effort to build the knowledge economy. Universities can play a central role as dynamos of growth. But they will only fulfill that mission if they match excellence in research and teaching with innovation and imagination in commercialising research. To do that they will need the skills and the infrastructure to translate science into products, services and marketable commodities*". Department of Trade and Industry (DTI), 2000.[26]

"*Today, once again, we are seeing a transformation in the purpose and self-image of universities. Today, academics and politicians are beginning to see the universities, not just as creators of knowledge, as developers of young minds, and as transmitters of culture, but also as major agents of economic growth in the economy. This change in the purpose and self-image of the university has been driven by the concept of the 'knowledge economy', an economy in which ideas, and the ability to manipulate them, are of more importance than the traditional factors of production*". Science Minister, Lord Sainsbury, November 2004.[290]

"*The modern university does not stand for anything . . . except efficiency and growth, or in other words, power. The university has become an institutional functionary in the technological system*".[291] Richard Stivers, Illinois State University, 2006.

In addition to measures of the knowledge-based economy such as patents and citations of scientific papers, the OECD emphasises the importance of 'knowledge networks', including the outsourcing of industry R&D to universities and 'knowledge transfer' from universities to the commercial sector.

This section considers the implications of the closer links between universities and business, and the drive to commercialise research that underpins the knowledge-based economy.

2.5.1 Knowledge, education and information

> "*A counterproductive strategy has been adopted: humiliating the intrinsic motivation to knowledge only for an illusory market reason.*
> *Are we in the process of demotivating research, studies, knowledge, culture with this ideological and practical subordination to utility, production and career?*". Cristiano Castelfranchi, Professor of Cognitive Science at the Faculty of Philosophy, University of Siena, 2007.[292]

In a 2004 speech[290], the then science minister, Lord Sainsbury listed the five attributes of a national university system which he considers are likely to lead to economic success in the 'knowledge economy':

- a high level of scientific excellence;
- a generously funded, peer reviewed and highly competitive system of allocating research grants;
- the location of most research in universities rather than in stand-alone research institutes;
- a high level of Knowledge Transfer;
- a high level of competition between universities for the best students and the best academic staff.

However, this competitive and technologically orientated system is not without its critics. For example, in the USA, Stivers states: "*If in the past universities were subject to religious and political pressures today these pressures are technological*". He argues that the modern university has become dominated by the quest for purely quantitative efficiency where research funding is an end in itself. Bureaucracy (driven by measures of accountability, such as numbers of publications and research grants) and specialization thrive, at the expense of theory.[291] Stivers argues that the technical education now favoured by US universities is the opposite of a theoretical education. The former means learning how to perform a task efficiently; the latter involves understanding why, reflecting on explanations, and criticising theories and the realities to which they refer. An example might be the technical education necessary to analyse DNA and to perform statistical genetic studies to find associations between genes and diseases, versus the theoretical understanding necessary to interpret the findings and critically assess the likely medical value of this type of information. The invention of the 'robot scientist' highlights the large numbers of repetitive tests in some genetic research, that can induce boredom and loss of concentration in human scientists.[293]

Nevertheless, there is considerable pressure for British universities to move closer to the American model in order to compete in the knowledge-based economy.

Becher and Trowler note that, as part of the changes taking place in Higher Education, "*there is evidence that marketised relationships have led to the commodification of knowledge: its treatment, discursively at least, as a 'thing' capable of being bought and delivered in module-sized chunks, with learning outcomes being the unit of currency*".[294]

They identify a growing convergence between the UK and USA as well as among other countries in the areas of science and technology policy, access, finance and university autonomy. The 'triple helix' of academia-industry-government relations is seen as a key component of any national or multinational innovation strategy. The four consequences of globalisation for universities are:

1. financial constraint by the state on discretionary activities, necessitated by fierce international competition;

2. the growing centrality of techno-science associated with international markets;
3. tightening relationships between governments and multinationals related to product development and innovation.

The changes involve more rapid technology transfer, increased movement of products and processes from the university to the market, a blurring of the boundaries between public and private sectors and a greater emphasis on applied science in universities.

Becher and Trowler describe how in each country the curriculum is becoming more vocationally-oriented while at the same time an expanded higher education system means more opportunities for access for lower status groups. Increasing state concern with 'quality' has accompanied public spending which has increased in total but declined per-capita. This has led to a consequent state intervention in the affairs of universities, involving increased surveillance and evaluation, with financial allocations tied to tightly specified performance. The result is a marketised system yet with considerable accompanying state intervention. They argue that academics and teachers have experienced 'deskilling' through the process of separating the conceptualisation from the execution of lectures and lessons, increasing bureaucratization and managerialism, central control of the curriculum and research strategies and extensive audit and control of their work. Arguably these changes reduce the complexities of learning, knowledge and judgment in communities and institutions to an over-simplified model of imparting information to individuals. In relation to these changes, Castelfranchi comments: "*It does not seem a society of knowledge at all, but rather one of technics and of information*".[292]

2.5.2 Knowledge-transfer and spin-out companies

In its 2003 report 'Turning science into business', the OECD claims that, for governments, granting Intellectual Property Rights (IPRs) to public research organisations (such as universities and research institutes) can lead to better use of publicly-funded research results that might otherwise remain unexploited, as well as to the creation of academic spin-offs or start-ups that create employment.[295]

Consistent with the idea of knowledge as something that is generated and patented and then exploited and traded, Knowledge Transfer Networks (KTNs)[296] are one of several mechanisms that have been set up by the UK government, industry and academia to facilitate the transfer of knowledge and experience between industry and the science base. The first KTNs were set up in 2005 and the network continues to grow. They are active in sectors, technologies and market-based areas and they interact strongly with the government's Technology Programme and overall technology strategy. Current KTNs include: Bioscience for Business; bioProcess UK; and Health Technologies.

The European Union is currently engaged in the 'Bologna process', which aims to create a European Higher Education Area[297], to increase mobility of employment within Europe.[298] At the same time, the European Commission has identified improving Knowledge Transfer as a key area for action, requiring universities and other research institutions to improve their links with industry across Europe.[299] Again, the UK and the EU are seeking to mirror the strong trend toward increased university-industry collaboration that has already taken place in the United States.

There are many different forms of commercial-academic relationship and the effects of the "commercial revolution" in academia are complex. In a 2006 UK study involving 32 biomedical scientists, several different types of relationships between academic and private sectors were identified[300]:

contracts between scientists or organisations (including collaborations; academic research financed by private funding; exchange of expertise);

commercialisation and patents;

the start-up, spin-off and incubation of companies in universities.

Lord Sainsbury's 2007 review of science and innovation[52] reports "*a dramatic increase in recent years in the amount of knowledge transfer from British universities*", using the measures shown in Table 1. However, Sainsbury also notes: "*The two most commonly used measures of innovation performance are the quantity of industrial research and the volume of patenting. The UK's performance is unimpressive on both counts*". A report by Library House also claims that the number of patents filed by universities is declining (citing 218 world patents by UK universities in 2006, compared to 281 in 2005), and that this could indicate either that the technology transfer offices of universities have developed a better understanding as to which ideas are worth patenting or that there is simply less research outcome to be patented.[301]

Table 1: Knowledge transfer from UK Higher Education Institutes 200001 to 200506

Indicator	2000-01	2001-02	2002-03	2003-04	2004-05	2005-06	Change
Patents filed	896	960	1,222	1,308	1,649	1,537	72%
Patents granted	250	198	377	463	711	576	130%
Licensing agreements	728	615	758	2,256*	2,099	2,699	271%
Income from IP (£million)	18	47	37	38	57	58	215%
Spin-outs	248	213	197	161	148	187	-25%
Income from business	104	122	168	211	219	236	128%

* From 2003-04 onwards, more Higher Education Institutes included software licences.

The creation of spin-out companies from universities is identified as falling in Table 1, however this still represents a significant increase since 1997, and a major change since the 1980s when spin-out companies were rare.[302] In a 2007 speech to the Foundation of Science and Technology, Lord Sainsbury claimed[303]: "*In the past 3 years 25 spin-outs from U.K. universities had IPO's* [Initial Public Offerings] *and today have a market capitalisation of more than £1.5 billion. In the past 18 months six spin-outs have been acquired for £1.8 billion*". The creation of spin-out companies from universities remains central to Government policy.[304]

However, despite the policy emphasis on bioscience, its contribution is relatively small. In January 2010, the Office of Life Sciences (OLS) reported that, in the last ten years, bioscience departments within UK universities have generated over 200 spin-out companies, which employ over 1,000 people.[166]

These biotech spin-outs are not generally profitable, and many may not survive the current economic downturn (see Section 5.2). Typically biotech startups have to raise capital on a yearly basis and are dependent on convincing venture capitalists to make risky investments. A longevity analysis of UK medical biotech companies performed in mid-2008 revealed that 67% of companies had less than two years of cash left and 45% had less than one year's cash left.[305]

Library House reports that university spin-out companies attract a significant proportion of the UK's venture capital. In absolute terms, university spin-out companies raised a total of around £160m in institutional investment during 2006, representing almost 12% of all venture capital investment in the UK. Over 16% of all venture capital deals targeted university spin-out companies.[302] However, even when the going is good, benefits to these investors is not necessarily the same as benefit to the economy as a whole.

In the UK biotech sector, Smith and co-authors note that the chances of a small company with a handful of early drug development programs reaching a major commercial success is small because of the vagaries of drug discovery and development.[305] Thus no launched blockbuster biopharmaceutical has originated in a Venture Capital (VC)-funded UK biotech. Humira (adalimumab)

originated from Cambridge Antibody Technology (set up in 1989, now Medimmune), but the company was funded by Peptech (Sydney, Australia), not by Venture Capital; Campath (alemtuzumab), the other UK-originated biopharmaceutical blockbuster, originated in an academic lab (the pathology lab at Cambridge University, in 1988). Smith's analysis blames under-capitalisation and excessive expenditure on items other than R&D, and especially on board- and executive-level salaries, concluding that: "*together, this lethal mix has resulted in an industry that cannot perform, and so is not supported*".

In addition, many of the technologies that biotech companies seek to market remain unproven, and high-profile scientific breakthroughs do not necessarily lead to commercially successful products. For example, the creation of Dolly the Sheep grabbed headlines around the world, but the company created to commercialise the technology was unsuccessful (see Box E). The likelihood of benefits was exaggerated and the major animal welfare concerns raised by the production of genetically modified and cloned animals were not considered in the rush to commercialisation.[306,307]

Box E: The Roslin Institute, PPL Therapeutics and Dolly the sheep.[308]
In the early 1980s, the UK Animal Breeding Research Organisation (ABRO) established a research programme to produce transgenic sheep and cattle that would produce human proteins in their milk.
The Roslin Institute was created in 1993 by combining the ABRO and several other institutes, located at the University of Edinburgh. The first of the Roslin Insitute's six commercial spin-off companies was PPL Therapeutics, which was established in 1987, next to the Institute, to exploit its technology to create transgenic animals. In July 1994, PPL was granted a US patent for its process to produce human proteins in animal milk. In 1995, the Roslin Institute filed two further patents, based on the production of two 'designer sheep', live lambs produced from cultured embryo cells. Dolly the sheep, the first mammal to be cloned from adult cells, using a technique known as nuclear transfer, was born on 5th July 1996, as a result of the work of a joint team from both the Roslin Institute and PPL Therapeutics, and announced in the journal Nature on 7th February 1997. A further sheep, Polly, was described in a paper in Science in on 19th December. Polly and other transgenic lambs were able to produce the blood clotting Factor IX in their milk, considered to be of major economic potential.
PPL Therapeutics was floated on the London Stock Exchange in 1996, with an initial commercial value of £110 million. However, in June 2003 PPL's German pharmaceutical partner Bayer AG decided to put on hold plans to develop a lung drug from the milk of genetically modified sheep. The firm had to slaughter up to 3,000 transgenic sheep, sack three-quarters of its workforce and sell its intellectual property to other companies.[309,310] By December 2003, PPL was up for sale, having made a loss of £13.6 million.

The creation of spin-out companies can also create conflicts of interest. There is a particular problem with companies that claim to market 'genetic information', because there is no independent pre-market assessment of the claims being made (Boxes F and G). These examples illustrate how 'knowledge' or 'genetic information' is becoming defined by what can be patented and/or marketed, rather than being informed by scientific evidence or technology assessment (see Section 2.2). The university 'brand' then becomes a tool to market misleading information.

Box F: G-Nostics and 'the smokers' gene'
The UK company G-Nostics is a 'spin out' company from Oxford University which markets a genetic test kit to smokers. The company was created in July 2004 by Isis Innovation, the University of Oxford's wholly owned technology transfer company, with the university as a shareholder.[311] Prior to its spin-out, approximately £3.5m was invested in the technology, and a total of £2.1m has been invested in the company since.[312] The test is based on research by Dr Robert Walton in the university's Department of Clinical Pharmacology, who became a co-founder of the company. The academic research was part-funded by the charity Cancer Research UK.

G-Nostics began marketing Nicotest, a test of two common genetic variants, combined with advice on quitting smoking, in December 2004. It claimed that its test included a gene which predisposed people to nicotine addiction, and provided advice on the best smoking cessation method to use. The test was launched amid a blaze of publicity which claimed that Oxford University scientists had identified 'the smokers' gene' and that: "*Smokers can now test themselves to find out if they carry a gene that predisposes them to heavy smoking and nicotine addiction*".[313,314] However, the claimed nicotine addiction gene does not have a statistically significant association with smoking, and the company had also published misleading information about smoking cessation rates on its website.[315] Both Oxford University and Cancer Research UK subsequently distanced themselves from the company and its claims.[316,317] G-Nostics now claims that it has new evidence that its programme 'doubles' quit rates (to 65% versus 35% at the NHS stop smoking service).[318] However, this unpublished assessment is based on a comparison after only 4 weeks of what the company calls a 'pragmatic' one-year clinical evaluation.[319] It is based on a self-selected population of smokers volunteering to take part via its website. They are likely to be much more motivated to quit than the other smokers in the study, biasing the findings.

In 2008, a review of the genetics of nicotine addiction concluded: "*Nicotine genomics is a very new and underdeveloped field. On the evidence to date, its advocates would be wise to avoid extravagant claims about its preventive applications*".[320] A more recent paper has highlighted serious limitations in the prediction of genetic susceptibility to nicotine addiction.[321]

Box G: Genosense Diagnostics

The Austrian company Genosense Diagnostics GmbH was founded in spring 2001 from its parent company VBC-Genomics Bioscience Research GmbH. VBC-Genomics had been founded in early 1999 at the Vienna Biocenter Campus by a core team of scientists originating from the Institute of Genetics and Microbiology at the University of Vienna.[322] Genosense's genetic tests are being marketed via private medical practices in 30 countries. Its UK partner is Genetic Health, based in Harley Street (see also Appendix A). GeneWatch UK conducted an assessment based on the description of the tests provided on Genosense's website in May 2007. Overall, the findings were:[323,324]

For most genes included in the tests, no large-scale evidence is available to conclusively establish a relationship between the common genetic variant identified (the polymorphism) and the claimed disease. Even where this relationship is clearly established, the clinical validity of the test is unclear and for most tests the predictive value is unknown.

For several genes included in the tests, large-scale evidence suggests that the association between the genetic variant and increased risk of a particular condition is invalid (i.e. the tested gene has nothing to do with the claimed disease).

Large-scale evidence of clinical utility in the general population is not available for any of the genes included in the tests (i.e. there is no evidence that taking particular advice or treatments based on the test results is of any benefit to health).

2.5.3 Scientific careers, disciplines and conflicts-of-interest

"*Molecular biological cancer research by 1984 appeared to new investigators to be the research line of choice. Scientists joined the bandwagon in order to build successful careers. For many new researchers, this decision to construct and solve problems on cancer in molecular biological terms was independent of whether or not the problems would yield cures for cancer. Building individual and collective careers was their foremost concern. While curing cancer would be a welcome reward, it was only one consideration among many for their decisions to jump on the bandwagon*". Prof Joan Fujimura, Stanford University, 1988.[325]

"*Funding, institutional and career dependencies are substantial inertial factors in many areas of science, including complex disease research. These things are widely acknowledged privately, but rarely publicly, for the very reason that public support is required for research*

and our society works by public persuasion. It would be highly disingenuous to deny that funding availability has a major effect on research directions and, hence, the way data are collected and inferences made…" Buchanan, Weiss and Fullerton (Penn State University and University of Washington Medical School), 2006.[326]

"*Current research in agriculture and food systems is fragmented into distinct projects, organised by disciplines, and focused on relatively narrow segments of the whole*". Agricultural scientists based in the US, Norway, Sweden and Denmark, 2008.[327]

The measures of the knowledge-based economy devised by the OECD also influence the careers of scientists and what research is done in publicly funded scientific institutions, including universities. The adoption of the biosciences and biotechnology as a key 'technology platform', central to the development of a new 'knowledge-based bio-economy' means that significant public and private investment has been made in creating new career paths, institutions and scientific journals all with a focus on molecular biology.

Thus, in the past, medical research was largely done by physician-scientists who also treated patients, but this changed with the explosion of molecular biology in the 1970s, when clinical and basic research started to separate.[328] Subsequently, there has been a marked decline in the numbers of trainees and professionals in physiology and pharmacology as the more reductionist disciplines of molecular biology and genetics have gained in prestige and influence.[329] The 1994 replacement of the Agriculture and Food Research Council (AFRC) with the Biotechnology and Biological Sciences Research Council (BBSRC), along with other changes which gave priority to the lab-based development of new crops, rather then on-the-farm research, has also resulted in a loss of skills. The BBSRC has recently identified shortages in specialist research expertise in areas such as agronomy, plant physiology, pathology and general botany, plant-soil interactions, weed science and entomology /pest biology.[330] The loss of agricultural extension services which used to supply 'on the farm' scientific and technical support to farmers is also now widely seen as a mistake.[259]

Academic disciplines and career paths influence what research is done.[331] The system of counting scientific publications and patents then tends to reward scientists who stay within a narrow discipline, rather than those who explore alternative understandings or approaches to a problem.

Guena and Nesta[209] suggest that the reasons for research activity are:

1) curiosity - researchers gain pleasure from the discovery process;
2) reputation - researchers want to become famous and contribute to posterity;
3) career - researchers want to make progress in their careers;
4) research money for the creation and development of a research team; and
5) personal income.

Careers and reputations depend on research funding, and on producing the outputs measured by the OECD, including scientific publications and patents. Thus, scientific careers have been strongly influenced by the investments, institutions and systems that have been created in the attempt to stimulate the 'knowledge-based bio-economy'.

Joan Fujimura describes a "*scientific bandwagon*" which "*exists when large numbers of people, laboratories and organisations commit their resources to one approach to a problem*".[325] Based on a study conducted in academic and private industrial cancer research laboratories in the USA in 1986, she describes how scientists are constrained by the requirements of career-building and how scientists and organisations make commitments to particular lines of research: in this case, research to study the molecular biology of cancer. The commitments which created the bandwagon included: *"(1) very large increases in funding allocations; (2) designated positions in academic departments, research institutes and private industrial laboratories; (3) easily accessible training and tools, including knowledge, standardised technologies, materials, and instruments; and (4) a cadre of researchers training in molecular biological skills*".

By providing funding, commercial companies can create or sustain such bandwagons when it suits their interests.

For example, the tobacco industry has been heavily involved in funding academic research into 'genetic predisposition' to lung cancer[332,333] despite the fact that twin studies show there is no significant inherited component.[334,335] The (false) idea behind this research was that only a minority of smokers who were predisposed to lung cancer would need to stop smoking in order to protect their health, and that the remainder of the population could therefore smoke with impunity. The concept of genetic predisposition to lung cancer was originally invented by the eugenicist Ronald Fisher, who was funded by the tobacco industry in the 1950s. Fisher's 1918 concept of the 'heritability' of complex diseases still underpins genetic research today.[336]

Research conducted by GeneWatch UK and Action on Smoking and Health (ASH), using internal tobacco industry documents, has highlighted the role of the tobacco industry in promoting the idea of screening for 'genetic predisposition' to lung cancer.[337] The documents include a memo of a secret meeting between Sydney Brenner of the Medical Research Council (MRC) and British American Tobacco (BAT) in March 1988, in the run up to the Human Genome Project (HGP). The meeting led to the establishment of a pharmacogenetics research unit at Newcastle University, jointly funded by BAT, the MRC, and the pharmaceutical company Bayer. The head of the unit, Professor Jeffrey Idle, published repeated misleading claims that genetic screening would in future enable scientists to predict which smokers would get lung cancer (so that smoking cessation could be targeted at these individuals, rather than the population as a whole).

The documents reveal how claims made by tobacco-funded scientists were endorsed by leading geneticists in the run up to the Human Genome Project (HGP) as they battled to convince the Thatcher and Reagan/Bush governments that the research would have industrial applicability. However, the evidence on which the claims were based turned out to be spurious. In practice, testing smokers for supposed 'genetic susceptibility' to smoking-related diseases could mislead them about the risk of smoking and falsely reassure some people into thinking that they do not need to quit.[338,339] This tobacco-funded research has also strongly influenced how the potential of human genetic screening to target lifestyle advice has been reported in the media (see Section 2.5.4).

Idle was also a co-author, with US National Cancer Institute researchers, of an early (1989) study of susceptibility to lung cancer in workers exposed to occupational carcinogens, which advocates screening and targeting of susceptible workers.[340] This idea is questionable on both ethical and scientific grounds.[341] In 1995, he co-authored a paper in *Pharmacogenetics* (a journal which he edited and founded) which advocates genetic screening of whole populations, with data stored on individual patient 'SMART cards', and expert computer systems on every doctor's desk, to assist prescribing.[342] Policy makers seem unaware of the history of this idea, or the long timescale over which taxpayers' money has been invested in developing it. Over twenty years after the pharmacogenetic research unit at Newcastle was set up in 1988, the Department of Health described the Wolfson Centre for Personalised Medicine, University of Liverpool, where it funds the NHS Chair of Pharmacogenomics, as: "*the first centre of its kind in the UK*".[165] Echoing the claims made by Idle in the journal Pharmacogenetics in 1995 on its website, the Wolfson Centre states: "…*some commentators have suggested that, in the future, we will all carry SMART cards, which will contain our genetic information. Using these SMART cards, a GP will able to prescribe the right drug at the right dose at the right time in order to ensure that it works effectively and does not cause serious side effects. This is achievable, but a lot of hard work and significant financial investment will be needed to realise the future*".[343]

Idle viewed his lung cancer findings as heralding a "*long overdue change in the practice of epidemiology*", involving a new focus on individual genetic risk factors, rather than limiting exposures for the general population. Many critics have questioned this shift away from traditional epidemiology towards a focus on individual biological factors (including genes).[344] However, for supporters, the Human Genome Project (HGP) became the "*quest for biology's holy grail*"[345] and the key to finding the 'causes' of cancer and predicting who will develop it.

The focus on genetic 'predisposition' or 'susceptibility' to cancer (and later to other diseases), promoted by tobacco-funded scientists, was a major shift from the original rationale for the HGP (which was first proposed by scientists who wished to examine the genetic damage caused by

radiation). Although recent studies of genetic damage caused by smoking (looking at so-called 'somatic' mutations, which arise during a person's lifetime[346]) have also depended on the original investment in the HGP, a strong political commitment to the concept of genetic susceptibility remains. This approach is dependent on the idea that there are important 'germline' genetic differences in people's inherited genetic make-up, which significantly influence an individual's risk of cancer and other common diseases. This concept continues to drive policies directed towards the idea of sequencing the genomes of every baby in the NHS, and the marketing of genome sequencing to adults, as well as research investments intended to quantify these genetic and biological risks in order to 'predict and prevent' disease (see Appendix A). The pros and cons of this approach to health are discussed further in Section 5.

Following the tobacco industry's lead, other industries also began to investigate the idea that a minority of individuals might be genetically susceptible to their products or pollution. For example, British Nuclear Fuels (BNFL) funded the 'North Cumbria Community Genetics Project' near its Sellafield plant in Cumbria, which collected DNA samples over a five year period from 1996.[347] Cord blood samples were collected from newborn babies by midwives, with consent from mothers, who were often hazy about what they had agreed to, whilst wanting to help with medical research.[348] The project included research on cancer and genetic susceptibility to radiation.[349] The National Radiological Protection Board (NRPB) subsequently questioned whether genetic screening could in practice ever be useful to reduce the incidence of radiation-induced cancers, and this approach was never implemented.[350]

As scientists and funders began to distance themselves from the tobacco industry in the late 1990s, the role of the food and pharmaceutical industries in promoting genetic susceptibility screening became more important. The commercial incentive for the pharmaceutical industry is a massive expansion of the drug market to healthy people, who could be treated on the basis that they are 'genetically susceptible' to developing a particular disease at some point in the future.[351,352] More recently, private healthcare companies and web-based companies such as Google, have adopted the idea of gene sequencing as a tool for 'personalised marketing' of future products and services.[353]

Similarly, the food industry's research in the area of diet-related disease is, not surprisingly, focused on developing new products and new ways of marketing, rather than questioning the politics and practices of global agriculture and the food supply, or exposing unhealthy food products or marketing practices. This then influences the research that is prioritised in universities and public research institutes, although meeting these commercial objectives may conflict with the best priorities for health.[354]

The International Life Sciences Institute (ILSI) was founded by Coca-Cola and other food manufacturers in 1978 to defend food industry interests.[355] It now describes itself as 'a nonprofit, worldwide foundation that seeks to improve the well-being of the general public through the advancement of science'.[356] Its members include all the major food companies worldwide.[357] ILSI says it aims to 'utilise its strategic alliances and global network to bring scientific solutions to important public health issues'. It has identified four key issues for research: overweight/obesity, food biotechnology, functional foods and risk assessment. ILSI is heavily involved in nutrigenomics (nutritional genomics) research, including research to develop 'personalised' (genetically-tailored) diets and new 'functional' foods with supposed healthy properties (including new GM crops with altered nutrient content).[354,358,359]

Commercial influences therefore help to create and sustain a research agenda that is focused on looking for the causes of smoking-related and diet-related diseases *within* the human body (to the supposedly determining genetic code), rather than *outside*, at the consequences of everyday life and people's environments.[2] The focus is on creating new markets – for genetic tests, medicines, and 'functional' and GM foods – and protecting existing markets from regulations designed to protect health or the environment. Scientific and technical solutions to problems like lung cancer and obesity may sound convincing and attractive, but they are often funded to distract from other approaches that are in conflict with commercial interests: such as tobacco control, or restrictions on junk food advertising, or the salt content of processed foods.

The long history of public investment in the bio-economy also means that new applications of molecular biology are often proposed as the solutions to complex social and environmental problems. Existing institutions, funders and the community of molecular biologists – now a well-established discipline – act as lobbyists to seek funding for potential new applications of the science. For example, a new generation of biofuels, produced using genetically modified micro-organisms (GMMs), has been proposed as a potential future solution for the current problems caused by the diversion of food and land into growing industrial-scale biofuels (agrofuels). This technical solution is extremely speculative and may introduce new problems of its own.[360] But the existence of a pool of molecular biologists and institutions with an interest in promoting this approach, means that it is more likely to be funded than some other approaches to reducing carbon dioxide emissions, which may have less powerful and well-established advocates.

2.5.4 Science, promises, the media and funding

> "*In a climate of increasing competition for funding and under increasing public scrutiny, scientists have recently increased their efforts to communicate their work to the public in an attempt to improve their public image…From an assessment of the language used in articles about human genetics in the popular media, I suggest that scientists often employ strategies which could not only mislead the public, but which could also create problems for the scientists themselves*." Dorothy Nelkin, 1994.[362]

> "*If science journalists are to regain relevance to society, not only must they master the new media, they must learn to analyse and interpret the findings – including the motives of the funders. And, as if that were not enough, they must also anticipate the social impacts of potential new technologies while there is still time to make a difference*". Science journalist Boyce Rensberger, 2009.

> "…*new companies, like new research projects, typically begin with the protagonist making wild promises to secure funding. The entrepreneur records his pledges in a business plan dispatched to a bank. The scientist frames hers in a grant application destined for a research council.*
> *Both are driven by an intuitive belief in an opportunity only they are brilliant enough to perceive. It could be a means of achieving cold fusion using only kitchen utensils and a few gallons of heavy water. Or it could be a low-cost mortgage bank financed entirely from the short end of the international money markets*". Journalist Jonathan Guthrie, Financial Times, 2007.[363]

> "*Of course, scientists have a strong incentive to make bold predictions namely, to obtain funding, influence, and high-profile publications. But while few will be disappointed when worst-case forecasts fail to materialise, unfulfilled predictions – of which we're seeing more and more – can be a blow for patients, policy makers, and for the reputation of science itself*". Science journalist Stuart Blackman, 2009.[364]

Hype about biotechnology (sometimes called 'genohype') has been widely criticised for misleading the public and distorting research priorities. Claims that the biosciences and biotechnologies will solve major social and environmental problems are made frequently in the press and media. The public and policy-makers can be strongly influenced by such claims, which may then influence how taxpayers' money is spent on research and development.

Dorothy Nelkin argues that, although scientists often dismiss the way their work is appropriated by the media as over-simplified and distorted, many scientists are prone to overestimate the benefits of their work and, in doing so, to contribute to overblown expectations that may ultimately undermine their base of public support.[361] Writing in 1994, she describes how human genome researchers use metaphors which contain three over-simplified related messages, which could mislead the public: a definition of the gene as the essence of identity and the basis of human differences; a promise that

genetic research will enhance prediction and allow control of behaviour and diseases; and an image of the genome as a text that will define a 'natural' order (the 'Book of Life').

Bubela and Caulfield examined 627 newspaper articles from major daily newspapers in Canada, the USA, Great Britain and Australia, which reported on 111 papers about gene discoveries and associated technologies published in 24 scientific and medical journals in 1995-2001.[365] They found that the majority of newspaper articles accurately reflected the claims made in the journal articles but that both the journals and the articles overemphasised benefits and downplayed any risks. They conclude that journalists may not always be the source of exaggerated claims.

Elsewhere, Caulfield has argued that the bias generated by commercial influence on journal articles is picked up by the press and conveyed, largely uncritically, to the public.[366] Caulfield describes a 'cycle of hype' about biotechnology, as it appears in the popular press, which is shaped by commercial pressure.[367] He cites evidence that, while it is likely that the media's desire for a good story may be at least partially to blame, much of the spin comes from researchers and research institutions. This optimistic 'spin', which minimises possible risks and limitations, is partly "*a result of the pressures placed on researchers by funding entities and the private sector*". Genetic research has to be "sold" to public funding agencies and politicians to secure long-term budgetary commitments. Private sector involvement then influences hype in two ways: by the bias toward publishing and reporting positive findings (Section 2.4.2) and by the need to "*speak with enthusiasm about possible near future profitable products in order to appeal to venture capitalists*". All the players – researchers, media, and industry – are complicit in, and benefit from, the hype, but can create expectations that are difficult to satisfy, potentially eroding public trust and investor confidence. More importantly, "*the hype may result in inappropriate research policy decisions within both the public and private sectors*".

In an analysis of stories appearing in three Australian newspapers in the late 1990s, Petersen found that there was rarely mention of the influence of non-genetic factors in diseases, or 'multifactorial' interactions, or any questioning of the goals, direction, methods, or value of genetic research.[368] Many articles relied heavily on the scientist's own descriptions and (positive) evaluations, and provided no independent confirmation of the research and its significance. Doubt was rarely expressed that a treatment would eventually be found and there was little debate about whether research could deliver what was promised, or whether funds used for research might be better spent in other ways. Petersen concludes that the scientists involved seek to persuade the public of the benefits of genetic research and that this is assisted by 'blaming' genes for disease.

Another study of articles published in the Sydney Morning Herald in 2003 found that cancer research findings reported in newspapers as "breakthroughs" are often not true breakthroughs, although they may be important for ongoing research. Based on expert reviews of the articles, it concluded that: "*Consumers are likely to be receiving an overly optimistic picture of progress in understanding and treating cancer*".[369]

Although the media usually gets the blame for distorting science, a 2002 study found that medical journal press releases did not routinely highlight study limitations or the role of industry funding, and that data were often presented using formats that may exaggerate the perceived importance of findings.[370] The journal Nature argues that society needs to see science scrutinized as well as regurgitated if it is to give science its trust, and journalists are an essential part of the process.[371] However, science journalists describe a process in which lack of time to explore the opinions of different scientists within a field can force them to resort to simply reproducing press releases, only asking a few questions of the study's main contributor: "*My colleagues felt that we reported on published papers without significant analysis, depth or critical comment: we just translated what scientists said*".[372]

Some journalists report becoming more wary of journal publications, following some high profile scandals, including the retraction by the journal Science of two papers on human cloning by the South Korean researcher Dr. Hwang Woo Suk.[373] However, most scientific bias stops well short of fabrication, and journalists will often be dependent on the interpretations and analysis of experts. Painting an accurate picture of the current state of knowledge is difficult because most scientific

discoveries (including genetic discoveries) are wrong (they are invalidated by later research), and because contradicted claims tend to persist in the scientific literature.[374] Conflicts of interest may also be well hidden (Box H).

Box H: Press stories about genetic susceptibility to lung cancer

In 2003, press reports based on a new scientific paper[375,376] claimed that a genetic test would be developed within three to four years to "*show which smokers face lung cancer death*"[377, 378, 379, 380, 381]. Document searches conducted by GeneWatch UK using the Council for Tobacco Research (CTR) website, reported in the Observer,[382] revealed that the study's corresponding author and press spokesman, Professor Zvi Livneh, had a history of tobacco funding (receiving $519,069 in funding from the CTR from July 1985 to June 1992). A statistical meta-analysis of studies of the gene, published five years later, found that individuals carrying the genetic variant do not in fact have significantly increased risk of lung cancer.[383]

The researcher was one of many funded by the tobacco industry in the past in order to promote the (false) idea that genetic screening would identify the one in ten smokers who develop lung cancer, allowing the rest of the population to "smoke with impunity". The scientists involved created a race to find the gene or genes that predispose smokers to lung cancer, driven by tobacco industry funding, without questioning whether lung cancer has a significant inherited component (without which a highly predictive test cannot exist). Although many spurious lung cancer genes were identified, the findings seem to be a result of statistical and other biases, rather than involving scientific fraud.[337]

The historian Robert Proctor reports that molecular epidemiologists were surprised when a 1994 NIH twin study found "*little if any effect of inherited predisposition on development of lung cancer*".[1] However, by this time, the myth that it would be medically useful to target smoking cessation measures at those at highest genetic risk was firmly established.

Funders, such as the Wellcome Trust, can also play a significant role in science communication. However, scientists are often under strong pressure to exaggerate the benefits of their work to secure funding, and not to "*bite the hand that feeds them*" by criticising research priorities.[384,385]

Gannon argues that hype is spreading for several reasons, including: the increasing pressure on institutions and researchers to secure funding from diverse sources; the requirement that scientists explain the relevance of their work to the general public; and the fact that many grant applications require the applicant to explain the impact of the work on society.[386] Because scientists are in a fierce competition to maintain and increase public support and funding: "*scientists over-promise by sending messages of being close to their goals even if this is not true*". Gannon notes that the promise that a cure is just around the corner after a few million more in funding is, more often than not, an exaggeration. However, when it comes to scientific publications and grant applications, reviewers do not usually comment on the credibility of the claims made for the future benefits that might arise from the research. Furthermore, they do not ask for the same level of proof for these speculations as they do, for example, for speculations on a mechanistic step. He argues that hype transmits a false message that carries a great danger for research.

Whilst Gannon focuses on hype in funding applications and the scientific literature, what scientists tell the public and the press is often more optimistic and over-simplified compared to what they say in private or in specialist publications. In 2008, in an article about the failure to identify significant genetic effects in complex diseases, the journal Nature reported that Francis Collins (the former head of the Human Genome Project in the US who is now Director of the US National Institutes of Health) "*agrees that the picture for disease prediction remains bleak, but is still optimistic about therapeutic intervention*".[387] Yet, in his popular science book 'The Language of Life', Collins continues to promote the vision of the future which he popularised in promoting the HGP. In the book, he describes a world where a fictional woman called Hope and most other people have had the entirety of their DNA sequenced and integrated with predictive models that make suggestions about diet, lifestyle, and treatments to optimise their health. The result for Hope is a healthy and productive life beyond age 100. He contrasts this with an alternative world for Hope that looks similar to our own, where a dysfunctional health-care system hasn't yet integrated 'personalised medicine' and Hope dies of a heart attack aged 50.[388]

This kind of 'vision-creation' can be harmful because it encourages investment in particular research priorities at the expense of others, and sidelines concerns about privacy and surveillance by making exaggerated promises of benefit. Professor Walter Willett, of Harvard School of Public Health, has noted that "*Over-enthusiastic expectations of the benefits of genetic research for disease prevention have the potential to distort research priorities and spending for health*".[389] This issue is considered further in Section 5.

The history of genohype, combined with seeing science in terms of technological rather than theoretical breakthroughs (see Section 2.5.1), also leads to a situation where technical progress in gene sequencing is automatically equated with delivering the vision of a 'genetic revolution'. For example, reports on breakthroughs in sequencing the human genome faster and more cheaply often include claims that it will then be possible to predict who gets complex diseases such as cancer or heart disease. These claims are not part of the research being published, but are simply stated by the scientist or journalist as justification for their work.[390]

Similar concerns arise in relation to GM crops, which have been touted as the technological solution to a wide range of global problems, including hunger, obesity, cancer and climate change.

For example, an industry press release at the launch of the 'Plants for the Future' Technology Platform in the European Parliament claimed that improved crops could be developed and grown to combat health problems such as cardiovascular disease, obesity or diabetes.[391] No such crops have yet been commercialised, and there are real problems with evaluating the possible benefits or harms of nutrient-altered crops, yet press releases from the scientific institutions involved in this type of research are already being used to promote this idea in the media (Box I).

Box I: The GM 'cancer preventing' tomato

In October 2008, a genetically-modified purple tomato created at the John Innes Centre in Norwich, working together with a number of European research partners, gained enormous publicity for its potential role in preventing cancer. The research had been funded by the earlier EU FP5 PROFOOD project and the FP6 FLORA project (see Section 3). The tomato is engineered to contain enhanced levels of antioxidant anthocyanins and the claims of health benefit were based on a single study in a strain of cancer-susceptible 'knock out' mice.[392] The press release from the John Innes Centre claimed that: "*Anthocyanins offer protection against certain cancers, cardiovascular disease and age-related degenerative diseases. There is evidence that anthocyanins also have anti-inflammatory activity, promote visual acuity and hinder obesity and diabetes*".[393] In on-line commentaries, Dr Andrew Wadge, Chief scientist at the Food Standards Agency, the NHS, and Cancer Research UK all pointed out that the evidence for any possible anti-cancer effects of anthocyanins in humans is very limited.[394,395,396] A Cochrane review of the impact of antioxidant supplements on human health, published shortly afterwards found no evidence to support antioxidant supplements for primary or secondary prevention, and that the commonly used antioxidant supplements, vitamin A, beta-carotene, and vitamin E, may increase mortality.[397] The idea that these antioxidants were good for health had been supported by previous research on animals, and some observational studies, and it was only when large clinical trials were done that lack of benefit, and possible harm, was identified.

Dominic Glover has examined the role of the US company Monsanto in promoting GM crops as a 'pro-poor technology', which would benefit poor farmers and consumers in the developing world.[398] He describes how Monsanto's managers embarked on a concerted campaign to depict GM crops as an essential tool for addressing critically important future challenges in hunger, environmental sustainability and international development. This view depends on a number of questionable assumptions about the ways in which technology will be developed and its likely impacts on poverty, hunger and the livelihoods of the poor (see also Section 5). It is also disconnected from the types of GM crops that have actually been commercialised. These depend on Monsanto's customer base of large-scale, commercial farmers in the industrialised world, and have been driven by a number of commercial and technical considerations, including the company's interest in extending the profitable life of its herbicide 'Round-Up', by marketing it as a package with its 'Round-Up-Ready' herbicide-

tolerant crops. In reality, the most profitable strategy (also adopted now by other companies) has been to package their own-brand herbicides with herbicide resistant GM plants.

Claims that GM 'Golden Rice' would bring major benefits to children in the developing world were first made in the press in 1999. GM 'Golden Rice' appeared on the front page of Time magazine in August 2000[399], with the headline "*This rice could save a million kids a year*", as well as in numerous press articles around the world. A deal with AstraZeneca was announced to offer vitamin-A-rich GM rice free to farmers in the developing world to combat blindness.[400,401] However, the intellectual property (IP) associated with Golden Rice was only donated to poor farmers after two major clinical trials (published in 1994 and 1996) found that its main ingredient, beta-carotene, unexpectedly increased the risk of cancer in smokers and asbestos workers (See Section 5). As a result, companies' plans to market beta-carotene enhanced GM foods to wealthy consumers as an anti-oxidant "functional food" – intended to reduce the risk of cancer – were abandoned. The claims of health benefits from GM Golden Rice remain controversial and it has not yet been commercialised – the issues are discussed further in Section 5.

A new PR push claiming that GM crops are needed to feed the world began in 2007, with ministers in Britain claiming that the technology is vital to develop higher yield and drought-resistant crops, as well as the develop new biofuels.[402] These claims are speculative, as discussed in Section 5. However, misleading claims that such crops already exist and are bringing benefits have been made in the press and media. For example, the former Chief Scientist Professor Sir David King told the BBC Today Programme in 2007 that crop trials around Lake Victoria in Kenya had shown how useful GM farming could be in feeding the Third World. However, this project uses agro-ecological farming methods, not GM.[403] This PR push has also seen a revival of claims for health benefits from Golden Rice, whose inventor claims that commercialisation has been delayed by 'excessive regulation', rather than by genuine concerns.[404]

Claims in the press and media about the potential of the biosciences and biotechnology to transform medicine and agriculture, and to solve a wide range of problems, including hunger, obesity and chronic disease, have thus become one of the key drivers of public investment in the 'knowledge-based bio-economy', reflecting and fuelling the 'vision-driven' approach to research investment described in Section 1.

2.5.5 Role of science in decision-making and in regulation

> "*It is a time of speculating in volatile bioeconomies, volatile life sciences, volatile concepts, and volatile bodies. Wonderful – let a thousand speculations bloom. As long as it is also a time of due diligence, utter honesty, painstaking effort, and extreme care*". Mike Fortun, 2008.[405]

> "*Ensuring that biotechnology developments are safe, environmentally sound and ethical is paramount.*
> *But if the UK is to benefit from the immense potential of biotechnology – and I am determined that we will – we need to strike a balance between public concerns about some aspects of the technology and the action that researchers and industry need to take to make progress*". Rt Hon Stephen Byers, then UK Secretary of State for Trade and Industry, 1999.[406]

Although the idea of the knowledge-based economy sees science primarily as an engine of technological progress and economic growth, science plays many other important roles in society, which are not considered in the OECD's measures. This includes the role that (changing and uncertain) scientific knowledge plays in influencing research investment decisions, and the role of scientific evidence in regulatory decisions.

Ziman argues that treating science as an instrument of policy, serving the interests of government and commerce, neglects the important 'non-instrumental' roles of science: including the creation of critical scenarios and world pictures; the stimulation of rational attitudes; and the production of enlightened practitioners and independent experts.[407] The role of independent experts and alternative

world views can influence decisions on research priorities, including investment decisions by both the public and private sectors, and policy advice, including regulatory frameworks and decisions.

The political commitment to the knowledge-based bio-economy, means increased dependence on scientists and experts. For example, GM crops create dependence on scientific risk assessment to determine which foods are safe, and also make farmers dependent more economically dependent on the performance of seeds supplied by distant corporations. Human genetic tests make healthy people dependent on genetic risk assessments, and large-scale application of this approach to health would make people's privacy increasingly depend on the security of databases managed by government institutions and/or commercial companies. At the same time, policy makers have become dependent on the scientific experts they promote and fund to provide them with assessments and appraisals of the future importance of their work and the extent to which its applications are in need of regulation.

As described in Appendix A, the idea that genetic screening will lead to genetic 'prediction and prevention' of disease has led to a significant investment in building large-scale 'biobanks' (databases of electronic medical records, linked to DNA samples). The idea of 'genetic predisposition' to different diseases and behaviours was originally developed by the eugenicist Ronald Fisher, based on his 1918 mathematical model of how genes and environments influence disease and other traits. The subsequent promotion of this idea has been strongly influenced by a succession of commercial interests, including significant amounts of research funding by the tobacco industry (Section 2.5.3). The theoretical underpinnings of this approach have long been disputed in the scientific literature (including the extent to which complex diseases are inherited, and the role that the complexity of interactions between biology and environments will play in limiting the predictability of such diseases[336]). However, numerous scientific critiques of this approach to health have had little impact on decision-makers, who have remained committed to significant investments in this area, despite growing evidence that it is unlikely to deliver significant benefits to health (Section 5.3.1). A 'cycle of hype' (Section 2.5.4) has driven these investments, based on the 'vision-led' approach described in Section 1 and facilitated by the 'scientific bandwagons' that have been created (Section 2.5.3). At the same time, the idea that regulation will stifle innovation has led to a situation where commercial providers of unregulated genetic 'services' can sell misleading claims about genetic risk to uninformed consumers.[336]

In the case of GM crops, significant public opposition and political tension has arisen due to a fundamental conflict between the what the US company Monsanto sees as its 'right to operate' and critics' emphasis on the 'right to choose' whether or not to eat GM foods, based on concerns about their potential impacts on health, society and the environment.[408] This tension arises because GM crops can irreversibly contaminate GM-free food supplies (and other related plants and crops) through seed-mixing (either deliberate or accidental), product mixing – again either deliberate (as happened when GM soybeans first entered the EU, for unlabelled use in a wide variety of processed foods), or accidental (for example, if new crops designed to produce pharmaceuticals or industrial chemicals end up in the food chain) – or through 'gene flow' (from GM plants to other related plants or soils), and because they are self-replicating. This means that consumers are dependent on regulatory assessments of the impacts of genetic-modification of plants on their health and the environment, and on regulatory controls, such as segregation and labelling, to preserve choice and protect the food chain and biodiversity.

The 'Public Acceptance of Agricultural Biotechnologies' project (PABE),[409] conducted using focus groups in 1998/99, found that the inter-connection of scientific innovation, regulation, commercial pressures and the complexities of social and ecological systems influenced opinions about genetically-modified organisms (GMOs). People's views are largely shaped by institutional behaviour in these areas, not public relations exercises: including the view that important decisions which influence their lives are made by unaccountable 'alien' institutions over which they have no control. Key questions revealed by the study were:

Why do we need GMOs?

Who will benefit from their use?

Who decided that they should be developed and how?

Why are we not given an effective choice about whether or not to buy these products?

Have the potential long-term and irreversible consequences been evaluated, and by whom?

Do regulatory authorities have sufficient powers to effectively regulate large companies who wish to develop these products?

Can controls imposed by regulatory authorities be applied effectively?

Who will be accountable in cases of unforeseen harm?

Claims about science and technology influence both research investment decisions in these areas, and regulatory decisions. The commercial aim is to 'add value' though science, by creating new products that can be sold at a premium to farmers or consumers. However, both farmers and consumers then become dependent on commercial and/or regulatory assessments of the new technologies (including 'health claims' for nutritionally-altered crops, seed performance for farmers, and assessments of potential risks to health and the environment). What science is done, the claims made about its likely future impacts, and how it is weighed up and used along with other factors, is not conducted in a vacuum, but is strongly influenced by institutional commitments to the 'knowledge-based bio-economy'.

The shift to closer university-industry collaboration, and the 'vision-based' approach to promoting bioscience investments, has led to concerns about a lack of 'counter-expertise': researchers able to ask critical questions about scientific claims. In addition to this 'missing expertise', 'absentee expertise' has been highlighted as a problem for developing countries, which may become dependent on international experts operating in a mode that is detached from local concerns and contexts.[410] This issue affects both research investment decisions and regulatory ones.

The EU argues that "*Regulation should encourage, not hinder, innovation*" and that, in the area of biotechnology in particular this means that "*Unnecessary administrative burdens on research and industry should be identified and removed*".[411] The UK Government has adopted a process of regulatory reform known as 'better regulation'.[412] The Hampton report,[413] published in 2005, is considered to be one of the cornerstones of the Government's better regulation agenda, alongside the Better Regulation Task Force's report 'Less is More'.[414] The widely-supported aim is to cut red tape and unnecessary burdens on business. However, one consequence has also been that regulating new technologies to protect consumers or the environment has met with increased political resistance.

In the context of the biosciences and biotechnologies, a key issue has therefore been the role of science and scientific experts in regulation, and whether and how regulation can allow consumers to make informed choices about new biotechnologies.

In the case of GM crops, public concerns have tended to be characterised by policy-makers as irrational, anti-science and creating an unnecessary block to progress.[415] However, this view neglects the role of values, uncertainties and unknowns in 'scientific' risk assessment.[416] Mayer and Stirling argue that key attributes of a precautionary appraisal system include humility, completeness, assessing benefits and justifications, making comparisons, allowing for public participation, transparency, diversity, and the mapping of alternative views rather than the prescription of single solutions.[417] In addition, socio-political concerns such as "*ownership, intellectual property, corporatism, and the appropriateness of technological solutions to what are often human problems*" lie completely outside the regulatory assessment process,[428] a situation which underlies increasing tension within the European Union about the authorisation process for GMOs.[418] Taking a precautionary approach involves a general process of broadening expertise and inclusion of a wide range of views. This includes highlighting uncertainties other than those dealt with by the scientific risk assessment process, such as uncertainties concerning biodiversity, co-existence of different types of agriculture, and the future of agriculture more generally.[419] Industry groups are concerned about the potential for precaution to stifle innovation or to be used as a tactic for delaying commercialisation, but others view it as an opportunity for greater fairness, openness and inclusiveness.

In May 2003, the USA, Argentina and Canada made a formal complaint to the World Trade Organisation (WTO) about the *de-facto* moratorium on GM crops and food in the European Union. Although the panel found in favour of the US Government, it made no finding as to the EC's right to require pre-market approval for the safety of GM products, and it did not revoke the right of WTO Members to choose whatever level of protection they want to provide to their people from risks to human health and the environment - including 'zero-level' risk.[420]

In December 2009, the EU's Environment Council adopted a resolution requiring improvements in the monitoring and evaluation of the long-term environmental impacts of GM crops and requiring the Commission to produce a report on the socio-economic implications of GM crops. The resolution also emphasised the need to take full account of specific regional and local characteristics, "*particularly ecosystems/environments and specific geographical areas of particular value in terms of biodiversity or particular agricultural practices*" and to allow the establishment of GM-free zones.[421] However, the issue of 'co-existence' of GM and non-GM, including liability for damage to biodiversity or contamination of non-GM and organic crops, may prove impossible to resolve.[422]

Controversy also remains about potential unintended effects of GM foods on human health, and the difficulties in assessing such effects using short term animal feeding studies.[423,424] If the nutritional composition of a GM crops is considered 'substantially equivalent' to its conventional counterpart, regulators currently consider it to be safe. However the concept of 'substantial equivalence' is disputed and some studies show unintentional alterations to the nutrient profiles of crops that have been genetically modified.[425]

Concerns about impacts on health, the environment, and economic liability, are likely to be exacerbated if and when 'second-generation' GM crops, with intentionally altered nutritional content, or designed to produce industrial chemicals or pharmaceuticals, begin to be marketed.[426] There are particular concerns about the health implications of producing pharmaceuticals in food crops.[427]

Peter Lund, a member of the UK Government's Advisory Committee on Novel Foods and Processes, notes that although the animal studies of GM foods submitted to the committee have never reported any significant ill effects: "…*these are generally neither peer-reviewed by independent professional toxicologists nor published in the scientific literature; moreover, they are often conducted by the very companies who are applying to market the foods that they are testing*".[428] Independent assessment and research on GM crops can be hampered by scientists having restricted access to seeds or by biotech companies preventing publication of damaging research.[429] In India, NGOs had to take a seed company to court to force disclosure of bio-safety data.[430]

In human genetics, there has been an ongoing dispute whether, and to what extent, human genetic tests should be regulated, in order to protect consumers from misleading claims about their health.[431,432] Government concerns about stifling innovation have led to a situation where companies are encouraged to commercialise misleading assessments of people's genetic risk of common diseases, without any independent assessment of their claims (see Section 5.3.1 and Appendix A).

More broadly, because the 'better regulation' concept treats regulating business as a burden, it emphasises 'light touch' regulation of both commercial products and industrial processes. This tends to encourage the development and marketing of new tests and treatments at the expense of controls on unhealthy products or pollution, even though the latter may be more effective at preventing ill-health (see Section 5.1).

The role of independent expertise (or 'counter-expertise') in appraising and evaluating research investment decisions, by both governments and industry, has been less widely discussed than the role of science in regulation.

Without a realistic appraisal, reliant on the existence of critical voices or 'counter-expertise', there is a danger that what the journalist Jonathan Guthrie calls "*wild promises to secure research funding*"[363] may be taken at face value by politicians, leading to potentially enormous waste of public money, especially on large-scale research infrastructure projects (see, for example, Appendix A). If there are

likely to be large externalities (such as potential irreversible damage to the environment), there is also a danger that these will not be adequately accounted for before significant investments in R&D are made (a concern that frequently arises in the context of GM crops).

It is well-known that major infrastructure projects – such as the Channel Tunnel – routinely result in massive cost overruns and underestimates of risks: including both economic and environmental risks.[433] The UK Treasury's guidelines on economic appraisal (known as the 'Green Book') now emphasise the need to assess such 'optimism bias' both before and during the process of implementing major projects.[434] The consequences of major investments in R&D infrastructure and research are highly unpredictable and technology forecasts are usually wrong.[435] Yet 'optimism bias' is rarely considered in these situations. Instead the structure of the knowledge-based bio-economy encourages scientists to promote unrealistic future visions to secure funding for research (see Sections 2.5.3 and 2.5.4).

Venture capital companies and investors routinely conduct 'due diligence', including 'scientific diligence' before making major R&D investments. But if independent expertise, or 'counter-expertise', is lacking (or silenced due to fear of losing funding), it may be hard to make a realistic appraisal of the likely risks and benefits of such investments. In the public sector, there is a danger that scientific diligence is by-passed altogether, as incentives to patent technologies and spin out companies take precedence over checking the validity of scientific claims or broader social or environmental consequences. In the private sector, lack of a realistic assessment can lead over-valuation, creating a 'bubble' that then bursts (as happened in the late 1990s); or losses for shareholders if substantial investment in new technology does not deliver (as happened with the revolution in drug discovery that was supposed to result from investment in genomics), or if it is rejected by the market, perhaps for social or environmental reasons. In the public sector, substantial amounts of taxpayers' money can be wasted as a result of 'entrapment' in innovation strategies based on false assumptions about science, innovation, or social or environmental impacts.

Major investments in the science, technology and infrastructure expected to underpin a 'genetic revolution' in both health and agriculture have arguably led to what William Walker describes as the "*politics of commitment*", in his study of the ramifications of an earlier British Labour Government's (Harold Wilson's) decision to construct the Thermal Oxide Reprocessing Plant (THORP) at Sellafield.[436]

Walker describes six predicaments that are characteristic of political "*entrapment*" in a particular innovation strategy:

> The preference for advance over retreat (the tendency "*to favour the investor over the protestor*");
>
> Commitments have to be 'dug in' to survive (the more risky, complex and costly the initiative, the more commitments have to be embedded at the outset, risking inflexibility);
>
> The necessary myth of certainty amidst uncertainty (leading to unrealistic 'vision-creation' as entrepreneurs try to build support for their proposals and downplay risks);
>
> Externalities politicise commitments (large and uncertain externalities, such as environmental costs, complicate choices and may lead to entrenched political commitments in the face of challenges to the legitimacy of government decisions);
>
> Commitments drive additional commitments (so states and industries feel compelled to forge future commitments in defence of the original one);
>
> Sunk costs and the escalation of commitments (leading to 'good money thrown after bad' as one project inevitably requires another before the promised benefits are realised).

Walker identifies GM crops as an example of a problematic commitment to a technology because it is unclear how the balance of costs and benefits will evolve and there are serious disputes over the values that should inform the assessment of costs and benefits. Arguably, the commitment to transforming Britain's National Health Service to implement the genetic 'prediction and prevention' of disease (see Appendix A) is also an example of entrapment (although with very different consequences).

In both cases the adoption of a vision-driven approach (see Section 1), rather than a system of ongoing, transparent appraisal and assessment, has made it hard to anticipate and address public concerns, as well as to respond to changing scientific understandings. This failure to assess both practical outcomes (costs and benefits) and the impact of new knowledge, on the bioscience-based 'visions' of the future (described in Section 1.2), contrasts with the ongoing process of counting patents, publications and R&D investment (as promoted by the OECD).

2.6 Summary of incentives, assessment and entrapment in the KBE

The OECD's measures of the knowledge-based economy now underpin much of the research funding system. Universities and researchers are rewarded for filing patents, creating spin-out companies and obtaining industry research funding and venture capital.

This system is intended to encourage a new form of 'academic capitalism' or 'science as a business', based on the increased commercialisation of intellectual property (IP), and expanded definitions of what can be patented.

However, there are concerns that:

- Patenting may be used to stifle, rather than encourage, innovation (for example, by blocking competitors) and a focus on patentable inventions and discoveries can distort research priorities;
- Incentives directed towards a narrow form of wealth-creation may not be the best drivers to improve health or sustainability, or to deliver other public benefits;
- Wealth creation is being narrowly defined in terms of economic benefits to particular commercial sectors, individual companies or venture capitalists (particularly those investing in bioscience and biotechnologies);
- Short-term measures of supposed wealth-creation (e.g. number of spin-out companies from universities) reflect what is largely a drain on private and public funds rather than a positive contribution to the economy;
- Investments are 'vision-led' and based on a 'cycle of hype' which misrepresents and over-sells the likely benefits;
- Access to independent expertise for technology assessment and risk assessment may be eroded, leading to poor policy and investment decisions, ineffective regulation, and the loss of public trust.

The major shift to measuring scientific output using patents on discoveries (rather than inventions) risks redefining knowledge as whatever can be patented and traded in the knowledge-based bio-economy, rather than though traditional methods of validating science, such as peer review and independent replication of results. There is also an increased emphasis on technical, rather than theoretical, education, leading to a lack of counter expertise and critical questioning of concepts and claims.

The system of incentives introduced to facilitate the knowledge-based bio-economy has also exacerbated biases in research assessment, publication, and media claims about the benefits of particular research agendas. Policy-makers, as well as members of the public, have become dependent on these claims when making decisions about how to best invest taxpayers' money in research and development. In science communication, via the press and media, telling stories to obtain and protect investments has now become routine.

The political commitment to developing a new bio-economy has tended to prioritise 'technologies of control', designed to monopolise markets and maximise profits, and to increase dependency on scientific expertise. For example, GM crops create dependence on scientific risk assessment to determine which foods are safe and also make farmers dependent on the performance of seeds supplied by distant corporations. Human genetic tests make healthy people dependent on genetic

risk assessments, and large-scale application of this approach to health will create increased dependency on the security of databases managed by government institutions and/or commercial companies.

Agricultural biotechnology companies invested in the genetic modification of plants because they could be patented, and their most profitable strategy has been to package their own-brand herbicides with herbicide resistant GM plants. The food and pharmaceutical industries supported genetic 'prediction and prevention' of disease in the hope that they could sell more medicines and added-value 'functional foods' to healthy people; and the tobacco, nuclear, chemical and food industries also wished people to blame their genes for smoking-related and diet-related diseases, rather than their products. They helped to create a 'scientific bandwagon' which was supported by public as well as industry funding.

The main limitations and adverse consequences of the system of incentives and assessment adopted in order to implement the knowledge-based bio-economy are:

- the consequences of turning scientific discoveries (rather than inventions) into 'intellectual property';
- the prioritisation of narrow commercial research priorities defined by vested interests, rather than the public interest;
- a strong incentive for researchers to make exaggerated claims about the benefits of particular research and technologies in order to secure funding;
- potential economic losses: due to the risk of public-private partnerships being borne by the taxpayer, and due to 'optimism bias' (including publication bias and 'rescue' bias) in the claims made about what can be delivered;
- 'entrapment' in particular research agendas, with no system of cost-benefit analysis or appraisal of success;
- misallocation of resources and the resulting opportunity costs;
- the potential for harm due to lack of regulation;
- the 'selling' (or mis-selling) of the claimed benefits of the 'genomic revolution', risking loss of public and investor trust in science if benefits are not delivered, or harms are not prevented;
- restrictions on the availability of independent knowledge and expertise, due to the pervasiveness of commercial 'partnerships'.

3. Research Funders and Funding Processes

In the broader context of the knowledge-based economy, and the incentives given to researchers to commercialise their findings, most countries have a system of awarding public grants to researchers based in universities and academic institutions.

Government policies regarding science, technology and innovation set the framework for research funding decisions, which are ultimately influenced by many different factors. These include the structures, priorities and strategies of the institutions funding, undertaking and using the research, and the decision-making processes used by the funders to choose which applications to fund. These usually involve scientific peer review and may also include other selection processes, often involving committees of experts appointed by the various funding bodies.

This section describes the UK system of Research Councils, which distribute public money to researchers, and the European Union's Framework Programme for research.

3.1 UK Research Funding

Public funding for research in UK universities is administered under a dual support system. In this system, the Higher Education Funding Council for England (HEFCE), the Scottish Funding Council (SFC), the Higher Education Funding Council for Wales (HEFCW) and the Department for Employment and Learning, Northern Ireland (DEL) provide block grant funding to support the research infrastructure, including the salaries of permanent academic staff, premises, libraries and central computing costs. In 2008-09 HEFCE received a grant of £7 billion, of which £1.4 billion was funding for science and research.[437] The majority is 'quality-related' funding, which is distributed based on the outcomes of the Research Assessment Exercise (RAE) described in Section 2.4.1.

HEFCE has developed a strategic plan which recognises that "*Higher education is critical to the development of a modern knowledge-based economy*".[267] In line with Government policy, HEFCE has recently developed plans to increase spending on engagement with industry and businesses (so-called 'third stream' activities), to engage 'users' of knowledge (including employers and members of the public), and to increase funding for the Higher Education Innovation Fund (HEIF).[438]

Grants for specific projects and programmes are provided by the Research Councils, charities, the European Union and government departments. The role of these bodies in funding bioscience research, in both health and agriculture, is discussed below.

The Technology Strategy Board (TSB) is a "*business-focused organisation dedicated to promoting technology-enabled innovation across the UK*".[439] It has a budget for 2008-2011 of £711 million plus aligned funding from the Regional Development Agencies of £180 million and at least £120 million from the Research Councils. The TSB works with Government Departments and the Devolved Administrations to further increase the funding from those organisations aligned with its industry-led strategy.

The Foresight programme looks beyond normal planning horizons to identify potential opportunities from new science and technologies.[440] It reports directly to the Government Chief Scientific Adviser and the Cabinet Office and is a part of the Government Office for Science within the Department for Business, Innovation & Skills. The programme focuses on three to four areas at one time, examining either a key issue where science might be part of the solution or a cutting-edge scientific topic where potential applications and technologies are yet to be realised. A high-level stakeholder group, comprising senior decision-makers and budget-holders from relevant Departments, Research Councils and other organisations, oversee all projects. The group is chaired by the Minister from the lead Department, and is responsible for agreeing an action plan. Each project reviews research

literature and undertakes horizon scanning. A network of scientific experts and stakeholders also work closely with the Foresight project teams, which include individuals with relevant research experience. In 2010, active Foresight projects relevant to the biosciences included: Global Food and Farming Futures; Land Use Futures; Mental Capital and Wellbeing; and Tackling Obesities: future Choices.

Government departments are also required to encourage innovation, over and above the research that they fund. In its 2000 report[26], the DTI required Departments to "*publish science and innovation strategies, drawing on Foresight, and focusing on how they can maximise the potential of science and technology activities and how they can drive innovation*". The strategies[441] are required to cover arrangements for commercial exploitation of research, following recommendations from the Council for Science and Technology (see Section 4.1), and to say how departments are encouraging innovation, through their approach to regulation, to procurement, and to the services they offer.

3.1.1 Agricultural research

The independent Food Ethics Council (FEC) describes how UK research on food and farming is funded in its 2004 report 'Just Knowledge? Governing research on food and farming?'.[202] It divides research into three bands: agricultural productivity; food processing and food safety.

Food safety research is mainly conducted by the Food Standards Agency[442], by awarding contracts to universities and research institutes. The FSA was set up in 2000, in response to public concerns about food safety, including the implications of BSE ('mad cow disease') for human health and the lack of research on the safety of GM crops and foods.[443] Food processing research is largely conducted by industry, including food processing, manufacturing and retail firms.

The main Research Councils involved in agricultural research are the Biotechnology and Biological Sciences Research Council (BBSRC, see Section 3.2.1) and (to a lesser extent) the Natural Environment Research Council (NERC).

The UK Government department most involved is the Department for Environment, Food and Rural Affairs (DEFRA). The Department for International Development (DFID) also supports agricultural research and development in Africa. DFID's spending is not analysed in this report, but GM Freeze has argued that some of this research funding encourages the intensification of agriculture and the use of GM crops.[444]

DEFRA uses research contractors, including universities, BBSRC-funded institutes and consultancy firms to undertake research. In January 2008, DEFRA launched a new Food and Environment Research Agency (FERA) to bring together its Central Science Laboratory, Plant Health Division, Plant Health and Seeds Inspectorate and the Plant Variety Rights Office and Seeds Division as one agency.[445] The aim is to strengthen its research in plant and crop protection, food chain safety, environmental risk assessment and crises response and promote better integration between policy development, scientific evidence and inspection services.

DEFRA is responsible for spending over £300 million annually on research, monitoring and surveillance activities.[446] This is small in comparison to funding by the Research Councils. As well as funding external research, DEFRA has three executive laboratory agencies, the Food and Environment Research Agency (Fera), the Centre for Environment, Fisheries & Aquaculture Science (Cefas) and the Veterinary Laboratories Agency (VLA).

DEFRA published its first Science and Innovation Strategy in 2003.[447] One of the Strategy's priorities was "Sustainable Farming Systems" (see Box J), which includes the aim of improving the efficiency of organic production and understanding and quantifying its environmental impacts in comparison with other types of farming. Another priority was "Exploiting Science", which includes an aim "*to harness genomics and other molecular approaches to support the genetic improvement of crops to improve crop quality, increase resource productivity and reduce environmental burdens*".

Box J: Setting sustainable farming research priorities

The UK Government set up a Policy Commission on Farming and Food in August 2001, chaired by Sir Don Curry, which published the Curry Report in January 2002.[448] In response, the Government published a Strategy for Sustainable Farming and Food[449] (followed up by a further report in 2006[450]), and, in 2003, established a Sustainable Farming and Food Research Priorities Group[451], with Professor Chris Pollock, Director of the Institute of Grassland and Environmental Research (IGER) as its Chair. In 2004, the Research Priorities Group undertook a stakeholder engagement exercise to inform their decisions on research priorities. In 2005, it published a report on the outcomes, which identifies 40 priorities in seven themes.[452] One of them involves including using genetics and genomics to create value-added 'functional foods' to tackle diet-related disease. The Group's second report assesses the response of the Research Councils and government departments.[453]

DEFRA established a broad-based Scientific Advisory Council (SAC) in February 2004, which reports to its Chief Scientific Advisor (CSA). The SAC replaces its earlier Science Advisory Group (SAG), established in 2002.

Between January 2005 and May 2006, DEFRA conducted its Evidence and Innovation Strategy project (EI&S), an analysis of its priorities and requirements for knowledge in the natural and social sciences, economics, engineering, statistics and other disciplines.[454]

DEFRA published an Evidence and Innovation Strategy in 2006[455], based on the outcomes of the EI&S, and a new version in 2010.[456] The Strategy defines evidence as "*reliable and accurate information that Defra can use to support sound decisions in developing, implementing, and evaluating policy*". It "*includes facts, risks, uncertainties, ambiguities and analysis of the limits to knowledge concerning current and future situations, and the viability of alternative options for future innovative solutions*". One of the key goals is to ensure that the evidence helps to foster innovation: this is defined broadly to include incremental innovation as well as radical and transformative innovation, and different ways of 'innovative thinking'. DEFRA's 'good practice' guidelines on the use of evidence include engaging stakeholders. The big challenges, identified following a stakeholder workshop, are seen as: climate change; a sustainable food supply; and protecting ecosystem services. The approaches identified are: interdisciplinary working, understanding and influencing behaviours, and innovation. DEFRA's research largely falls between the 'basic/strategic' research of the Research Councils and the near market and technology development activities of the private sector and near private sector bodies such as the Technology Strategy Board (TSB).

In 2010, the Technology Strategy Board (TSB) announced a new five year Innovation Platform for agri-food with funding of up to £80m, including £30m from DEFRA and a contribution from BBSRC available for joint funding with industry. This will replace several existing LINK programmes sponsored by DEFRA and others in the agriculture and food areas.[456] The new Innovation Platform, called 'Sustainable Agriculture and Food'[457] seeks to "*increase the productivity of crops and animals and, simultaneously decrease the environmental impact of the industry*". It will focus on four interlinked areas:

- Crop productivity including protection and nutrition
- Sustainable livestock production
- Waste reduction and management
- Greenhouse Gas Reduction Technologies and Methodologies

The TSB has a commitment to 'bioscience' as a key technology area, stating: "*Biotechnology will drive expansion of the global economy, increasing wealth while reducing our environmental footprint*".[458] The Innovation Platform is part of its Biosciences Strategy.[161] The Platform is focused on "*technology-based solutions*" and its Board contains no expertise in food and farming.[459] This decision raises concerns because it appears to exclude farm management approaches (including organic farming and agro-ecological approaches) and small farming businesses, in favour of partnerships with multinational companies developing pesticides and GM crops. Examples of

projects that might lose out include those funded under DEFRA's sustainable arable LINK programme, many of which involve small-scale organic producers,[460] and some of which incorporate new techniques such as marker-assisted breeding.[461]

In Scotland, The Scottish Government Rural and Environment Research and Analysis Directorate (RERAD) provides around £70 million of funding each year towards a wide range of environmental, biological and agricultural research.[462] RERAD funds research largely through its main research providers: the Macaulay Land Use Research Institute, the Moredun Research Institute, the Rowett Research Institute, the Scottish Crop Research Institute, the Scottish Agricultural College and the Royal Botanic Garden Edinburgh.[463] The Scottish Government differs from the UK Government in that it intends to maintain a moratorium on planting GM crops in Scotland. It has set five strategic objectives: to be wealthier and fairer; healthier; safer and stronger; smarter; and greener.[464] In this context, it has conducted a review of the areas where science in its broadest sense can make a contribution to policy development relevant to Scotland, in order to help shape the next Scottish Government Rural, Environment and Marine research strategy.[465] The review will be used to develop a policy framework, which will then be consulted on.

Scotland's review sought to identify policy relevant drivers, trends and challenges over the next 30 years; together with knowledge gaps and potential research needs, from the perspective of a range of stakeholders, including government, researchers and civic society. A number of important knowledge gaps were identified. In addition, key findings were:

> Many of the drivers of change and associated knowledge gaps are linked, and research programmes should take account of this interconnectedness. This approach requires a shift from analytical thinking to contextual thinking. Indeed Scotland could be considered as a national ecosystem – with the need to address the social, economic and environmental aspects of the system.
>
> There would be benefit from developing mechanisms for better integration of research into policy and better integration across policy areas.
>
> Scotland's environment, agriculture and marine resources cannot be studied in isolation from changing patterns of societal demands and expectations or Scotland's economic welfare.
>
> There are advantages in understanding the role of the natural environment in the economy as well as understanding links between environment, vibrant communities and entrepreneurship, particularly for rural areas.
>
> It is important to note the need for research programmes to be fuelled by and to increase innovation. This involves dialogue, networking and collaboration in shaping and developing the research. In addition, barriers to innovation such as planning and licensing issues should be considered at an early stage to ensure that desired outcomes can be achieved.

The Department of Agriculture and Rural Development Northern Ireland (DARDNI) and the Department of Environment Northern Ireland (DOENI) also fund some research, but on a much smaller scale. The College of Agriculture, Food and Rural Enterprise (CAFRE) is an integral part of the Northern Ireland Department of Agriculture and Rural Development.

DEFRA and the relevant devolved departments are also members of the Environmental Research Funders Forum[466] and part of a ten year (2007-2017) co-ordinated programme called Living with Environmental Change (LWEC), which also includes the Research Councils.[467] The LWEC programme aims connect natural, engineering, economic, social, medical, cultural, arts, and humanities researchers with policy-makers, business, the public, and other key stakeholders.

The Levy Boards traditionally represented different agricultural sectors in the UK (such as dairy farming) and were also responsible for funding some research. In June 2006, the Government announced it was restructuring the Levy Boards into one single over-arching Board.[468] The new structure, announced in June 2006, is intended to "*release the sector companies from the requirements associated with being public bodies*", whilst still making them accountable to levy payers (and ultimately to Ministers). A new overarching Agriculture and Horticulture Development Board has been created.[469]

3.1.2 Health research

The main public funders of health R&D in the UK are the Medical Research Council (MRC) and the Health Departments of England, Wales, Scotland and Northern Ireland.

The Department of Health's budget for health R&D in 2010/11 is approximately £1 billion, of which £992 million will be distributed by the National Institute for Health Research (NIHR), with the remainder allocated to policy research.[470] In 2008/09, the MRC spent £704.2 million on research. The BBSRC (section 3.2.1) also plays a growing role in funding research in areas such as genomics, systems biology and cloning.

However, total spending on medical research is dominated by the pharmaceutical industry. In 2007, the pharmaceutical industry spent £4.5 billion on research and development (R&D) in the UK.[471]

The Wellcome Trust, Cancer Research UK and the British Heart Foundation, the three largest charity funders, together fund more than 80% of UK charitable health related research. They have annual research spends of about £600 million, £350 million and £80 million respectively. The Wellcome Trust is the largest charity in the UK and has been particularly influential in influencing funding decisions since 1997, with much government research being conducted in public-private partnership with the Trust, particularly in the area of human genomics (see Appendix A).

A 2002 King's Fund report found that public sector research funding is influenced by commercial research priorities and certain kinds of research attract little if any funding, either because results cannot be patented or they are of little scientific interest.[4] More recently, the UK Clinical Research Collaboration (UKCRC) analysed the research portfolios of the 11 largest government and charity funders of health related research in the 2004/2005 financial year – a total of 9638 peer reviewed awards and total spend of £950 million.[472] This included funding from the health departments in each of the countries in the UK, the research councils and the three largest health charities. The report concluded that what research gets funded is influenced by scientific opportunity, size and quality of the workforce, the 'researchability' of a topic, burden of disease and level of charity fundraising.

'Best research for best health', a new national health research strategy for the NHS, was published in January 2006.[140] The 2006 Cooksey Review[142] (see Appendix A), also proposed changes intended to ensure that knowledge from discovery science 'translates' into health and wealth benefits. A new National Institute for Health Research (NIHR) was set up in England, to provide the framework within which NHS research, research staff and research infrastructure can be managed. The annual budget for the National Institute of Health Research (NIHR) now incorporates all previously existing funds for NHS research in England.[473] The MRC has traditionally focused attention on basic research, while the Health Departments have focused more on applied research. However, a major recommendation of the 2006 Cooksey Review was that the MRC should collaborate better with NHS R&D. The Office for Strategic Co-ordination of Health Research (OSCHR) was established in order to play a major new role in setting research priorities. It now takes an overview of the budgetary division and research strategy of both the MRC and NIHR.

OSCHR's mission is to facilitate more efficient translation of health research into health and economic benefits in the UK through better coordination of health research and more coherent funding arrangements to support translation. It was jointly set up as a Government office in January 2007 by the Department of Health in England (DH) and the Department for Innovation, Universities and Skills (DIUS) with responsibility for:

- Translational Medicine Research
- Public Health Research
- E-Health Records Research
- Methodology Research
- Human Capital

Three Boards – a Translational Medicine Board (TMB), an E-Health Records Research Board (EHRRB) and a Public Health Research Board (PHRB) – have been established to provide strategic oversight in these areas. These Boards do not have a direct funding role.

Following the launch of the Office for Life Sciences in 2009, and its Life Sciences Blueprint, OSCHR began leading on the establishment of a series of Therapeutic Capability Clusters, the initiative by which industry, academia and the NHS will focus on areas of translational medicine, particularly early and exploratory development, where the potential for collaboration is regarded as substantial.[165]

3.2 The UK Research Councils

> "*Science and innovation underpin the UK's position in the global economy. The UK needs to maintain its position as a world leader in high value added industries to ensure growth in our prosperity and quality of life*.
> *Research Councils have pivotal roles, both as funding bodies and as leaders of the research base.*"
> The Warry Report, 2006.[48]

The Research Councils are the main public investors in fundamental research in the UK and also manage a significant proportion of the knowledge transfer budget. Around 80% of the Government's Science Budget is currently delivered through the Research Councils.[48]

The research councils were established following the publication of the Haldane Report in 1918, which created the Councils to administer 'general research', as distinct from research that met the immediate needs of government departments.[474] This decision was underpinned by the Haldane Principle, which implies that researchers are best placed to determine detailed priorities; that government's role is to set the over-arching strategy; and that research councils are guardians of the independence of science from too much government interference. It is often cited to state that scientists rather than politicians should determine how research funds are spent. However, in reality, research funding policy has been based largely on a customer-contract model since the 1970s.

Total expenditure by Research Councils in 2007-08 was £2,791m, with the budgets split as follows[47]:

Arts and Humanities Research Council (AHRC) £97m
Biotechnology and Biological Sciences Research Council (BBSRC) £382m
Council for the Central Laboratory of the Research Councils (CCLRC) £213m
Engineering and Physical Sciences Research Council (EPSRC) £721m
Economic and Social Research Council (ESRC) £150m
Medical Research Council (MRC) £546m
Natural Environment Research Council (NERC) £367m
Particle Physics and Astronomy Research Council (PPARC) £315m

The Science and Technology Facilities Council (STFC) was formed as a new Research Council on 1 April 2007 through a merger of the Council for the Central Laboratory of the Research Councils (CCLRC) and the Particle Physics and Astronomy Research Council (PPARC) and the transfer of responsibility for nuclear physics from the Engineering and Physical Sciences Research Council (EPSRC).

Research Councils UK (RCUK) is a partnership of all seven Research Councils.

The Research Councils receive annual 'grant-in-aid' funding from Government distributed via the Department for Business, Innovation and Skills (BIS). Although government-funded, the Research Councils are independent in their choice of which research to support. All the Research Councils therefore have processes and structures they use to:

- Set a funding strategy, including a vision for the future and how they intend to deliver it;
- decide which projects and institutes to fund in order to deliver the strategy;
- manage the projects and investments that they make, including the translation of knowledge into intellectual property;
- evaluate their investments.

The Research Councils are nevertheless required to operate within the context of the Government's overall science and innovation policies and budgets, and in 2008 MPs criticised ministers for interfering in how they spend their money.[475] The Commons Innovation, Universities, Science and Skills Committee expressed concerns that Science Budget increases do not fully cover Government-determined spending commitments and expenditure on new bodies like the Technology Strategy Board (TSB) and claimed that: "*Additionally, large parts of the budget are tied to cross-council programmes that largely follow a Government agenda*".

In its budget allocations in 2004, the DTI (now part of BIS) set a new Public Service Agreement target requiring the Research Councils to: *"Improve the relative international performance of the UK research base and improve the overall innovation performance of the UK economy including through effective knowledge transfer amongst universities, research institutions and business".* Each Research Council is required to publish a Delivery Plan, which is part of a comprehensive Performance Management System to enable the Office of Science and Innovation to assess how it is achieving government targets. This system includes a series of performance measures (the 'Outputs Framework') and a set of targets and milestones arising from the activities set out in the Delivery Plan (the 'Scorecard').

In July 2006, the Warry Report (Box K) recommended ways to increase the economic impact of research councils. It followed a series of other reports on Research Council Knowledge Transfer, including by the House of Commons Science and Technology Committee[476] and the 'Independent External Challenge' panel[477], and refers to reports on related subjects from the University Companies Organisation, the British Venture Capital Association and the Council for Industry and Higher Education.

Box K: The Warry Report[48]

The Research Council Economic Impact Group was chaired by Peter Warry, Chairman of Kier Group plc, Victrex plc and BSS Group plc. Its members included representatives of research councils and universities, plus Dr David Chiswell (Chairman of several biotechnology companies) and John Murphy (of BAE Systems and the CBI).

Its report recommended that the Research Councils' emphasis on knowledge transfer should continue to increase and that one of the Research Council chief executives should be nominated by RCUK to champion the work on economic impact across all Councils.

Sources of evidence for the report included universities, research councils, businesses, investors, the House of Commons Science and Technology Committee, charities (Cancer Research UK and the Wellcome Trust) and 'independent commentators'. The businesses were: the Confederation of British Industry (CBI); the Home Grown Cereal Authority; Campden and Chorleywood Food Research Association; the Association of the British Pharmaceutical (ABPI) Industry; the Bioindustry Association; Shell; BT; GlaxoSmithKline (GSK) and PriceWaterhouseCoopers. The 'independent commentators' were: London Technology Network; Council for Industry and Higher Education; The Research Council External Challenge Group; Trinamo; QI3; Foundation for Science and Technology; Higher Education Policy Institute; Public Support for Research in Universities (Mark Schankerman); Centre Management Public Organisations.

In 2007, the Research Councils are embarked on a new range of thematic research programmes, with a planned investment of almost £1.3bn[478]:

The **Life long health and wellbeing** programme aims to improve understanding of the ageing process (including Alzheimer's, Parkinson's, diabetes and strokes) and "*what can be done to keep people healthy throughout their lives*".

Living with environmental change is a research and policy programme examining the pressures on natural resources, ecosystems, economic growth and social progress.

The **Energy** programme brings together energy-related research across the Councils to address the issues of climate change and security of energy supply.

The **Global threats to security** programme integrates research in crime, terrorism, environmental stress and global poverty.

There are two further multi-disciplinary programmes on nanoscience and the digital economy, which build on the existing work of the Research Councils.

This report covers only research funding in the biosciences, principally in the areas of health and agriculture. Only funding by the BBSRC and MRC are discussed in detail, although other research councils – particularly the NERC and the ESRC – also fund some relevant research. The European Commission's Biopolis report identifies the BBSRC and MRC as the most important funding agencies for biotechnology-related research in the UK.[479] However, the Biopolis report for the UK also identifies other roles being played other research councils and government departments, and by charities, which are not considered further here.

A Government announcement made on 7 March 2007 breaks down the three years of spending on science for April 2007-2011. Total spend over all 4 years will top £10 billion, reaching nearly £4 billion in 2010-11.[480] The allocations for the BBSRC, MRC and (for comparison) Science and Society are shown in Table 2.

Table 2: Relevant research council funding allocations

Research Council	07-08 allocation in £000's (Includes Capital Investments)	08-09	09-10	10-11	% increase in 10/11 against 06/07
BBSRC	386,854	427,000	452,563	471,057	21.8%
MRC	543,399	605,538	658,472	707,025	30.1%
Science & Society	11,411	13,441	15,441	17,441	52.4%

3.2.1 The Biotechnology and Biological Sciences Research Council (BBSRC)

> "*The drive for commercially relevant research has resulted in a significant penetration of public sector research institutions and policy-making committees by industry, including those involved in private sector companies involved in developing GM food and GM crops*". Barling & Henderson, 2000.[168]

The Biotechnology and Biological Sciences Research Council (BBSRC)[481] is the UK's principal funder of basic and strategic biological research. It was formed in 1994, replacing the Agriculture and Food Research Council (AFRC), during the re-organisation of the Research Councils which followed the 1993 Government White Paper 'Realising our Potential'. The creation of the BBSRC therefore played a key role in the UK's political commitment to biotechnology and the biosciences as a driver for growth.

The BBSRC supports research and research training in universities and research centres throughout the UK; and promotes knowledge transfer from research to applications in business, industry and policy, and public engagement in the biosciences.

It invests around £470 million per annum in the biosciences in areas including:

Genomics, stem cell biology, and bio-nanotechnology, that provide a basis for new technologies in healthcare, food safety, plant and livestock breeding, and bioprocessing;
Whole organism biology relevant to understanding of diet and health, ageing, animal health and welfare, infectious diseases and immunity, and crop productivity;
Biological populations and systems that underpin agricultural sustainability, biodiversity and novel bio-based and renewable processes for energy and manufacturing.

In 2000, a report by Barling and Henderson at the Centre for Food Policy, Thames Valley University, mapped the then institutional framework for public sector research into the genetic modification (GM) of crops and food. The report found that, to achieve the Government's wealth creation goals, industrial expertise had been integrated into the decision making processes for allocating research budgets: including strong industry representation of the BBSRC's Committees on Agri-food, Plant and Microbial Sciences, and Genes and Developmental Biology. The report also concluded that a culture had been created in which scientists find it extremely difficult to avoid close association with industrial interests.

There have been some changes in priorities and personnel since 2000, however the over-arching commitment to biotechnology as a driver for wealth creation remains in place.

The BBSRC's mission is to promote and support post-graduate training in biological sciences and: "*To advance knowledge and technology (including the promotion and support of the exploitation of research outcomes), and provide trained scientists and engineers, which meet the needs of users and beneficiaries (including the agriculture, bioprocessing, chemical, food, healthcare, pharmaceutical and other biotechnological related industries), thereby contributing to the economic competitiveness of the United Kingdom and the quality of life*".

The Chief Executive and the Chairman of Council report to the Director General of Science and Innovation in the Office of Science and Innovation.

Professor **Douglas Kell** was appointed as BBSRC's Chief Executive in 2008: he was director of the Manchester Centre for Integrative Systems Biology, and is reportedly a strong supporter of GM crops.[482] Professor **Julia Goodfellow** was Chief Executive from 2002-2007, after more than 20 years at Birkbeck College, University of London, where she was Vice-Master and head of the School of Crystallography. She is a fellow of the Academy of Medical Sciences and the Institute of Biology and the wife of geneticist Dr Peter Goodfellow (see Appendix A).[483] Julia Goodfellow replaced **Peter Doyle**, a Director of the biotech firm Syngenta and the former Executive Director of Zeneca (now part of Syngenta).

Sir Tom Blundell has been Chair of the BBSRC since 1 July 2009 and was its founding Chief Executive. He was President of the UK Biosciences Federation between 2004 and 2008, a Non-Executive Director of Celltech from 1996 to 2005 and has been involved in science advisory roles with Pfizer, UCB and SmithKlineBeecham. He co-founded the biotech company Astex Therapeutics. His predecessor, **Dr Peter Ringrose**, was former Chief Scientific Officer of Bristol-Myers Squibb (BMS).

The BBSRC's **Council** determines its policies and strategies. The Council comprises the Chairman, the Chief Executive and between 10-18 other members at least half of whom are appointed for their qualification in science and engineering. Users of research, in Government and industry, are also represented.[484]

The Council receives reports, recommendations and advice from several boards and committees, which cover the range of BBSRC's activities, and from the BBSRC.

BBSRC-sponsored **Institutes** receive core strategic grants from Council. They can also apply for research grants, up to a cap that controls the overall ratio of university and institute funding. Institutes are also supported through a mix of funding sources including government departments, industry and the EU. They have charitable status and are companies limited by guarantee. The governance of each institute is through a Governing Body that comprises senior scientists and figures from the user communities. Currently, the seven institutes are split between three categories of research. Those covering 'Sustainable Agriculture and Land Use' are:

Institute of Grassland and Environmental Research
John Innes Centre
Rothamsted Research

The BBSRC institutes covering 'Animal Health and Welfare' are:

Institute for Animal Health
Roslin
Institutes covering 'Biomedical and Food Sciences' are:
Babraham Institute
Institute of Food Research

The BBSRC also funds six 'Systems Biology' centres, jointly with the Engineering and Physical Sciences Research Council (EPSRC), six 'Structural Biology' centres, based in universities, plus two research collaborations (with other Research Councils) in nanotechnology and one in tissue engineering.

The **Strategy Board** advises Council on key strategic issues across BBSRC's remit. It receives reports and advice from seven **Strategy Panels**, each of which considers strategic and policy issues in area of high strategic importance to BBSRC; and, via the BBSRC Executive, input from seven **Research Committees** that primarily perform the scientific assessment of research proposals.

Much of the research grant funding activity and development of scientific strategy is conducted by the Strategy Panels and Research Committees that report into the Strategy Board. The Strategy Board meets five times a year. Each of its panels takes a strategic oversight for areas of the BBSRC Ten-Year Vision and Strategic Plan for which it is responsible, monitoring the existing portfolio and producing an action plan. The current ten-year vision (2003-2013) is sub-titled 'Towards Predictive Biology' and anticipates a major shift in biology from a descriptive to a predictive science (see also Appendix A)[485]. The current Strategic Plan (2010-2015) is called 'The Age of Bioscience'[486]. Its strategic priorities are: food security: bioenergy and industrial biotechnology; basic bioscience underpinning health.

The BBSRC's **Strategy Panels** cover:

Bioscience for Industry
Bioscience for Society
Bioscience Skills and Careers
Healthy Organism
Integrative & Systems Biology
Sustainable Agriculture
Tools and Resources

The 'Bioscience for Industry' strategy panel includes representatives of the biotech, food and pharmaceutical industries, including Unilever, Syngenta, Pfizer and GSK. The other panels are more mixed: for example, the 'sustainable agriculture' panel includes representatives of Syngenta and the Royal Society for the Protection of Birds (RSPB). However, its focus is on the role of the biosciences and biotechnology, rather than farming practices such as agro-ecology.

The Strategic Panel on 'Bioscience for Society', supersedes the BBSRC's Advisory Group on Response to Public Concerns and is intended to play a more central role in BBSRC business. It includes social scientists and civil society representatives as well as scientists and business people. It provides a “high level overview” of the opportunities and appropriate avenues for engaging with different stakeholders and make proposals for integrating ethical and other social issues into its planning on policy and funding. The BBSRC has organised a number of participatory processes, beginning in 1994 with a Consensus Conference on Plant Biotechnology. Recent dialogue activities have covered the areas of nanotechnology, stem cells and synthetic biology. In 2005, the BBSRC published a report on public attitudes to diet and health, and in 2006, two further reports on public attitudes to industry-funded research and to ageing research. In 2009, it consulted on future directions in research relating to food security.[330]

The four BBSRC **Research Committees** have responsibility for peer review of research proposals. They identify new research opportunities, delineate priority areas in which they wish to see applications and identify lower priorities that may receive reduced support in the future. The Committees are:

Animal systems, health and well-being
Plants, microbes, food and sustainability
Technological and methodological development
Molecules, cells and industrial biotechnology

Companies with representatives on the Research Committees include: GlaxoSmithKline, McNeil Nutritionals Limited, MedImmune, Shell, AstraZeneca, Pfizer and GSK.

The Research Committees' interests are represented on the Strategy Board by the BBSRC Director of Science and Technology, who also chairs meetings of the chairs of the Research Committees. There is also cross membership of Research Committees and the Strategy Panels.

Committees operate two mechanisms for funding research grants.

The bulk of the BBSRC's funding is allocated in "responsive mode" where researchers can apply at any time for funding for research which is within a committee's remit, preferably in priority areas identified by the committee. Occasionally committees will identify areas that need specific funding outside of normal responsive funding, and will set up a research initiative in that area, which runs for a set period of time. In addition to priorities that cross all Committees, there are research areas of priority to two or more Committees (identified as Joint-Committee Priority Areas).

The BBSRC Research Grants Guide explains how grant applications are assessed.[487] Assessment of research quality is undertaken by UK and overseas experts in the field from academia, government or industry against: scientific excellence; industrial and stakeholder relevance; relevance to BBSRC strategy; economic and social impact; timeliness and promise; cost effectiveness; staff training potential of the project.

In addition, the BBSRC attaches “particular weight” to Industrial Partnership Awards (IPA), which are viewed favourably in its assessment for Responsive Research Grants. A responsive-mode IPA project that is judged to be of appropriate quality would normally be funded in preference to a standard grant of equivalent scientific merit, “*because of the significant user interest demonstrated by the industrial contribution to the cost of the proposed research*”.

BBSRC usually assigns responsibility for IP management and exploitation to the universities and institutes that undertake the research. Therefore while BBSRC does not itself hold the IP, it supports, through its **Business and Innovation Unit** (BIU), a range of mechanisms to facilitate the innovation process. BBSRC has responsibility for promoting an environment in which opportunities for knowledge transfer within the bioscience community are maximised, encouraging the translation of Intellectual Property (IP) and expertise into exploitable processes and products.

The BBSRC's **Technology Strategy**[488] is overseen by its 'Bioscience for Industry' Strategy Panel. It identifies areas where increased research investment is needed to meet industrial needs. It informs the thinking of the Technology Strategy Board (TSB) as it develops national strategy for innovation and enables the Council to work with the TSB in priority areas such as bioprocessing. Between 2008-2011 the BBSRC will provide £34M for collaborative and complementary activities with the Technology Strategy Board (TSB).

The BBSRC Technology Strategy priorities are: bioprocessing; integrated mammalian biology; exploiting systems biology; biocatalysis and biotransformations; genomics underpinning healthcare; intelligent storage, retrieval and analysis of large databases; crop sciences; and bionanotechnology.

BBSRC also supports a number of schemes aimed at improving industrial uptake of new science and the exchange of knowledge.

Collaborative research is encouraged through the LINK scheme (where the industrial contribution is 50% of total costs) and the Industrial Partnerships Scheme where the contribution is less. Industrial CASE studentships, the Industry Interchange Programme, Knowledge Transfer Partnerships and Industry Fellowships encourage the exchange of technology and expertise between academic institutions and commercial enterprises.

3.2.2 The Medical Research Council (MRC)

The Medical Research Council (MRC) was originally established in 1913 and is generally regarded as having a strong track record in funding original research, including funding 27 Nobel prize winners. The MRC spent £704.2 million on research in 2008/09. It supports research in almost all areas of basic and applied biomedical and health research and is the UK's largest non-commercial funder of clinical trials for medicines.

The MRC supports medical research in three main ways:

- by providing research grants and career awards to scientists in UK universities and hospitals
- by funding research centres in partnership with universities
- through funding of MRC's own research facilities.

Its mission is to:

- Encourage and support research to improve human health.
- Produce skilled researchers.
- Advance and disseminate knowledge and technology to improve the quality of life and economic competitiveness of the UK.
- Promote dialogue with the public about medical research.

Consistent with the international trend towards investing in molecular biological research, described in Section 2.5.3, the MRC's estimated spend by research area in 2006/07 was: molecular and cellular medicine, £192.1m; neurosciences and mental health, £108.7m; infections and immunity, £85.8m; physiological systems and clinical sciences, £97.3m; health services and public health research, £89.8m.[489]

Unlike the BBSRC, the MRC puts a higher proportion of its funding into its units and institutes than into its 'response-mode' funding stream. The advantage of this approach is that researchers can develop long-term strategic plans for their research, knowing that funding is relatively secure.

Sir John Chisholm was appointed **Chairman** of the MRC in October 2006. In 1979 Sir John founded the start-up CAP Scientific Ltd, which grew rapidly to become a core part of the CAP Group plc, a computer software company, which floated on the London Stock Exchange in 1995. In 1991, he led the UK Defence Research Establishments to form one new organisation, which was privatised in 2001 as QineticQ, with Sir John as Chief Executive, and controversially sold to the US private equity group, Carlyle in 2003. Sir John invested £129,000 in QinetiQ and now has shares worth £23m.[490] He became Chairman of the company in 2005.

Sir Leszek Borysiewicz was appointed **Chief Executive** of the MRC in September 2007.[491] Sir Leszek was Deputy Rector at Imperial College London, having joined the College in 2001 as Principal of the Faculty of Medicine. Previously he was Professor of Medicine and Head of the Department of Medicine at the University of Wales, Cardiff. He was a founding fellow of the Academy of Medical Sciences in 1996 and Chairman of HEFCE's main Clinical Medicine panel for RAE 2008. He was a member of the Council of Cancer Research UK from 2002 to 2005, a governor of the Wellcome Trust from 2006 to 2007, a member of the MRC Council from 1995 to 2000 and chair of the MRC's Molecular and Cellular Medicine Board from 1996 to 2000.

The MRC's governing body is the MRC **Council**, which directs its scientific strategy and corporate policy. The Council consists of the Chairman, the Chief Executive and Deputy Chairman, and 10 to18

other members. Council membership is is largely drawn from the academic and research communities, with one member currently from Pfizer.

In December 2008, the MRC held a Health Research Opportunities meeting[492], which was used to inform the development of the MRC's new Strategic Plan 2009-2014[493]. At the same time, the Office for Strategic Coordination of Health Research (OSCHR) is co-ordinating a multi-stage project with the overall objective of identifying and prioritising UK health research opportunities over the next decade. The MRC's four strategic aims for 2009-2014 are: picking research that delivers (seeking research priorities which are most likely to deliver improved health outcomes); research to people (i.e. a focus on translation); going global (accelerating progress in international research) and supporting scientists. This last aim includes an objective to maximize sharing and linking of data from electronic medical records.[494] The priorities identified under the first aim are grouped into two themes: 'resilience repair and replacement'; and 'living a long and healthy life'. The latter includes genetics and disease, as well as lifestyles and environment.

The MRC's Strategy Board is responsible for developing, co-ordinating, and overseeing implementation of and evaluating the MRC's strategic plans. The board is chaired by the Chief Executive. Membership consists of chairs of the four research boards and of four overview groups. The overview groups are: global health, population health, training and careers, and translational research. Most members are academic medical researchers. Currently, Pfizer is represented on the training and careers group and GlaxoSmithKilne is represented in the translational research group. The four Research Boards represent the main divisions of the MRC's research portfolio:

Molecular and cellular medicine

Population and systems medicine

Infections and immunity

Neurosciences and mental health

The Health Services and Public Health Research Board (HSPHRB) was disbanded in 2008. The molecular and cellular medicine board is now responsible for research into environmental factors, as well as genetics and genomics. It is also responsible for MRC's investment in UK Biobank. The decision to fund UK Biobank did not follow the MRC's usual research assessment processes: this history is described in Appendix A.

The MRC Boards hold their own budgets and manage and review scientific activity within their specialist area, including making funding decisions. They also advise the MRC Council on strategic development of their areas. The majority of board members are academics and clinicians, although some have made declarations of interest as consultants to the pharmaceutical industry. However, additional industry members have recently been appointed to the Boards. Currently they represent GlaxoSmithKline, Domainex, AstraZeneca, Pfizer, Eli Lilly and Roche.

All research proposals the MRC receives are assessed through a two-stage process. First, they are reviewed by independent scientific experts in the UK and abroad, then they are shortlisted for consideration by the MRC research boards. External reviewers and research boards/panels assess proposals against three core criteria:

Importance: how important are the questions, or gaps in knowledge, that are being addressed?

Scientific potential: what are the prospects for good scientific progress?

Resources requested: are the funds requested essential for the work, and do the importance and scientific potential justify funding on the scale requested?

Research Boards then consider whether proposals effectively address needs or strategies identified by MRC or other key organisations such as the Department of Health or the Department for International Development. Reviewers and research boards/panels also identify any ethical issues or risks to human participants that need further attention. In addition, some MRC grant schemes have scheme-specific criteria and subsidiary questions which they will consider.

In 2008, the MRC put in place a new translational research strategy, coordinated with the National Institute for Health Research (NIHR), under the Office for the Strategic Coordination of Health Research (OSCHR) and its Translational Medicine Board.

The MRC, as the lead for the Office for the Strategic Co-ordination of Health Research (OSCHR), is developing a 'stratified medicine' strategy in partnership with the Technology Strategy Board (TSB). 'Stratified medicine' is a new term now being used for the co-development of uses of medicines and of genetic (or other) tests for drug response (known as 'pharmacogenetic tests'). This has been identified as a priority following the Review and Refresh of Bioscience 2015 report (BIGTR2) in May 2009. The TSB and MRC have organised a stakeholder workshop that will inform the MRC's strategy and investment plans and the case for a potential innovation platform on stratified medicine.[165]

In 2007, the MRC set up a public lay panel to add patient or public perspectives. Panel members are invited to provide advice and guidance to the MRC on a project-by-project basis.[495] The MRC has undertaken public consultations on: the use of human embryos in medical research (in 2003); BSE ('mad cow disease') and human health (in 2004); the use of animal models in medical research (in 1999 and 2005); ageing research (2006); the use of personal information in medical research (in 2007); and stem cells (in 2008).[496]

The MRC has its own affiliated company, **MRC Technology**, which works with industry to commercialise its research.[497] MRCT was set up in 2000, following a decision to merge the MRC's Technology Transfer Centres in London and Edinburgh. The London (Mill Hill) Technology Transfer Centre (originally called the Collaborative Centre) was first established in the late 1980s. MRCT and its predecessors have been involved in the creation of 17 start-up companies, including two of the UK's largest biotech companies, Celltech (founded in 1980, see Section 1.4.1) and Cambridge Antibody Technology (founded in 1989 and bought by AstraZeneca in 2006 to create MedImmune). The technology developed by Cambridge Antibody Technology was used to create adalimumab, the pharmaceutical industry's first fully human antibody blockbuster drug. Up to the beginning of 2008, royalties arising from the licensing of MRC intellectual property to industry had generated £390 million. Any income the MRCT generates goes back to the MRC to fund further research.

The MRC Open LINK Grant scheme is designed to facilitate collaboration between academic researchers and the biotechnology and pharmaceutical industry.

In response to the Cooksey Review, the MRC launched a strategic review to examine the impact of the proposed changes on the organisation's role, structures, and operations, and appointed the consultants Ernst & Young to conduct the review jointly with the MRC. The 2007 review report[498] noted that after several decades of investment in biomedical research, there is an increasing pressure on research organisations to demonstrate a clear return on investment through the delivery of health and benefits. It recommended that the MRC should create:

- a Translation Directorate to develop strategy and to promote partnering and work with the OSCHR's joint MRC/NIHR Translational Medicine and Public Health Boards.
- specific funding routes, with different evaluation and management approaches, for its more goal-oriented research.
- a Strategy Advisory Group (SAG) and a new strategy-setting process which clearly addresses UK health needs, is evidenced based and engages external stakeholders.
- a Strategy & Evaluation Directorate (SED), to bring together the development and evaluation of science and organisational strategy and engage stakeholders.
- two new cross-cutting MRC Research Boards, Translation & Population Sciences, which should be core to decision making, plus more user representation on all Research Boards.
- a more strategic Executive Board, comprising the Chief Executive Officer, Chief Operating Officer, Director of Research & Training, Finance Director and Human Resources Director, plus two new appointments Director of Strategy & Evaluation and Director of Translation.
- a smaller and more strategic Council, removing Health Departments' representatives but retaining experience of user sectors such as the health service and pharmaceutical industry.

greater separation between Council's governance role, and the processes of strategy development and Board funding.

At its December 2007 meeting, the MRC's Council agreed that, as a result of the changes, it would disband its Health Services and Public Health Research Board (HSPHRB) and create the four overview groups that now advise the new Strategy Board.[499] In November 2007, the MRC announced that, to further strengthen its support for translational research, it would join forces with the new Technology Strategy Board (TSB), by making calls for proposals in cell therapy research and technologies for health.[500]

3.3 European Union research funding

The Treaty of the European Union identifies two core strategic objectives for the European Research Framework Programmes: (i) strengthening the scientific and technological bases of industry to encourage its international competitiveness and (ii) supporting other policies of the European Union.

The European Framework funding schemes have been progressively developed since the 1980s, and comprise various funding mechanisms and research themes. Research related to the biosciences and biotechnology has received substantial funding from the Framework Programmes. This section describes how the Framework Programmes operate and the increasing role of industry in setting research priorities.

3.3.1 Early European Framework Programme support for biotechnology

The European Commission's support for biotechnology research began in 1982 under the First Framework Programme (FP1) with the EUR 15 million Biomolecular Engineering Programme (BEP, 1982-1986)[501], followed by the EUR 17 million Biotechnology Action Programme (BAP, 1985-1989)[502] and the EUR 100 million Biotechnology Research for Innovation, Development and Growth in Europe (BRIDGE, 1990-1994)[503]. The 65 million Euro ÉCLAIR (European Collaborative Linkage of Agriculture and Industry) programme, which ran from 1998-1993 also included some agricultural biotechnology projects.[504] The EC spent EUR 15 million on the HUMGEN programme from 1990-1992. The EUR 151 million BIOMED I[505] and EUR 186 million BIOTECH I[506] programmes ran from 1990-1994, followed by BIOMED II and BIOTECH II (EUR 374 million and EUR 595 million, respectively, from 1994-1998).

The EU's Framework Programme 5 (FP5) ran from 1999-2003. By this time the Framework Programme had evolved into a set of instruments geared towards the attainment of a set of broader economic objectives, involving research funding geared towards industrial organisations (particularly 'small and medium-sized enterprises', SMEs) as well as academic institutions and research institutes.[507] About 108 million Euros was allocated to agricultural biotechnology research in FP5.[508]

3.3.2 The Sixth Framework Programme (FP6)

According to the European Commission, the 6th Framework Programme (2002-2006)[509]:

> Allocated €500m to supporting exchanges, training and fellowships in the area of life sciences and biotechnology, as part of the Marie Curie Actions. This funded about 1000 full-time PhD positions and supported the creation of 45 new research groups. It also supported 11 top-level "Chairs", attracting world-class researchers (back) to Europe.
>
> €2.5 billion was used to fund 613 projects in the field of life sciences, genomics and biotechnology for health, looking at issues such as fundamental genomics, poverty-related diseases, cancer, cardio-vascular diseases, diabetes, age- and brain-related diseases and rare diseases.
>
> €756 million funded 186 projects in the field of food quality and safety, looking at food processing and safety, nutrition, food-related diseases, animal and plant production systems, forestry, animal and plant biotechnology.

€20 million was awarded to projects to develop biomass, under the sustainable development theme.

Support was given to specific actions to promote the debate on ethical, legal, social and wider cultural aspects of life sciences and biotechnology including on issues such as human embryonic stem cell, animal cloning, genetic testing etc.

Small and Medium Enterprises (SMEs) were strongly represented, accounting for 17% of all participants and 14% of funding in the health theme, and 19% and 12% respectively in the food quality and safety theme.

Other parts of FP6 (funding of infrastructures, international co-operation and coordination of national and regional research programmes) also supported research in the field of life sciences and biotechnology.

Under FP6, around €2.5 billion were awarded for 'Life sciences, genomics and biotechnology for health' research: this included about 613 projects, involving more than 7600 participants. Another €756 million were awarded for 'Food quality and safety research'. These funds went to 186 projects, involving more than 3032 participants, with projects ranging from food processing, safety, nutrition and food related diseases to animal and plant production systems, forestry, plant and animal biotechnology. [510]

FP6 projects related to agricultural biotechnology included CO-EXTRA [511] (a project on the co-existence of GM, conventional and organic crops); NOFORISK [512] (a project looking at the risk assessment of 'novel foods', including a GM potato); TRANSCONTAINER [513] (a project developing controversial 'biological containment' systems for GM plants); GMO-COMPASS [514] (a communication project) and SIGMEA [515] ('Sustainable Introduction of GMOs into European Agriculture': another project investigating the co-existence of GM and non-GM crops). In September 2005, the Commission also established the SMEs Virtual Platform on Agro-food Sector (SPAS) under FP6. [516] The FP6 FLORA project (following on from the FP5 PROFOOD project) funded the development of the GM 'purple tomato' described in Box I.

Under FP3 to FP5 (application phases 1990-2002), 40 projects dealt explicitly with the development of '2nd generation' GM plants with modified use properties. Industrial materials dominated the field with 20 projects. In FP6, only isolated relevant projects for plant-made pharmaceuticals and functional foods were identified in a German technology assessment. The authors state that is only possible to derive trends from this to a very limited extent, as both the promotional instruments (integrated projects, excellence networks) and the promotional philosophy (greater orientation towards problems and markets) have been changed. [517]

According to Friends of the Earth Europe (FOEE), about 100 million Euros were allocated to agricultural biotechnology research under FP6[508] and at least eight FP6 projects and three Technology Platforms (Plants and Health, Plants for the Future and White Biotech) directly involved the industry association, EuropaBio (Box L). [518] Technology Platforms are discussed further in Section 3.3.5.

Box L: EuropaBio

EuropaBio (the European Association for Bioindustries) describes itself as "*the political voice of the biotechnology industry in Europe*", covering applications in health, agriculture and industrial biotechnology (sometimes known as red, green and white biotechnology, respectively). EuropaBio is a strong advocate of GM foods: for example, it claims that "*Genetically modified fruit and vegetables can offer higher nutritional value, better taste, longer conservation, all to the benefit of the consumer*". [519] It is an industry body representing 87 corporate and 8 associate members operating worldwide, 6 Bioregions and 25 national biotechnology associations (representing some 1,800 small and medium sized enterprises, SMEs). Its members include the main companies producing GM crops: Bayer CropScience, DuPont/Pioneer, Monsanto and Syngenta.

3.3.3 Evaluation of FP5 and FP6 and development of FP7

Following the European Union's adoption in 2000 of the Lisbon Goal "*to become the most competitive and dynamic knowledge-based economy in the world*", there was increased political interest in transforming the Framework Programmes into drivers for growth.

There are two levels of development of the Framework Programmes. Firstly, there is a consultation process involving researchers and their organisations, in which industry representatives are often also involved. Representatives of civil society organisations, including consumer groups and trade unions are also occasionally involved via advisory groups on particular topics or programmes. Secondly, there is a decision-making process to adopt the Framework Programme, involving the European Commission, the relevant public authorities of the member states, and the elected representatives of the European Parliament. The consultative processes are important, not just for developing the Framework, but also to help set the annual Work Programmes, which determine how the Framework will be implemented. To prepare the Work Programmes, the Commission relies on advice from consultations, including from the European Technology Platforms (see Section 3.3.5) and from specific advice of a series of advisory groups.

The largest consultative group involved in developing the Framework Programmes is the European Research Advisory Board (EURAB), created in June 2001.[520] EURAB is an advisory committee of academics and industry, plus a representative of the European Trade Union Institute's research department. It provides advice on the design and implementation of EU research policy, including, for example, on the establishment of European Technology Platforms.[521] It had 45 members from 2001 to 2004.[522] In 2004, a new Board was appointed.[523]

Groups of experts are also established for short periods to write reports for the Commission. The European Group on Life Sciences (EGLS) met from 2000 to 2004 and published a report in 2004, with a view to shaping priorities for FP7, via EURAB and others.[524,525] The EGLS report concludes that "*The one lesson to emerge after a decade of controversies (GM food, stem cells, reproductive technologies...) is that research, development and innovation can hardly prosper in the face of social opposition to science*".[526] It claims that the 'gene revolution' and agricultural biotechnology "*are powerful and certainly essential tools for generating sustainable agriculture, increased productivity, new markets for plant-derived products, and for making developing countries more independent*" and that "*Despite past controversies, Europe cannot give up the hope raised by their* [GM Plants'] *potential applications in agriculture, environmental bioremediation and plant-based pharmacology*". The report argues that the cost of regulation "*creates an extraordinary burden on the development of GM food*" and inhibits innovation, and that: "*The ongoing paranoia over intellectual property rights often puts in place an unethical barrier to access by developing countries to the benefits of agricultural and health-related biotechnologies*".

Evaluations of the Framework Programme from 1999-2003 covering FP5 and the early years of FP6 highlighted that the aim of encouraging risk-taking and increased participation from industry and new member states had not been as successful as hoped.[527,528] Overall, these evaluations have concluded that low-level project-specific goals, normally relating to knowledge and networking, are generally achieved, together with outputs such as journal articles and patents. However, socio-economic benefits from projects are generally speculative and hard to assess and the Framework Programme is "*flawed as a way to (or plan to) reach specific policy goals*".[529]

As one means to address this, the 2005 expert panel review of the Framework Programme "*supports the idea of establishing a limited number of 'technology platforms', with the objective of establishing European leadership in key emerging technologies, thereby increasing private investment in RTD*" (see Section 3.3.5). It states that; "*These large collaborative programmes should be industry-driven, with public/private partnerships for both funding and execution. They should involve academic institutions, large and small companies and, often, participants from outside Europe. Excellent management of pooled resources, from Framework Programme, national sources and industry will be needed to make an impact*".[530]

The process of developing FP7 began with the European Commission's report 'Communication on Investing in research: an action plan for Europe', which was endorsed by the European Parliament's Committee on Industry, External Trade, Research and Energy in November 2003.[531] In 2004, the Commission issued new Guidelines for future European Union policy to support research, which, as well as emphasising wealth-creation and the Lisbon goals, included a new commitment to "*Placing research at the service of security*".[532] An online consultation on research themes for FP7 was also held in 2004, which received over 1,800 responses.[533] In April 2005, the Commission announced its proposals for Fp7[534], accompanied by a Communication on the European Research Area (ERA), entitled 'Building the ERA of knowledge for growth'.[535] The elected members of the European Parliament were also involved in the decision-making process.

Following Europe's complex co-decision procedure[536], FP7 was finally adopted by the Council of Ministers in December 2006[537] and the first call for proposals was issued.

3.3.4 The Seventh Framework Programme (FP7)

The 7th Framework Programme for Research and Technological Development (FP7) and the first EU Competitiveness and Innovation Programme (CIP) both run from 2007-2013.

FP7 is the EU's main instrument for funding research in Europe, however despite its budget of over 50 billion Euros it still constitutes less than 10% of all research funding in the EU.[538]

The broad objectives of FP7 have been grouped into four programmes: Co-operation**,** Ideas**,** People and Capacities.[539] Most of the budget is in the 'Co-operation' programme, which supports industry-driven public-private partnerships of universities, companies, research centres and public authorities and contains ten priority research themes.[538] The Co-operation work programme's ten research themes are shown in Table 3. The Ideas programme includes the European Research Council (Box O) as its flagship component, whereas the People programme funds training and links between industry and academia. The Capacities programme includes investment in large-scale research infrastructures (often as public private-partnership) and, on a much smaller scale, the 'Science in society' initiative aims to encourage Europe-wide reflection and debate on science and technology and their relation with society and culture.[540] There is also a separate FP7 for nuclear research activities (under the Euratom Treaty) which runs from 2007 to 2011.

Table 3: Indicative budget breakdown among the non-nuclear FP7 programmes (in EUR million)[541]

Programme	Theme	Budget
Co-operation	Health	6 100
	Food, agriculture and fisheries, and biotechnology	1 935
	Information and communication technologies	9 050
	Nano-sciences, nano-technologies, materials and new production Technologies	3 475
	Energy	2 350
	Environment (including climate change)	1 890
	Transport (including aeronautics)	4 160
	Socio-economic sciences and the humanities	623
	Space	1 430
	Security	1 400
	SUB-TOTAL	**32 413**
Ideas		**7 510**
People		**4 750**
Capacities	Research infrastructures	1 715
	Research for the benefit of SMEs	1 336
	Regions of knowledge	126
	Research potential	340
	Science in society	330
	Coherent development of research policies	70
	Activities of international cooperation	180
	SUB-TOTAL	**4 097**
Non-nuclear actions of the Joint Research Centre (see Box M)		**1 751**
TOTAL		**50 521**

Box M: Europe's Joint Research Centre

Europe's Joint Research Centre (JRC) undertakes activities to support the European Commission's Seventh Framework Programme (FP7) and the Seventh Framework Programme of the European Atomic Energy Community (EURATOM). It was originally set up as the Joint Nuclear Research Centre (from 1957 to 1969), to support the expansion of nuclear power in Europe, under the Euratom Treaty.[542] It now has seven institutes (Environment and Sustainability; Health and Consumer Protection; Prospective Technological Studies; Energy; Reference Materials and Measurements; Transuranium Elements; Protection and Security of the Citizen).

The Institute for Health and Consumer Protection (IHCP) works in support of European legislation associated with: chemicals (REACH) and biocides; genetically-modified organisms (GMOs); cosmetics and animal welfare; consumer products; food and food-contact materials.

In addition, the JRC runs six reference laboratories, including the Central Reference Laboratory for GMOs in food and feed.[543]

Within FP7, the programmes identified as of interest to biotechnology small and medium-sized enterprises (SMEs) include the 'Research for benefit of SMEs' initiative under the 'Capacities' programme. Other aspects of interest to SMEs include the health theme and food, agriculture and biotech theme in the 'Co-operation' program; the 'Technology Platforms' and 'Joint Technology Initiatives' (also in the 'Co-operation' program); and the Marie Curie initiative within the 'People' program (which supports partnerships between academia and SMEs).[544]

According to the Commission, within the FP7 Co-operation Programme, €8 billion are specifically dedicated to Life Sciences and Biotechnologies.[509] Some €6 billion will support health research with another €2 billion supporting research on food, agriculture and fisheries, and biotechnology. SMEs are expected to account for 15% of these budgets, meaning funding of 1.2 billion euros. However, these budgets are not always reached. Life Sciences and biotech companies also expected to "*stand to gain considerably*" from the Risk Sharing Finance Facility, which will use money from the research programme to access credit from the European Investment Bank (EIB) to support the development of major new research infrastructures.

The EU's Competitiveness and Innovation Programme is completely separate – run by DG Enterprise rather than DG Research – but is also aimed at implementing the Lisbon Strategy. It runs from 2006 to 2013 and has a budget of approximately Euros 3.6 billion.[545] Of particular interest to biotechnology SMEs are the financial instruments in its Entrepreneurship and Innovation Programme (EIP).[544]

The EU also has a EUROTRANS-BIO initiative[546] which aims to "*foster the competitiveness of European's biotechnology industry*" and the Eureka network, which "*aims to enhance European competitiveness through its support to businesses, research centres and universities who carry out pan-European projects to develop innovative products, processes and services*".[547] It has also been developing the concept of the European Research Area (ERA) (see Box N) and a new European Research Council has been launched (Box K).

Box N: The European Research Area (ERA)[548]

The objective of the European Research Area initiative combines three related and complementary concepts:

- the creation of an "internal market" in research, an area of free movement of knowledge, researchers and technology, with the aim of increasing co-operation, stimulating competition and achieving a better allocation of resources;
- a restructuring of the European research fabric, in particular by improved coordination of national research activities and policies, which account for most of the research carried out and financed in Europe;
- the development of a European research policy which not only addresses the funding of research activities, but also takes account of all relevant aspects of other EU and national policies.

Box O: The European Research Council (ERC)[549]

The ERC was launched in February 2007 with a seven year 7.5 billion Euro budget. It is a flagship component of the 'Ideas Programme' of FP7. It is intended to be 'investigator-driven', or 'bottom-up', in nature, allowing researchers to identify new opportunities and directions in any field of research, rather than being led by priorities set by politicians. Scientific excellence, determined by peer review, is intended to be the sole selection criterion. This approach is intended to ensure that funds are channeled into new and promising areas of research with a greater degree of flexibility.

3.3.5 European Technology Platforms, Joint Technology Initiatives and Research Infrastructures

European Technology Platforms (ETPs) involve the development of an industry-led "Vision" document, focused on how research and technological development can improve growth and competitiveness in the relevant sector.[550] A process of consultation amongst industry stakeholders

then leads to a “Strategic Research Agenda” (SRA). Implementation is led by industry, but each strategy involves obtaining complementary public finance at national and European levels. The SRAs are used to influence the Framework Programme and the national research programmes of the member states.

The aim of the ETPs is to orientate FP7 to better meet the needs of industry. The ETPs “*Provide a framework for stakeholders, led by industry, to define research and development priorities, timeframes and action plans on a number of strategically important issues where achieving Europe's future growth, competitiveness and sustainability objectives is dependent upon major research and technological advances in the medium to long term*”.[551] The Commission states that ETPs are “*proving to be powerful actors in the development of European research policy, in particular in orienting the Seventh Research Framework Programme to better meet the needs of industry*”.

Objectives of the ETPs include[552]:

- Tailoring FP7 to better meet industry's needs
- Mobilising and aligning public funds at European, national and regional level
- Mobilising funds of industrial stakeholders
- Mobilising other funds, such as debt and equity financing, or other schemes (such as public-private partnerships) for implementing research and development activities
- Addressing regulatory and other barriers to the optimal development, deployment and use of the relevant technologies

Technology Platforms for road, rail and aeronautics were established in 2001/02, but a major expansion of the programme began in 2004.[553] There are now more than 30 ETPs at various stages of development.[554] The ETPs most relevant to biosciences are the “Plants for the Future”[555], “Food for Life”[556], “Biofuels”[557], “Farm, Animal Breeding and Reproduction” (FABRE), “Global Animal Health”[558], “Forest-based Sector”[559], “European Aquaculture”[560], “Nanomedicine[561]” and “Innovative Medicines for Europe”[562] technology platforms. Biotechnology also plays a role in the “Future of textiles and clothing”[563] and “SusChem”[564] (Sustainable Chemistry) technology platforms.

Although the ETPs are industry-led, they are meant to involve other stakeholders. However, a 2008 evaluation report found that NGOs (non-governmental organisations) and end-users (consumers) have a small presence, whilst industry and knowledge-generating (academic) institutions are well represented.[552]

The bioscience-based ETPs developed to promote the Knowledge-Based Bio-Economy (KBBE) are seen by the biotechnology industry as the key to reviving the fortunes of GM crops and food in Europe and to developing new patentable products to achieve food industry growth (see Boxes P,Q and R). For example, the 'Food for Life' Strategic Research Agenda (Box Q) states that “*good links have been established with other ETPs, especially those addressing agriculture and biotechnology. These links will ensure that the knowledge-based bio-economies of the EU Framework Programme can combine to address effectively the serious challenge of global competition that Europe currently faces*”.

Knowledge and the bio-economy are narrowly defined to be restricted to patentable technologies, rather than broader knowledge about crop rotation systems. For example, Europe's DG Research refused to fund a Technology Platform on organic agriculture, even though the market for organic foods in the EU is much larger than for GM crops.[565]

Box P: 'The Plants for the Future' ETP

In March 2003, the EU Council recommended the setting up of an ETP on Plant Genomics.[566] The EC asked European Plant Science Organisation (EPSO)[567] and EuropaBio (Box L) to develop the initiative. A 'Brainstorm meeting' was then held with a group of representatives from companies including EuropaBio, Syngenta, Bayer, BASF and Nestlé, who drafted the vision together with scientists from EPSO, INRA (France), Ceres (US), the John Innes Centre (UK), the Max Planck Institute (Germany) and VIB (Belgium).[568] EPSO and EuropaBio then submitted an application for a Specific Support Action (SSA) to FP6 to develop the proposal.[569]

The Vision paper[570] for 'Plants for the Future' was published in June 2004, accompanied by press releases from EPSO[571], EuropaBio[572] and the EC[573]. The report claims that increased investment in plant genomics and biotechnology would lead to "*major advances in our lifestyle and prosperity*", including better quality, healthy food; environmental sustainability and enhanced competitiveness and that *"The deterioration of the EU's scientific base, the loss of markets for European agricultural products and an increased dependence on food and feed imports are at stake*" as a result of Europe's failure to grow GM crops. The Vision estimates that public and private funding for the strategy at EU, national and regional level "*will have to exceed 45 billion EUR over the next ten years if Europe is to remain competitive*".

The Plants for the Future 'Stakeholder proposal for a Strategic Research Agenda'[574,575] was launched in July 2005, followed by a Draft Action Plan 2006-2010.[576,577] The ETP's Mid-Term report to the European Commission states that it has established a Steering Council and a European Parliament "Mirror Group", consisting of a Chair plus 7-10 MEPs; and plans to establish a two further "Mirror Groups" for the Commission and for Member States.[578,579] The report also claims that the recommended research priorities are already being taken into consideration by academic and private research institutions, as well as by Commission and Member States, in preparing the plant genomics and biotechnology component of FP7.

The final Strategic Research Agenda (SRA)[580,581] for 'Plants for the Future' was launched in the European Parliament in June 2007.[582] A joint press release by EPSO, EuropaBio, the European Seed Association (ESA), the Committee of Agricultural Associations (COPA) and the General Confederation of Agricultural Cooperatives (COGECA) claimed that: "*For example, improved crops could be developed and grown to combat health problems, such as cardiovascular disease, obesity or diabetes. New or improved feed could also be used for farm animals to reduce Europe's dependency on foreign imports of animal feed, such as soybeans. Furthermore, plant science is a key technology for addressing the challenges of climate change by replacing fossil fuels with renewable sources of biomass for energy, including biofuels*".

Box Q: The 'Food for Life' ETP

The Vision paper of the ETP 'Food for Life' was launched in July 2005.[583] 'Food for Life' was created by the Confederation of the Food and Drink Industries of the EU (CIAA - Confederation des Industries agro-alimentaires de l'UE), chaired by Dr Jan Maat from Unilever. Its Board, Operational Committee and Working Groups include representatives from Nestlé, Kraft, Unilever, Bayer Crop Science, Cargill, Danone, Danisco and the Dutch food ingredients company, DSM. The Vision claims that it will deliver "*innovative, novel and improved food products*" and that these products will have a positive impact on quality of life 'adding life to years' and significantly reducing healthcare costs.

The 'Food for Life' Strategic Research Agenda (SRA) to 2020[584] and a draft implementation plan[585] were published in September 2007. The SRA argues that the European food and drink industry's competitiveness is at risk and rapid innovation will be needed to reverse the decline, by producing new 'value-added' products. It claims that implementation will ensure "*tailor-made, personal nutrition (nutraceuticals, functional food, food ingredients and supplements) that will provide better, healthier food that will form part of a diet with improved health attributes*". It also states that: "*All goals have the potential to increase competitiveness of European SMEs as well as larger companies. The building up of basic knowledge in the areas of priority would generate patentable innovations, some of which would be suitably exploited by research-type SMEs.*

Box R: The 'Biofuels' ETP

In 2001, the EC published a Communication on an Action Plan and two Proposals for Directives to foster the use of Alternative Fuels for Transport.[586] In May 2003, the EU adopted Directive 2003/30/EC, which sets a target of increasing the use of biofuels in energy consumption to 5.75% by 2010.[587] The following year, a stakeholders' meeting was held about establishing a new Biofuels Technology Platform.[588] The Biofuels Research Advisory Council (BIOFRAC) includes a representative from EuropaBio, as well as numerous other industries (including car, oil and agricultural commodity companies), and held its first meeting in June 2005.[588] BIOFRAC developed its Draft Vision Report for the Biofuels Technology Platform in 2006[588] and launched the final version in June.[589] The Vision estimates that between 4 and 18% of the total agricultural land in the EU would be needed to produce the amount of biofuels to reach the level of liquid fossil fuel replacement required for the transport sector in the Directive 2003/30/EC.[590] It notes that different sectors – food, feed, fibre, chemicals and energy – compete for biomass from agriculture and forestry, and that biomass production for energy therefore has to be as efficient as possible per unit area in order to minimise the competition for land. The Vision includes the development of 'second generation' biofuels and claims that genetics can be used to improve the quality characteristics of the crop, e.g. decrease lignin content, so that whole crop use becomes efficient. The Biofuels Technology Platform published its Strategic Research Agenda (SRA) in January 2008.[591]

Technology Platforms have been influential in affecting Europe's innovation policy more broadly, particularly via its commitment to 'lead markets' (Box S).[592] The EC states that they "…*will provide a means to foster effective public-private partnerships…and this will deliver the impetus to mobilise the research and innovation effort and facilitate the emergence of 'lead markets' in Europe*", and that the Platforms should "…*address both the technical and non-technical barriers to and requirements for the optimal development, deployment and use of technologies…*".[593]

Box S: The lead market initiative for Europe[594]

On 21st December 2007, the European Commission published its Communication 'A lead market initiative for Europe'. Six markets were identified for the initial stage of the initiative; eHealth, protective textiles, sustainable construction, recycling, bio-based products and markets for renewable energies. The process of identifying these markets involved developing criteria and holding stakeholder workshops and expert groups with the European Technology Platforms (ETPs) and Europe INNOVA (a network set up to drive European innovation[595]).[596] The Thematic Action Plan for the lead market initiative in the area of bio-based products envisages that future revisions of the Common Agricultural Policy (CAP) could provide opportunities to examine the various elements of non-food policy in order to give positive incentives to the cultivation of crops for industrial uses.[597] It plans to set up a high-level advisory group, including Member States and industry, in 2008.

Joint Technology Initiatives are a major new element of the EU's 7th Research Framework Programme.[598] They provide a way of creating new partnerships between publicly and privately-funded organisations involved in research, "*focusing on areas where research and technological development can contribute to European competitiveness and quality of life*". The Commission sees this approach as signaling "*a real change in how Europe promotes industry-driven research, designed to establish European leadership in certain technologies that are strategic to Europe's future*".

The first two JTIs were proposed in May 2007[599], and are in the fields of embedded computer systems (ARTEMIS: Advanced Research and Technology for Embedded Intelligence and Systems) and Innovative Medicines (IMI). The Innovative Medicines Initiative (IMI)[600] is a proposed a public-private partnership (PPP) involving the EC and the pharmaceutical industry, represented by the European Federation of Pharmaceutical Industries and Associations (EFPIA). Currently, other candidate JTIs are: Clean Skies ('greening' of the aviation industry), Nano-electronics, Hydrogen & Fuel Cells, and Global Monitoring for Environment and Security (GMES[601]).

In 2002, the EU also set up ESFRI, the European Strategy Forum for Research Infrastructures, which has developed a European roadmap for the construction of the next generation of large-scale Research Infrastructures[602], including EATRIS (The European Advanced Translational Research Infrastructure in Medicine[603]) and 'European Biobanking and Biomolecular Resources'[604] (see Appendix A). As Technology Platforms develop, ESFRI expects future editions of the roadmap to further reflect the Research Infrastructures needs of industry, provided there is some open access to all researchers.

3.4 Summary of research funders and funding processes

In Britain, the Biotechnology and Biological Sciences Research Council (BBSRC) was established in 1994 to help drive the expected new bio-economy. Expertise from a narrow range of industries seen as key to the KBBE has been integrated into its decision-making processes. Following the public concern surrounding GM crops and foods, the BBSRC has become more open to consulting on some of its priorities and strategies. However, it is still focused on narrow biotechnological solutions to issues such as food security, energy and health, with a new emphasis on industrial biotechnology and industrial-scale biofuels (agrofuels). It has focused on developing a narrow range of skills in lab-based molecular biology, whilst other areas have been neglected (see Section 2.5.3). Funding for on-farm research in agro-ecology has recently been cut further due to an increased role for the industry-led Technology Strategy Board, which is seeking partnerships with multinational companies rather than small farming businesses.

A significant re-structuring of health research funding has taken place in the UK as part of a push to ensure 'translation' of findings in the biosciences into benefits for patients. Like research funding bodies across the globe, the Medical Research Council (MRC) is under increasing pressure to 'translate' basic molecular research into clinically important interventions. Significant spending on bioscience research has increased understanding but not delivered the expected major breakthroughs in new therapies, and total income from technology transfer has been low. The MRC's portfolio is more diverse and less industry-led than the BBSRC's. However, although public health research is funded, it is given a lower priority than molecular biology, genetics and genomics.

Industry representatives appointed to research funding boards are likely to influence research strategies and choose research priorities from their own perspective. This is taken to a new level by the European Technology Platforms, where research strategies in food, health and agriculture are being determined by the 'vision' of the relevant commercial sectors. In this context, the research funding system allows significant public investment in particular research trajectories to be made with very limited public or democratic oversight. This tends to skew research priorities towards the perceived needs of certain sectors, whilst alternative priorities are ignored. Thus, food manufacturers' drive for growth leads to investment in researching and developing new 'functional foods', rather than in more fundamental reforms to food and agriculture policy, that could be a cheaper and more effective means to tackle diet-related disease. Agricultural biotechnology is favoured for similar reasons, particularly because genetically-modified (GM) crops can be patented (see Section 2.2.4). Better health is seen primarily as an outcome of molecular biology and the translation of genetic and genomic information into new diagnostics, therapies and treatments.

Increasingly, early-stage public R&D investment is seen as critical to remaining competitive in a globalised economy. Patients and the public are more widely consulted than they used to be about some aspects of medical research. However, decisions about research investments are largely made behind closed doors, with little public input. The next chapter considers the role of experts and advisors in influencing these decisions.

4. People and Power – Who Influences Research Priorities?

The development of science and technology policy can easily become strongly influenced by a small circle of 'expert' advisors. Often, ministers know little about the issues for example, former UK Prime Minister Tony Blair, a strong advocate of expanding computer databases, reportedly did not know how to use a computer. Because scientific training is highly specialised, expert advisors themselves may know little about science and technology outside their own area of expertise. And, because science is about exploring the unknown, uncertainty and ignorance about the future is likely to be high. The system policy makers adopt for gathering advice and influencing policy decisions can therefore have a major impact on what research is prioritised, and whether potential problems are anticipated and assessed.

4.1 Who influences research strategy in the biosciences in Britain?

"*You could have your first publication, maybe only one, maybe two, in a scientific journal somewhere, and you may even be a chief scientific officer, or even a chief executive of your little start-up company, which you just started and raised a few bob from someone like me and you may have discovered something useful and be a millionaire – all in ten years from now! Because I was only ten years older than you when I started my first company. You won't be a Prime Minister because I think that Tony Blair will probably still be the Prime Minister, ten years from now and ten years after that!*" Professor Sir Christopher Evans, biotech entrepreneur and Labour Party donor, April 2002.[605]

There is an official system for overseeing science policy in Britain, and an informal network of Government advisors. A few key individuals from the Venture Capital, biotechnology, pharmaceutical and nuclear industries often act as members of task forces and ad-hoc advisory committees, or play central roles in a small number of influential lobby groups.

Lord Sainsbury was science minister from 1998 to 2006 (Box T). **Lord Drayson** (one of the New Labour "biotech barons", see Appendix A, Box A) became Minister for Science and Innovation in October 2008.[606]

Box T: Lord Sainsbury

Lord Sainsbury resigned as science minister on 10th November 2006. He was first appointed Parliamentary Under-Secretary of State for Science and Innovation in July 1998, with responsibility for the Office of Science and Technology and the Research Councils.[607] He previously had been Chairman of J Sainsbury plc, and still retains a 6.3% per cent shareholding in the family supermarket chain.[608] David Sainsbury became Lord Sainsbury of Turville in October 1997. He was a member of the Commission on Public Policy and British Business run by the New Labour think tank IPPR from 1995 to 1997, influencing the development of policy. Sainsbury has been a major donor to New Labour – reportedly giving the party a total of £16 million – and was one of a number of donors investigated by the police during the "cash for honours" inquiry.[609] In July 2007, the Crown Prosecution Service confirmed that it had insufficient evidence to charge anyone in the case.[610] Lord Sainsbury has long been an enthusiast for biotechnology and invested in numerous biotechnology businesses before entering Parliament. His investments were subsequently managed in a 'blind trust' amid accusations of conflict-of-interest.[611] A newspaper report in 2006 revealed that the Sainsbury Laboratory, which researches GM crops, had received a 400% increase in government funding since Labour came to power in 1997, with grants of £8.7m, and that a further £4.2m over 5 years had been given to Plant Bioscience, a company set up by Sainsbury's charitable foundation, which markets spin-offs from the laboratory.[612]

The Ministerial Committee on Economic development has a sub-committee on science and innovation (known as EDSI), which is chaired by the Minister of State for Science and Innovation and includes ministers from all other departments. Its terms of reference are to consider issues relating to science and innovation; and report as necessary to the Committee on Economic Development.[613]

The Government Office for Science, headed by the Government Chief Scientific Adviser (GCSA), is located within the Department for Business, Innovation and Skills (BIS), headed by **Lord Mandelson**. The GCSA is responsible to the Prime Minister and Cabinet for the quality of scientific advice to them on scientific and science policy issues.
The GCSA also:

- oversees the Government's Foresight programme and Horizon Scanning Centre;
- chairs the Global Science and Innovation Forum which co-ordinates the UK's international science and innovation strategy and delivery;
- co-chairs the Prime Minister's Council for Science and Technology;
- heads the Science and Engineering profession in Government.

Professor **John Beddington**, Professor of Applied Population Biology at Imperial College London, became Chief Scientific Advisor and Head of the Government Office for Science with effect from 1 January 2008.[614] He is Chair of DEFRA's Science Advisory Council and has served on the Council of the Natural Environment Research Council, as well as holding several other appointments relating to fisheries and conservation. Beddington was made a Fellow of the Royal Society in 2001 and was awarded the CMG in 2004 for services to fisheries science and management. His predecessor, **Sir David King** (Chief Scientific Advisor from October 2000 to December 2007) was previously Master of Downing College, Cambridge and Head of the University Chemistry Department.[615] On his departure, King trumpeted the benefits of nuclear power, culling badgers and growing GM crops – erroneously claiming that an African project had used GM crops to tackle pests[616,617] – and (incorrectly) stated that he had converted ministers to supporting new nuclear power stations.[618] King succeeded Sir Robert May, who became President of the Royal Society (the current President, whose five-year term began on 1 December 2005, is Lord Rees of Ludlow).

The Chief Scientific Adviser's Committee (CSAC) is the principal committee at official level dealing with issues relating to science, engineering and technology (SET). Its membership consists of the Government Chief Scientific Adviser, Professor John Beddington, acting as the Chair, and the Chief Scientific Advisers or their equivalent from all government departments and devolved administrations. There are 18 Chief Scientific Advisors in total, including three from Government agencies (the Food Standards Agency, the Forestry Commission, and the Health and Safety Executive).[619]

The Director General of Science and Innovation at the Department of Universities, Innovation and Skills (DIUS) – which later became part of BIS – was the statistician **Professor Adrian Smith**, who worked for the UK Government Department of the Environment from 1991-1998 as a Statistical Advisor to the Nuclear Waste Inspectorate and for the Ministry of Defence from 1982 to 1987 as adviser on Operational Analysis.[620]

His predecessor Professor **Sir Keith O'Nions** became Director General of the Research Councils on 1 January 2004 and was appointed Director General of Science in April 2006. In July 2008, he left to take up an appointment as head of a new Institute for Security Science and Technology at Imperial College London.[621] He was previously Chief Scientific Adviser at the Ministry of Defence (MOD) from January 2000 to July 2004 and in charge of the 'Missile Defence Centre', set up to support Bush's missile defence plans (also known as 'Son of Star Wars').[622] He was a member of the Council of Science and Technology (CST) from 1998-2000 and received a Knighthood for services to Earth Sciences in the 1999 Queen's Birthday Honours. He is a geologist who has supported plans to bury highly radioactive nuclear waste deep underground in Cumbria (see Box U).

Box U: Professor Sir Keith O'Nions and radioactive waste

Sir Keith O'Nions (Director General of Science and Innovation from 2004-2008) was head of Earth Sciences at Oxford University from 1995. In 1995, O'Nions was the only geologist not directly employed by the nuclear waste disposal company Nirex to give evidence in favour of its plans for a Rock Characterisation Facility – the first phase of an underground nuclear waste dump – near Sellafield.[623] Following extensive evidence that nuclear waste buried at the site would leak and contaminate the environment[624], the planning inspector ruled that the site was unsuitable[625] and the plans were rejected by the then Conservative Environment Minister John Gummer shortly before the 1997 election that brought New Labour to power.[626] Despite this decision, the Government now plans to return to the site to bury high-level nuclear waste.[627,628,629] Ministers are following a plan developed by the House of Lords Science and Technology Committee following the inquiry, which aimed to overcome local objections to returning to the site.[630] Planning procedures for major infrastructure projects have been changed so that they can be decided by central Government; compensation is to be paid to the local community for blight; and a committee was set up to reach a public 'consensus' on deep disposal of nuclear waste without revisiting the scientific evidence about the dangers: all recommendations made by the Committee in 1999.[631] During O'Nions' tenure as DG of Science and Innovation, new geological criteria were chosen so as not to exclude the Sellafield site.[632,633,634] The government proposes to invite communities to volunteer to host the underground repository in return for benefits including extra government funding for local facilities: however the local borough of Copeland near Sellafield is the only site in the country that is likely to be persuaded to agree.[635,636] Thus the original planning decision, and the examination of the scientific evidence on which it was based, has effectively been overturned and removed from public scrutiny.

DEFRA's Chief Scientific Advisor is currently **Professor Bob Watson**, appointed in September 2007, who was previously at the World Bank where he was the Chief Scientist and Senior Advisor for Sustainable Development. He took over from Sir Howard Dalton, who also chaired the Environment Research Funders' Forum from 2004-2007.[637]

Professor Dame Sally Davies (see Appendix A), is Director General of Research and Development and Chief Scientific Advisor at the Department of Health. She developed the new government research strategy, Best Research for Best Health, and is responsible for implementation of the National Institute for Health Research (NIHR). She is a Board member of the Office of the Co-ordination of Health Research (OSCHR), and chairs the UK Clinical Research Collaboration (UKCRC). She was a member of the steering group for the Biotechnology Innovation and Growth Team, chaired by Sir David Cooksey and the Health Care Industry Task Force, and is a member of the UK Health Innovation Council.

The **Council for Science and Technology** is the Government's top-level advisory body on science and technology issues, with members appointed by the Prime Minister. It is chaired by the Government's Chief Scientific Advisor. **Professor Janet Finch**, a sociologist, was appointed as co-chair in March 2007.[638] Other current members are:
Professor Geoffrey Boulton, Vice Principal and Regius Professor of Geology and Mineralogy at the University of Edinburgh, who chaired the Royal Society's working group on radioactive waste in 2002 and also led its 2006 report[639,640];
Professor Peter Davies, Chief Economist at oil company BP;
Professor Alan Gilbert, an Australian historian, who came to Manchester University (where UK Biobank is based: see Appendix A) in February 2004 as President & Vice-Chancellor-elect, after leading a financially disastrous attempt to create a private university spin-off at the University of Melbourne[641];
Professor Wendy Hall CBE, a computer scientist who advocates extensive data-sharing (see Appendix A);
Dr Hermann Hauser, co-founder of Amadeus Capital Partners Limited and various computing firms;
Professor Alan Hughes, Director of the Centre for Business Research (CBR) and Margaret Thatcher Professor of Enterprise Studies at the Judge Business School;

Dr Sue Ion, Group Director of Technology and Chief Technology Officer of British Nuclear Fuels PLC (BNFL) from 1992 until 2006 (where she was responsible for the commissioning of the failed Sellafield MOX Plant[642]), President of the British Nuclear Energy Society (BNES) between 2004 and 2006[643] and an advocate of new nuclear reactors;
Sir Paul Nurse, the Nobel prizewinning cancer biologist (see Appendix A);
Dr Raj Rajagopal, who was Chief Executive of BOC Edwards and an Executive Director of the BOC Group plc until November 2006[644];
Dr Philip Ruffles who was Director of Engineering and Technology and a Main Board member of Rolls-Royce plc from 1997 to 2001 and is presently a Non Executive Director of Diamond Light Source Ltd (see Appendix A);
Professor Michael Sterling, an engineer and Vice-Chancellor of the University of Birmingham;
Professor Kathy Sykes, Professor of Sciences and Society at Bristol University;
Dr Mark Walport, Director of the Wellcome Trust (see Appendix A).

Previous members of the CST include **Sir Richard Sykes** and **Professor Sir Chris Evans** (see Appendix A) and Professor Sir Keith O'Nions (see Box U).[645]

In September 1998 the CST agreed to establish a subgroup to prepare a report about the Government's Science and Technology spending plans, under the leadership of Sir Robin Nicholson with Sir Richard Sykes, Dame Bridget Ogilvie, Dr Chris Evans and Professor Keith O'Nions.[646] The sub-group's report was published in July 1999.[647] Another sub-group, led by Professor Julia Higgins, was set up to consider education and a third sub-group, led by Professor Sir Alec Broers, concentrated on issues concerning the growth of technology based businesses in the UK .

Several past and present members of the CST have been closely linked with the promotion of the UK Biobank research study and the idea of genetic 'prediction and prevention' of diseases using DNA linked to electronic medical records (see Appendix A). Many others have been influential in promoting investment in new nuclear power stations and other nuclear developments.

The House of Lords Science and Technology Committee supported the idea of a centralised system of electronic medical records linked to DNA (first proposed by **Sir George Poste**, see Appendix A), and have also been influential in nuclear waste policy (Box U). The Committee launched an inquiry into the Setting of Science and Technology Research Funding Priorities in July 2009. Committee members include Lord Cunningham of Felling (former pro-nuclear MP for Sellafield, and a former Secretary of State); Lord Warner (the former Department of Health minister who advocated screening every baby's DNA at birth, see Appendix A) and Lord Krebs (the former head of the Food Standards Agency, who is strongly pro-GM).

The Technology Strategy Board (TSB) is made up largely of business people and venture capitalists, from the IT, aeronautics and biotechnology industries.[648]

The Office for the Strategic Coordination of Health Research (OSCHR) is chaired by **Professor Sir John Bell** (see Appendix A) and was set up on the recommendation of **Professor Sir David Cooksey** (see Appendix A).

Informal networks of influence are harder to document, but include organisations such as the influential Foundation for Science and Technology,[649] the Royal Society[650] and the Science Council.[651] The latter is led by **Sir Tom McKillop** who was formerly chief executive of AstraZeneca PLC, president of the European Federation of Pharmaceutical Industries and Associations, and chairman of the British Pharma Group.[652,653] McKillop was forced to resign as Chair of Royal Bank of Scotland (RBS) when the bank had to be bailed out by taxpayers following the credit crunch in 2008.[654] In January 2009, Prime Minister Gordon Brown accused RBS of taking irresponsible risks under McKillop's chairmanship, when it warned it could report an annual loss of up to £28 billion.[655] McKillop also led the Treasury's UK Science Forum, set up in 2004 to monitor implementation of the Government's 10-year framework for science and innovation.[656,657]

Whilst these advisors have worked closely with Government in formulating its science and biotechnology policies, they remain impatient that the Government has not done even more to

subsidise the sector. For example, Sir Richard Sykes (see Appendix A), former Rector of Imperial College, told the Government to: "*Just get on with it*" at the 2007 launch of Lord Sainsbury's review of science.[658] In May 2009, the venture capitalist Sir David Cooksey described Government support for biotech as "*disappointing*" and called on the Treasury to discriminate in favour of the industry and to set aside specific pools of money for biotech firms.[659]

4.2 Case study: UK Biobank and electronic medical records

> "…*we can now see a future where the doctor will swab a few cells from inside your cheek, put them into a DNA-sequencing machine and a computer will spit out a complete reading of your unique genetic makeup all 30,000 or so genes that make you who you are. From that, doctors could pinpoint flawed genes and gene products and predict what diseases you are likely to develop years in advance of any symptoms and how to help you avoid them*"… "*We have a unique resource in this regard in the national health service. There are crucial issues of privacy of genetic information that we need to deal with. But our national, public system will enable us to gather the comprehensive data necessary to predict the likelihood of various diseases – and then make choices to help prevent them*". Prime Minister Tony Blair, 2002.[7]

A striking aspect of the many reviews and advisory bodies conducted to review UK policy in the biosciences (Box B) is the small number of people and institutions who re-appear repeatedly on multiple committees and task forces. This is particularly true of Britain's health research strategy.

In order to document more closely how these informal networks influence research priorities, Appendix A (published online in January 2009 at: http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/UK_Biobank_fin_1.pdf) documents in detail the decision to fund the UK Biobank genetic research project and to centralise NHS electronic medical records.

The Appendix reveals how the idea of a 'genomic revolution' in healthcare, was promoted by a small circle of government advisors, including Sir George Poste (formerly of SmithKline Beecham, and subsequently Chair of Orchid Cellmark and President Bush's bioterrorism advisor); Sir Richard Sykes (until recently, Rector of Imperial College, and former Chairman of GlaxoSmithKline); Sir David Cooksey (founder of Advent Venture Partners and author of the Cooksey review of UK health research funding); Professor Sir Mark Walport (Director of the Wellcome Trust); and Professor Sir John Bell of Oxford University (President of the Academy of Medical Sciences, Chair of UK Biobank's Scientific Committee and now Chair of the Office of Strategic Co-ordination of Health Research, OSCHR). The aim is to link electronic medical records to DNA samples and genomic data and to win the race to commercialise the human genome by implementing a public-private partnership for the genetic 'prediction and prevention' of disease. The proposal to create a national genetic database, linking DNA and electronic medical records, was first made by Sir George Poste and later endorsed by the House of Lords Science and Technology Committee.[660] The UK Biobank research project was developed as a pilot study for this universal genetic database.

As a result, the Government has invested billions of pounds of NHS money in the idea of 'early health', which includes using people's genetic make-up (their genomes) and information stored in their medical records to try to predict which diseases they will get and treat them while they are still healthy.

Consistent with the Government's commitment to the knowledge-based bio-economy, industry documents submitted to the Ministerial Medical Technologies Strategy Group (until recently, co-chaired by the US company GE Healthcare):

1. Promote the idea that 'early health', involving human genome screening and health surveillance, is the future of medicine and will improve public health and save the NHS money;

2. Oppose any pre-market regulatory assessment of genetic tests, and other medical tests, on the grounds that this would stifle innovation;
3. Argue that public procurement by the NHS should be used to stimulate innovation, along the lines proposed in the 2006 Cooksey Review of health research funding and Lord Darzi's 2008 review of the NHS.

However, many doctors and scientists are sceptical that 'early health' will be good for health. The 2009 House of Lords Science and Technology Committee's report 'Genomic Medicine' continues to promote this approach to health, but nevertheless reports a seminar that concluded (page 108): "*On the question of the desirability of "genomicising" medicine, it was assumed that most of the medical profession would not like to move towards genomics in healthcare, and the pressure for this change may need to come from the science*". Further (page 113): "*The view was expressed that the use of currently known genetic variants as part of genetic testing to predict development of common diseases did not add substantially to risk prediction by using conventional risk factors*". There are also major privacy concerns associated with this approach to health.

Despite the enormous investment made in creating a centralised system of electronic medical records in order to implement this plan, there is no evidence that this approach will be good for health, or cost-effective. Consistent with the 'vision-led' approach to research investments described in Section 1, the claims made by commercial companies and a narrow circle of advisors were never assessed by Government before it invested substantial amounts of taxpayers' money in this approach to health. To date, no genetic variants – either singly, or in combination - meet medical screening criteria for the general population, and there is increasing scientific scepticism that any will ever do so (see Section 5).

Appendix A describes how, in January 2009, data-sharing proposals, hidden in Clause 152 of the Coroners and Justice Bill, would have allowed DNA stored in the NHS including the blood spots taken from every baby at birth – to be analysed without consent and genetic data to be linked to electronic medical records and shared with any company or government agency: including foreign governments and the police.[661] Following massive public opposition, the Secretary of State for Justice, Jack Straw, was forced to drop the plans.

However, plans to access NHS data without consent are being re-considered, not abandoned, and data-sharing is still likely to take place via the 'secondary-uses service' for electronic medical records. In 2009, the Wellcome Trust Sanger Centre **"***encouraged the NHS Care Records Service to prepare for the integration of significant amounts of genetic and genomic information into patient records*" and argued that: *"If robust systems are in place…….the benefits of research will outweigh the risks associated with the use of identifiable information"* (including information that patients have requested to be kept confidential in 'sealed' and 'locked' envelopes).[163]

4.3 Summary of who influences research priorities

A small number of advisors, often with close links to a narrow range of commercial interests, are highly influential in setting the research agenda for the biosciences. These people and institutions re-appear repeatedly on multiple committees and task forces.

These individuals are largely unaccountable and have been allowed to produce advice that is rarely open to proper public or democratic scrutiny. Key UK Government decisions have been taken behind closed doors, often with the only parliamentary endorsement coming from the un-elected House of Lords Science and Technology Committee.

5. The Right Research Priorities?

This section considers whether a commitment to the biosciences and biotechnologies as a key part of the 'knowledge-based bio-economy' has achieved its aim of generating wealth and improving quality of life. It also considers public attitudes to this type of research and to the idea of the knowledge-based economy.

The benefits and harms of genetic technologies – particularly of controversial ones, such as genetically-modified (GM) crops – are highly contested. Although some aspects of the dispute are about the performance of the technology itself, Glover argues that the fundamental disagreement is over whether the starting point should be the technical performance of the technology or the social problems it is supposed to solve.[662] This sustains ongoing disagreements about the relevance and value of GM crops for small-scale farmers in the developing world, without bringing the dispute closer to a resolution.

Future scenarios for the development of genomics depend on a number of key drivers, including: functionality of genomics (how well do the applications work); regulation; business forces; genomics itself (the science and institutions); politics and geopolitics; demand; social attitudes; social mobilization (for or against developments); governance of knowledge (including intellectual property rights); events; risk; and the environment.[663,664]

The investments made in the biosciences and biotechnology as part of the push to a new 'knowledge-based bio-economy' have undoubtedly lead to some new beneficial products, such as new biopharmaceuticals, including some new cancer drugs. But have these investments been good priorities for health, the environment and the economy? What are the scientific and technological limitations to the claims being made for future benefits? Is this a good approach to innovation and has it won public support?

5.1 Good for health, hunger and sustainability?

> "*Unrealistic expectations are dangerous as they lead to poor investment decisions, misplaced hope, and distorted priorities, and can distract us from acting on the knowledge we already have about the prevention of illness and disease*". Nightingale & Martin, 2004.[665]

> "*Society's huge investment in technological innovations that only modestly improve efficacy, by consuming resources needed for improved delivery of care, may cost more lives than it saves. The misalignment of priorities is driven partly by the commercial interests of industry and by the public's appetite for technological breakthroughs, but health outcomes ultimately suffer*". US researchers in family medicine, 2005.[666]

> "*I'd like to think that the South African government will come to the* [genomics] *party, but then when you look at the nature of the other challenges that the country is facing…well, where does scientific research fit into all of that? And it is easy for educated scientists who've got a vested interest to say, well of course what we are doing is incredibly important and an integral part of all those challenges for the country*." Interviewee in South Africa, cited by Hardy *et al.*, 2008.[667]

Andersson points out that the notion of public-private partnership in the knowledge economy presumes that the interests of the market, state and citizens are the same and that no differences or conflicts of interest exist.[14] The role of the state is seen as creating the environment for innovation, through strategic investment in education, research and knowledge infrastructure, particularly information and communication technologies. The market provides creativity and entrepreneurship and becomes "*the arbiter of what knowledge, skill and creativity are useful in society*".

In the knowledge-based bio-economy, conflicts between commercial priorities and the public good are presumed not to exist: wealth creation and better quality of life go hand in hand (Section 1). However, conflicts between different interests are pervasive in the bioeconomy, and wealth creation is often directed at narrow, vested interests, rather than society as a whole. In their book on the politics of food, Lang and Heasman conclude: "*Food is such an enormous sector of the economy, so vital to people's needs and contexts and so powerfully fought over by companies wishing to capture markets that conflict is inevitable*".[3] Further, as Altieri notes[668]: "*The globalised economy has placed a series of conflicting demands on existing cropland*", which is now expected to produce food for a growing human population, as well as meet the increased demand for industrial-scale biofuels (agrofuels): and do so in a way that preserves biodiversity and reduces greenhouse gas emissions, whilst representing a profitable activity to millions of farmers. At the same time, intensive farming and subsidised monocultures degrade and deplete the water, soil, climate and ecosystems that underpin nature's capacity to meet future food, fibre and energy needs.

Particular tension arises around GM crops because, as Levett argues: "*If some people are allowed to choose to grow, sell and consume GM foods, soon nobody will be able to choose food, or a biosphere, free of GM. It's a one way choice…once it's made it can't be reversed*."[669] However, health research priorities may also give rise to conflicts. Researchers at the University of California have argued that the way we view health and medicine has changed significantly due to increasing corporate involvement in science and technology. They describe several interacting processes have led to the 'biomedicalisation' of health, involving: major political economic shifts; a new focus on health and risk and surveillance technologies; the 'technoscientisation' of biomedicine; transformations of the production, distribution, and consumption of biomedical knowledge, and transformations of bodies and identities.[670]

The current system of research funding, in the context of the knowledge-based bio-economy, means that – with some exceptions – most public research funding tends to follow the research investment strategies set by a narrow range of industries and vested interests, rather than being focused on solving the real problems of global hunger and malnutrition. The food industry's priorities are not necessarily those which benefit health or sustainability[3], and important gaps in health research reflect biases within the health research economy which mean that research that is unlikely to be profitable or is of little scientific interest tends to be neglected.[4]

This section considers how a strong political commitment to the knowledge-based bio-economy distorts research priorities in ways that may be harmful and/or prevent better approaches from being developed.

5.1.1 Health and medicine: the right research priorities?

> "*Who will pay for research on what works in tackling obesity? The European Union's programme for health research from 2007-13 favours biotechnology studies over those on public health and health services and industry has little incentive to fund such work*." Trish Groves, Deputy Editor, British Medical Journal, 2006.[671]

> "*If a mere fraction of the billions spent on technological research were spent instead on simpler things like, yes, early education to improve diet and promote exercise, the benefits could grossly dwarf even the greatest plausible genetic successes, especially with regard to late-onset disease*". Buchanan, Weiss and Fullerton (Penn State University and University of Washington Medical School), 2006.[326]

> "[Public health] *problems are exacerbated by the concentration of funding on biomedical research and the failure to confront and work with vested interests, which promote and sustain unhealthy behaviour patterns*."
> Robert Beaglehole (World Health Organisation) and co-authors, 2004[672]

> "*The dearth of* [public health] *evidence is not unrelated to the lack of funding of public health intervention research – with funding from research organisations and the private sector heavily directed towards clinical, pharmaceutical, biological and genetic research – and the lack of a clear and coherent set of Government priorities for the public health research which does exist.*"
> Derek Wanless, UK Treasury advisor, 2004[673]

Although there are clearly benefits to the role that the pharmaceutical industry plays in developing new drugs, a market-driven approach to health will not generally identify the best priorities for public investment in terms of improving health or saving taxpayers' money. This is because ill-health is strongly correlated with poverty and hence lack of funds to buy healthcare or eat healthily.

The market-driven biases within pharmaceutical research are well known: including the neglect of developing country diseases[674], the emphasis on 'me too' (copy-cat) drugs rather than genuinely new products[675] and the increasing medicalisation of ordinary life in order to expand markets.[676] Put simply, rich, healthy people are a better market for health products than poor, sick people are.

In 1990, the international Commission on Health Research highlighted what became known as the "10/90 gap": that 90% of all research funding for health was devoted to the health problems of wealthy countries, whilst only 10% was for research on the health issues of low-income countries. In 2000 the World Survey of Funding for Genomics concluded: "*Even more than for medical research in general, the skew of research funding is heavily directed toward the developed economies with large pharmaceutical markets*".[677] With a few exceptions, such as collaborative efforts on malaria, research is directed towards conditions affecting large populations in rich countries. Whilst biomedical research has had some successes, new biopharmaceuticals are not without their problems and covering the costs has proved difficult even for wealthy countries.

Perhaps more importantly, the '10/90 gap' is not the only gap in medical research. In 2007, Leroy and colleagues highlighted another even more serious, compounding gap, which they call the '3/97' gap.[678,679] Based on analysis of funding by the US National Institutes of Health (NIH) and by the Bill and Melinda Gates Foundation, they found that 97% of research grants aimed at reducing child deaths in poor countries were for developing new technologies. Only 3% of research grants were for research on delivery and use of technology, yet, according to their calculations, the reduction in deaths that could be achieved with new technology was only one third of what could be achieved if existing technologies were fully utilised. The authors cite examples such as ensuring HIV drugs reach those in need, teaching healthcare workers how to administer oral measles vaccine and vitamin A capsules, and programmes to supply oral rehydration therapy for diarrhoea, or encourage and support breast feeding.

Studies by Woolf and colleagues in the USA have reached similar conclusions, based on analysis which shows that technological advances must yield dramatic, often unrealistic increases in efficacy to do more good than could be accomplished by improving the 'fidelity' of healthcare: that is, improving systems to ensure the delivery of care to all patients in need.[666,680,681] Woolf concludes that inattention to how research priorities are balanced can indirectly claim lives, contribute to disease, and generate costs that would not occur if priorities were in greater harmony with potential gains.

In short, biomedical advances save fewer lives than modifying the social conditions that influence health, and: "*Lives are lost in developed and developing countries by concentrating too many resources on advancing biotechnology and concentrating too few on the fidelity of healthcare delivery*".[682]

Sarraci and co-authors echo this view when they argue that health systems research has also been neglected in Europe. They argue that the EU needs to implement "*a clear, coherent research strategy for all citizens' health rather than be the sum of studies plugged into projects conceived primarily in biological or biotechnological terms, often with industrial production development as the key objective*".[683]

Although the UK benefits from a publicly-funded health system, and other EU countries also have smaller health disparities than the USA, there are still important gaps in the types of research that are likely to be funded.[4] For example, public health research has been neglected in the UK despite its enormous importance in reducing the incidence of disease. The 2002 report by Derek Wanless to the Treasury concluded that a scenario in which the public are "fully engaged" in disease prevention could save the health service billions of pounds as well as improving health.[120] Yet, not more than 0.4% of UK academic and research output (measured by journal publications) is relevant to public health intervention research[684]. The later 2004 Wanless report on public health warned that "*pharmacological solutions might become the focus of primary prevention with considerable financial implications*" and that: "*Substantial investment, or reprioritisation, is necessary if this imbalance in research funding is to be addressed*".[134]

For example, European investment in biomedical research into diabetes, obesity and so-called "diabesity" (the increase in incidence of type 2 diabetes associated with the current global epidemic of obesity and overweight) has increased four-fold, rising from €44.5 million during the EU's Fifth Framework Programme (1998 to 2002) to €188 million in the Sixth (2002-2006).[685] Yet the cause of the increase in obesity and type 2 diabetes - too many people eating too much and exercising too little – is well known, and evidence also exists that medical solutions are less effective than lifestyle interventions, or tackling the social, economic and environmental factors that underlie the problem.[686,687,688]

The 'early health' model of disease prevention proposed by the life sciences industry suggests that health scans will in future include screens of all or part of people's genomes, linked with advice on medicines, supplements, cosmetics and functional foods (such as cholesterol-lowering margarines) that they can buy.[353] In this vision of the future, screening people's genomes (their genetic make-up) will routinely be applied to identify high risk individuals and populations, and it is claimed that "*tailored prevention programmes*" will improve personal and public health.[689] Industry will communicate more directly with patients and there will be "*more innovation that will blur the regulatory boundary between drugs, biologics, devices, cosmetics and nutritionals*". There will be increasing consumerism, including ordering directly over the internet, bypassing medical professionals, and more suppliers will be engaged in "*nurse-led care*". The companies involved envisage:[690]

- routine genetic screening – using whole or partial genome scans conducted by gene testing companies delivered by nurse-staffed pharmaceutical outlets in supermarkets and other stores;
- widespread use of home diagnostics and remote health monitoring, with blood samples collected via Blackberrys and iPods;
- smart cards including electronic health records and DNA;
- consumer-driven personal health planning, involving companies such as Google Health;
- tools to monitor medication regimens to drive compliance, and tools to measure physical activity and diet, linked to online work-outs and incentive programmes (such as paying people to lose weight);
- roaming nano-devices in blood vessels to diagnose and fix problems, and nano-particles to add nutrients to food;
- a shift from 'one size fits all' healthcare to personalisation, prediction, prevention/disease pre-emption and patient responsibility.

Whilst this represents a shift away from only treating disease to considering disease prevention, it in fact involves a new approach to monitoring and medicating healthy people, which is expected to significantly increase the market for pharmaceuticals and other healthcare products and services.[351,352,690] The vision includes having your genome stored on your smart-phone, so that you can scan supermarket barcodes and be recommended 'personalised' products.[691] The aim is to "*capitalise on the trends toward wellness and consumerism to enable tailored approaches to prevention and care*", and family health practitioners are expected to be sidelined as gatekeepers to medical services.[692] In the UK National Health Service, it is envisaged that the research (or data-mining) needed to produce personalised biological risk assessments (based on individual genomes, perhaps

combined with other biomarkers) will be conducted initially in UK Biobank and then rolled out to the entire population (see Appendix A).

The companies involved have been lobbying to avoid regulation of genetic tests, so that they can feedback research results when they are not validated and do not meet medical screening criteria (see Appendix A). Google and 23andMe, and other gene testing companies, want the power of information to be "*wrested from the medical profession*".[693] They have recently set up an online campaign to lobby for people's "right to know" this information.[694] But companies like theirs – which interpret people's genomes to tell them their supposed genetic risk – will have the power, not their customers. Individuals will be dependent on the (unregulated) interpretations they are given of their risk and the products they should buy in order to reduce it.

Selling medication to treat risk factors rather than diseases is immensely profitable for the pharmaceutical industry: for example, statins (to lower cholesterol levels) are now the biggest selling prescription drugs in the world and their high costs are putting a strain on healthcare services.[695] Sales of statins grew 11.2% between 2003 and 2004, bringing the pharmaceutical industry $30.2 billion in sales.[696] Whilst statin drugs can save lives, expanding their use to ever larger numbers of people has been criticised by some doctors because lifestyle changes are usually cheaper and more effective and avoid the risk of side-effects.[697] The role of the pharmaceutical industry in influencing guidelines for lowering cholesterol has sparked [698]and there is some evidence that many people dislike preventive medication and prefer alternatives, such as lifestyle changes[699,700].

Functional foods – foods with claimed health benefits, such as cholesterol-lowering margarines – are also seen as a major area of growth by the food industry.[701] Although health and wellness has become the latest trend in food industry marketing, the Food Ethics Council argues that the current policy shift towards 'personalisation' in preventive health tends to support personalised marketing of functional foods, neglecting more effective approaches to tackling diet-related disease, such as: better cross-government co-operation to reduce poverty; healthy public food procurement policies; and a greater emphasis on public health research.[702]

Despite the growing evidence that attempts to predict genetic 'susceptibility' to common diseases will not in general be useful or cost-effective (see Section 5.3.1 and Appendix A), this model of 'personalised' prevention is being exported to countries as diverse as Mexico[703], India[704], Thailand and South Africa[667]. Major research investments are being made, backed by unsubstantiated claims that large-scale human genotyping initiatives will deliver significant health benefits, reduce healthcare costs and achieve economic development.[706,707] For example, in Mexico, the food manufacturer Nestlé is collaborating with the large-scale genotyping project INMEGEN, which aims to predict individual genetic risk of diet-related diseases such as obesity and type 2 diabetes. The company is funding a new Nestlé Chair in Nutrigenomics (nutritional genomics) and two fellowships. This approach is driven by a marketing strategy aimed at selling functional foods (see also Section 2.5.3), rather than by an assessment of the likely benefits, and is arguably much more likely to confuse public health messages and undermine public health initiatives than to reduce the incidence of these conditions.[354]

Petersen argues that, although it is doubtful that many of the promised benefits of genetic research will be delivered (see also Section 5.3.1), an increasingly pervasive genetic worldview and expectations about future genetic innovations are profoundly shaping conceptions of health and illness and priorities in healthcare.[708]

Environment plays a major role in most types of cancer[709] and environmental factors such as air pollution also contribute to many deaths from heart disease.[710] However, research on the environmental causes of disease is rarely a high priority. The environmentalist George Monbiot notes that in the 1999 UK Government White Paper on public health 'Saving lives: our healthier nation' the only atmospheric pollutant named is radon – which happens to be one of the only pollutants in Britain which does not result from the activities of large corporations.[711] Genetic research projects such as UK Biobank (see Appendix A), although claiming to research the combined effects of genes and environment, do not in practice involve meaningful measurements of environmental exposures, so

will not be able to identify the role of pollution in disease.[712] Further, the claimed benefit of a genetic approach – the potential to save lives through targeting reductions of exposures in those believed to be at highest genetic risk – is extremely limited.[341]

A recent report from the World Health Organisation (WHO) has highlighted the enormous health disparities across the globe, and even within wealthy countries such as the UK.[713] The report argues that social justice is a matter of life and death, and that governments should take global action on the social determinants of health and end inequity within a generation: addressing issues such as urban planning, land use, environmental degradation, fair employment and social protection. The WHO's press release highlights that a child born in a Glasgow can expect a life 28 years shorter than another living only 13 kilometres away; a girl in Lesotho is likely to live 42 years less than another in Japan; and in Sweden, the risk of a woman dying during pregnancy and childbirth is 1 in 17 400, compared to 1 in 8 in Afghanistan. It states: "*Biology does not explain any of this. Instead, the differences between and within countries result from the social environment where people are born, live, grow, work and age*".[714]

The 2010 Marmot Review of health inequalities in England[715] found that the poorest people in England live seven years less on average than people living in the richest neighbourhoods, and have on average 17 years less disability-free life. The Review estimated that up to 202,000 early deaths could be avoided, if everyone in the population enjoyed the same health as university graduates. It estimates that inequality in illness accounts for productivity losses of £31-33 billion per year, lost taxes and higher welfare payments in the range of £20-32 billion per year, and additional NHS healthcare costs associated with inequality are well in excess of £5.5 billion per year.

A focus on individual biological differences is therefore unlikely to deliver significant improvements in public health.[716] There is a danger that 'mainstreaming' a genetic or genomic approach to prediction and prevention acts as a distraction to tackling the social, economic and environmental issues that could make a substantial difference to reducing the global burden of disease. A more population-based approach to disease prevention, such as that proposed in the Marmot Review, involves a greater emphasis on initiatives such as increasing the minimum wage, increasing access to green spaces and healthy food, and moving beyond economic growth as the sole measure of a successful society. The Review highlights six policy objectives: giving every child the best start in life; enabling all children young people and adults to maximise their capabilities and have control over their lives; creating fair employment and good work for all; ensuring a healthy standard of living for all; creating and developing healthy and sustainable places and communities; and strengthening the role and impact of ill health prevention. Although the latter can include the use of medical interventions – such as statins, vaccinations and smoking cessation programmes – this is only one aspect of a new approach, which might also include the use of health trainers to help people from disadvantaged and hard-to-reach communities.

Similar problems arise with the emphasis on pharmacogenetics or pharmacogenomics (genetic tests for drug response) as a means to improve drug safety. In his book on personalised medicine, based on interviews with clinicians, researchers, regulators and company representatives, Hedgecoe describes how supporters of this approach, including industry representatives, frequently cite a US study which found that in 1994 in the US, 106,000 deaths were caused by Adverse Drug Reactions (ADRs), making adverse drug reactions between the fourth and sixth leading cause of death.[717] A similar 2004 study in the UK found that ADRs represent a considerable burden on the NHS, accounting for 1 in 16 hospital admissions and 4% of the hospital bed capacity.[718] Hedgecoe describes how, when the risk of ADRs are stated, commentators implicitly accept that the underlying cause is necessarily genetic and that the solution therefore lies in 'personalised medicine': "*Few of the reviews, editorials and opinion pieces written to promote personalised medicine are prepared to disentangle ADRs from an automatic genetic cause, with Ruth March of AstraZeneca, who accepts that 'only a small number of these [ADRs] will be from genetic causes', being a rare exception*" (page 15).

Whilst there is potential for some new useful pharmacogenetic tests to be developed, their role in tackling adverse drug reactions (ADRs) is likely to be limited by the complexity of drug response, which also involves many non-genetic factors (see Section 5.3.1). The Audit Commission found that

reported deaths in England and Wales from the adverse effects of medicines rose nearly five-fold between 1990 and 2000.[719] The reasons for this increase are poorly understood, but cannot include an increase in 'genes for adverse drug reactions'. Some relevant factors could include:

- the increasing toxicity of some new medicines;
- the limitations of safety testing and monitoring of new medicines;
- the increasing use of medicines, including multiple medicines and more 'over the counter' sales.

There is a danger that these factors will be given less attention than pharmacogenetics, even though they may be more important. Tackling some of them might imply imposing tighter restrictions on the use of some medicines, meaning lower profits for the companies selling them. Other methods, such as better monitoring of ADRs and improving packaging, are less exciting than genetic science and require political will and government investment to make them happen. Another aspect of 'personalised medicine' the promotion of genetic testing for disease susceptibility (not just drug response) is another factor that could lead to more healthy people taking medication and increase, rather than reduce, the number of people who suffer side-effects.

Although promoted as leading to uncontested benefits (longer, healthier lives) the commitment to genetics and genomics as a research priority for the knowledge-based bio-economy in practice involves a commitment to a highly medicalised and individualised system of disease prevention, involving a considerable degree of monitoring and control over whole populations. Although enthusiasts claim that genetic information will empower individuals, a genetic approach to tackling common diseases can be disempowering because it over-emphasises the role of inherited genetic factors that people cannot change, and because it increases dependency on scientists and commercial companies to interpret this information, and governments to regulate and store it safely. The alternative view of empowerment, highlighted by advocates of a focus on inequalities rather than genetic differences, involves "*changing power structures to remove barriers that prevent people from participating in the issues that affect their lives*", rather than increased health surveillance.[715]

Even advocates of whole genome sequencing acknowledge that privacy can no longer be protected if a universal genetic database exists, linked to electronic medical records. People will be both tagged and categorised by their genetic information, because DNA is left wherever someone goes and can also be used to identify relatives.[720] Even if this were technically successful (see Section 5.3) it is questionable whether it will prove publicly acceptable.[721,722]

Thus, health research priorities in the knowledge-based bio-economy are clearly skewed towards the interests of the various industrial sectors that have promoted the 'early health' approach, and the claims made by the small circle of advisors who have advocated it (see Section 4). Following the commitments made to the 'knowledge-based bio-economy' described in the first part of this report, there has been no in-depth analysis of the pros and cons of this approach to health, or any consideration of potential mismatches between the priorities of vested interests and public health priorities.

5.1.2 Food and agriculture: the right research priorities?

> "*Even if the Life Sciences paradigm* [for the future of food and agriculture] *reduces its reliance on GM and exploitation of biology, we think it will still be folly for governments to rely on it; it is the Ecological paradigm which deserves stronger backing…a diet that is good for biodiversity is also good for human health, providing a rich variety of nutrients*". Lang and Heasman, 2004.[3]

"…*there is little or no evidence to date that the high level of investment in plant science is having a significant impact on strategic and applied research in crop science. Indeed there was considerable scepticism amongst respondents to the questionnaire about the effectiveness of knowledge transfer from models to crop production and a view that the gap between plant and crop science is widening*".[723] The Crop Science Review Panel, 2004.

"*I will leave others to discuss whether GM really has any value to the poor. But there is a choice angle. Ultimately it is our choices – to eat far more meat than we need, to throw away lots more, to fatten livestock on grain rather than grazing and scraps, and now to develop biofuels as a sop to climate change rather than curb our hyper mobility – that are driving malnutrition and starvation*".[669] Roger Levett, sustainability consultant, 2008.

"…*the reality* [is] *that Africa is once again being given what the world thinks it needs and not what it actually needs*".[724] Botha & Viljoen, GMO Testing Facility, South Africa.

In 2000, the WorldWatch Institute estimated (based on United Nations and World Health Organisation figures) that the number of overweight people in the world for the first time matched the number of undernourished people – at least 1.1 billion each.[725] The World Health Organisation (WHO) now refers to a global 'epidemic' of obesity and has warned that many low and middle-income countries are suffering a 'double burden' of both under-nutrition and obesity.[726]

Companies such as Monsanto describe meeting global needs for feed, fuel and food as essentially a problem of production. The company argues that projected growth in global consumption of meat and biofuels – the former mainly in non-OECD countries, the latter mainly in the USA – will require either the area of land under production to be increased, or productivity to be improved on existing farmland.[727] Although both these options will have environmental consequences, Monsanto argues that the negative consequences of increasing crop yields on existing land are generally less onerous. In its view, the solution lies partly in increasing the use of modern (industrial) farming practices in developing countries, and partly in developing a new generation of high-yielding GM crops.

Critiques of this view rest partly on doubts about the potential for GM technologies to increase yields (see Section 5.3), as well as disagreements about the downsides of the technology. However, most critics also disagree fundamentally about Monsanto's characterisation of the problem as primarily an issue of production, and are critical of policies which increase the area of land devoted to growing biofuels. Based on grain consumption figures calculated by the Food and Agriculture Policy Research Institute (FAPRI),[728] Monsanto argues that production of grain for animal feed must increase by 50 million tonnes a year by 2017/18 to meet the expected increased demand for meat, and by 60 million tonnes a year to meet biofuels production targets. It argues that its corn breeding programme will achieve these targets partly by introducing new hybrids and transgenic traits, but that 80% of the increase could already be met by raising corn yields in the ten largest below-average producing countries to the global average. However, because wheat and rice – largely used as food, rather than as fuel or feed - lack large private breeding programmes, the company states that increased public support is needed to develop new varieties of these crops.[725]

The alternative view is that the diversion of potential food growing land to produce industrial-scale biofuels is part of the problem, not the solution to global hunger, as is excessive grain-fed meat consumption in rich countries. Whilst increased biofuels production is treated as a policy *assumption* in the FAPRI figures, Monsanto and other companies have in fact been actively lobbying for government subsidies for biofuels.[729] Ten per cent of global GM crop production is currently used in biofuel production.[730] The evidence suggests that a significant proportion of biodiesel and bioethanol currently on sale is likely to be derived from GM feedstocks, and claims that a new generation of GM biofuels will avoid the serious problems associated with diverting land and food supplies to fuel production are, at best, speculative.[360] The EU's Joint Research Centre (JRC) notes that the use of maize-based ethanol production in the US (which frequently uses GM maize) is more likely than to not exacerbate global warming, if indirect effects on land use are included in the assessment.[877]

There are significant opportunity costs because there are better ways to achieve greenhouse gas savings and security of supply enhancements than to produce biofuels. Grain-fed meat production is also significantly more resource intensive and damaging to the environment than pasture-fed meat production, so an emphasis on expanding GM maize and soya production for animal feed neglects important alternative steps that could be taken to make the production of meat and dairy products more sustainable.

The potential for population growth to outpace food supply has been hotly contested since Thomas Malthus published 'An essay on the principle of population' in 1798.[731] Malthus argued that population would grow geometrically (doubling every year), rapidly outstripping food supplies, which could only grow additively. He has been strongly criticised by social historians for arguing that any attempt to relieve poverty during the social upheavals of the industrial revolution was foredoomed to failure, because it would only encourage the poor to breed.[732] Further, his assumptions about both population growth and agricultural productivity were purely speculative and neglected human agency and capacity to both restrain birth rates and increase agricultural productivity. Malthusian theory has nevertheless consistently overwhelmed other explanations of poverty because it acquitted the property-owning class and the political economic system of accountability.[733]

Central to the critiques made of Malthus' theory at the time, which continue to underpin debates about 'feeding the world' today, is his failure to consider how entrenched systems of power and inequality lead to poverty, and how people can take responsibility for feeding their own families (rather than out-breeding their own food supplies) provided they have sufficient control over their own lives and resources. Or, as one of his many critics stated at the time: "*My objections to him arise from his want of science; his infinite contradictions; his inhumanity; his loud abuse of the people; his silence respecting the hard-heartedness of the opulent; his general indemnity for kings and ministers.*"[734] The main alternative to the Malthusian view – articulated by the Nobel Prize winner Amartya Sen and others – is that hunger results from a lack of political freedom and the limited power of the poor over their own food supplies: "*Starvation is the characteristic of some people not having enough food to eat. It is not the characteristic of there being not enough food to eat*".[735] These arguments are not mutually exclusive as, of course, rising populations do need greater food supplies, however they underline that food availability is not merely an issue of production.[736]

Although a global increase in population is expected to increase food consumption, the world currently produces more than enough food for everyone. Despite concerns about over-population, and the existence of serious environmental degradation in many areas of the world, it is over-consumption in rich countries that is the source of the greatest environmental impacts.[737] Pearce cites evidence that the carbon emissions of one American today are equivalent to those of around four Chinese, 20 Indians, 30 Pakistanis, 40 Nigerians, or 250 Ethiopians. Thus, even if a woman in Ethiopia has ten children and a hundred grandchildren, the entire family will still emit less carbon dioxide than one person in Europe or North America. Continued economic growth – predicted to increase by 600% by 2050 – is likely to put much greater pressure on world resources than population growth, which is predicted to increase by 50% (from 6 to 9 billion) over the same period. Although the predictions are highly uncertain, this population bulge is expected to decrease later in the century, when the number of children born to women in Africa is expected to begin to fall. The timing of this demographic shift is likely to be influenced significantly by social and economic policies, including the extent to which people are empowered to take control over their own lives and escape from poverty.

A plant-based diet could feed the predicted population, provided it was fairly distributed, but an 'American-style diet', very high in meat and protein, could not, because such a diet requires much greater inputs of land and energy to feed the same number of people.[738] The current world grain harvest of around two billion metric tons could feed 10 billion Indians at current consumption levels but only 2.5 billion Americans, largely because 90% of US grain consumption goes to the indirect production of milk, meat and eggs.[739] Although meat consumption is increasing in India and China, these countries remain net grain exporters.

Currently, many people in developing countries cannot afford a minimum healthy diet. For the poorest people in Bangladesh, for example, this costs three times what they usually earn.[740] When families do

not have enough money for a nutritious diet, they are forced to eat food that is not nutritious enough for their children to be healthy or protected from sickness. Under-nutrition, caused in part by poor diets, impairs growth and development. This results in lower achievement in school and lower productivity in adulthood. As a result, poverty is entrenched in the next generation, in part because parents cannot afford to feed their children sufficiently.

At the same time, over-consumption of unhealthy foods is creating a global 'epidemic' of obesity. In Europe, there are now major concerns about the impacts of poor diets on health. As Lobstein explains, there are major 'upstream' problems which are shaping consumption patterns, such as trade and agriculture policies.[741] In both rich and poorer countries, this includes 'fat dumping' (the segregated marketing of unwanted high fat, high sugar and high salt food to lower socio-economic status populations).[742,743,744]

Large amounts of food are also wasted, and buying food which is then wasted reduces overall supply and pushes up the price of food, making grain less affordable for poor and undernourished people in other parts of the world.[745]

Food production (farming and fishing), processing, storage and transport, has major impacts on the environment. The unintended consequences of intensive agriculture include reduction in the genetic diversity of crops, increasing dependence on finite energy and other production resources, and new concentrations of harmful pesticides, nutrients and harmful greenhouse gases in the environment.[746] Other issues include over-fishing, soil depletion, and loss of biodiversity. Environmental impacts also affect the current and future availability of nutrients, and hence people's diets and health. Industrially produced ('factory-farmed') meat, for example, contains different types of fats from traditional game meat, and hence has very different implications for health. In addition, industrial meat production requires much greater energy inputs than the food energy it outputs, creating an unsustainable system of production that contributes to malnutrition in low-income countries.[747] Food and agriculture policies affect social justice and the working conditions of packers and farm labourers.[748]

Processing and packaging also affect nutrients, such as the levels of vitamins and minerals in packaged salads and white flour. Additives such as colourings and flavourings are often used in foods of poor nutritional value and some food preservation methods can make unhealthy processed foods (such as canned fatty meats) cheaper than fresh, healthy ones.[738]

The approach to these problems that is embedded in the idea of the 'knowledge-based bio-economy' involves investments in scientific and technological solutions, intended to drive growth in the agricultural biotechnology and food manufacturing sectors. Thus, new 'functional foods', underpinned by biological research and marketed at a premium to rich consumers, are claimed to be the solution to diseases related to the increase in obesity. Some of these functional foods are expected to use GM technologies (such as the purple tomato, described in Box I), and GM agriculture is also proposed as the key to improving yields and nutritional value of crops in poorer countries, as well as providing a new source of fuel for cars. The proponents of this approach also claim that environmental benefits will be delivered and that increases in the efficiency of food production will offset the diversion of more land to the production of industrial-scale GM biofuels (agrofuels) and of industrial chemicals in GM plants.

In this context it is worth noting that the Vision articulated in the European Technology Platform 'Plants for the Future' (Section 3.3.5) bears a striking resemblance to the 'Vision for agricultural research and development in the 21st century' prepared by the US National Agricultural Biotechnology Council (NABC) back in 1998.[749] The NABC vision claimed that biobased products "*will provide security and sustainability in food, health, energy, environment and economy*" and would "*improve the healthfulness of foods*" as well as producing new "*bio-industrial crops*" (fuels, chemicals and materials) and revitalising the agricultural economy.

In a speech made at the US 12th Annual National Agricultural Biotechnology Council (NABC) meeting in 2000, the environmentalist Ralph Nader raised many concerns about this vision, including the role of power – "*including corporate power and the governmental power it reflects*" – in deciding future directions. Nader argued that industry had failed to address critical aspects of agricultural

biotechnology, including ecology, nutrition and disease dynamics, and basic molecular genetics.[750] Another speaker at the meeting, Lois Levitan of Cornell University, whilst supportive of a new biobased economy, argued that land, energy and resource constraints must be factored in to any vision "*otherwise they are fantasy*". For example, if maize-based ethanol were to meet US fuel needs, it would require four times as much land as is potentially available for all crops grown in the USA.[751]

These criticisms seem prophetic, given the acknowledged role of increased pressure on land-use including the diversion of food crops to biofuels and the increase in consumption of grain-fed meat[752] – and speculation in grain markets, in the global food crisis triggered by soaring food prices in 2008.

As described in Section 2.2.4, investment in agricultural biotechnology has been driven largely by the opportunities it provided commercial companies to control the global seed market, underpinned by the assumption that in the knowledge-based bio-economy this would also lead to public benefits (as described in Section 1). As well as the global seed market becoming concentrated in the hands of a few powerful companies, there has been a significant shift in the focus of agricultural research, away from the land and into laboratories, resulting in the loss of important skills and agricultural extension services (see Section 2.5.3).

The proponents of this approach claim that a new 'gene revolution' will match and extend the 'Green Revolution' that took place from the 1940s to about 1985. The Green Revolution combined high yielding hybrid crop varieties, fertilisers, irrigation and agrochemicals, to increase the production per unit area of food crops. A hallmark of the Green Revolution was that land productivity increased faster than labour productivity as a result of the new technological packages, thus increasing employment and wages, and that total factor productivity in agriculture increased faster than the fall in food prices, so both poor producers and consumers benefited.[753] It achieved food security for some sectors of the population across large areas of Asia and Latin America. However, there were also downsides:

- The spread of hybrids and use of agrochemicals caused a loss of biodiversity, less varied diets and exposure to toxic pesticides, affecting ecosystems and human health.
- Crop diversity also decreased so that a limited number of four main crops (maize, rice, wheat and barley) now dominate.
- The benefits of new technologies were unevenly distributed. The gap widened between those who owned or rented land and the landless, particularly women and labourers, as rural employment opportunities diminished and wages did not keep up with the rising price of land.

Thus, whilst the Green Revolution undoubtedly increased food production, it did not increase food availability for the poorest people or help the poorest farmers. Further, a 'Green Revolution' similar to Asia's is considered unlikely to occur in Africa because of the region's diversity, reliance on rain-fed smallholder systems, its immense size and poor infrastructure.[754]

The UN's Special Rapporteur on the right to food has highlighted that, although commercial seed varieties may improve yields in the short term, their higher performance often has been a response to inputs (fertilisers) and to water availability, making it difficult for poorer farmers unable to reap their benefits. Farmers may also find themselves trapped in a vicious circle of debt as a result of a bad harvest and consequent impossibility to reimburse input loans. Commercial seed varieties may be less suited to the specific agro-ecological environments in which farmers work, and for which landraces (traditional farmers' varieties) may be more appropriate. The expansion of surface cultivation with commercial seeds also accelerates crop diversity erosion, as an increasing number of farmers grow the same crops, using the same, 'improved' varieties on their fields (creating 'monocultures').[755]

The idea of new 'Gene Revolution' involves portraying GM crops as a 'pro-poor' technology, which will spread the benefits of technology to Africa as well as Asia. However, the 'Gene Revolution' suffers from many of the same limitations as the 'Green Revolution'. It also differs from the 'Green Revolution' in that the claimed new high-yielding varieties do not yet exist, but are assumed to be developed in the future, as a result of increased public investment in research and development of GM crops. Claims that GM technology will allow the production of new crops with increased yield or new properties, such as drought-tolerance and salt-tolerance, are at best speculative (see Section

5.3); and raise new socio-economic issues: including the consequences of driving poorer farmers onto more marginal land, and questions about who carries the economic risk if production gains are only temporary. The role of new technologies in agriculture is critically dependent on their socio-economic context, including whether they are likely to drive poorer farmers into debt, and the loss of autonomy involved buying seeds and chemicals from large corporations.[756,757]

Thus, claims that GM crops can help to tackle third world hunger are hotly contested. For example, reviewing the evidence on GM crop yields after more than 20 years of research and 13 years of commercialization in the United States, the Union of Concerned Scientists has concluded that: "*a hard-nosed assessment of this expensive technology's achievements to date gives little confidence that it will play a major role in helping the world feed itself in the foreseeable future*".[758]

Glover has documented a mismatch between claims made by the US company Monsanto and others that GM crops would be developed in ways that would be 'pro-poor', benefiting poor farmers and consumers in the developing world and the reality of Monsanto's investment strategy, which is focused on large-scale commercial farmers and crop-trait combinations that are both technically feasible and commercially viable.[397]

Rosett argues that there is no relationship between the prevalence of hunger and our ability to produce enough food. In fact, per-capita food production increases during the past 4 decades have far outstripped human population growth.[759] The real causes of hunger are poverty, inequality, and lack of access to readily available food by people who are cash poor. Rossett also argues that when transgenic varieties are used in small-scale marginal cropping systems, the risks of crop failures are much greater than in green-revolution, large, wealthy farmer systems or farming systems in northern countries, and the economic risks affect poor farmers much more severely than wealthy ones. Rossett concludes that proponents of genetically engineered varieties are repeating the very top-down errors that led first-generation green-revolution crop varieties to have low adoption rates among poorer farmers, and that participatory breeding organised by farmers themselves – which takes into account the multiple characteristics of both seed varieties and farmers – is essential.

As Scoones describes, in India, South Africa and Brazil: *"the debate about GM crops has become a much wider one: about the future of agriculture and small-scale farmers, about corporate control and property rights and about the rules of global trade. In sum, a debate not just about the pros and cons of a particular set of technologies, but about politics and values and the future of agrarian society*".[760]

One of the most contentious issues in the development of GM plant technology has therefore been attempts to develop sterile GM seeds (known as 'genetic use-restriction technologies' or GURTs), to prevent farmers from saving, exchanging and re-planting seeds. As Smyth notes: "*In brief, plants and people cannot be trusted to do what markets require. As a result, genes move, creating co-mingled traits in the food system and liabilities in the transfer of technologies between markets*". He concludes that "*new biological control mechanisms are needed to manage many of the risks and liabilities of GM crops*" but concedes that: "*As Monsanto's initial interest in* [seed] *sterility technology was prompted not by environmental concerns, but by the need to protect its intellectual property and prevent "brown bagging"* [seed exchange by farmers] *convincing opponents that terminator technology is a solution to gene flow is likely to be an uphill struggle*". However, Smyth notes that Monsanto's decision to halt the development of Terminator technology has not prevented other companies from developing and patenting new sterile-seed technology.[895]

Eicher *et al.* note that GM crops are currently grown commercially in only one country in Africa – South Africa – and examine the development of seven GM crops (six food staples and cotton) over the past 15 years.[761] They note that in practice, the number of GM traits under development in Africa is rather limited: insect and virus resistant sweet potato; insect resistant Bt potato, Bt maize, Bt cowpea and Bt cotton; disease and insect resistant banana; and virus resistant cassava. Although the authors are enthusiastic about the potential for GM crops in Africa, their case studies reveal a number of unexpected scientific, legal, economic and political barriers to the development of GM crops and long delays in developing and implementing national biosafety regulations and guidelines. They conclude that most GM crops are at least 10-15 years or longer from reaching smallholder farmers in Africa.

A further major area of research investment is seeking to develop GM crop varieties with increased amounts of essential vitamins and minerals, and 'improved' profiles of 'nutraceutical' compounds (functional foods).[762]

The attempt to produce new 'functional foods' is driven by the food industry's need for growth in industrialised country markets. However, plenty of healthy foods already exist and are likely to remain cheaper than premium-priced functional foods. Although access to fruit, vegetables and whole grains can be a problem for lower socio-economic groups, who may live in 'food deserts' or not be able to afford these foods, this problem will not be solved by introducing new, more expensive products. The priority for health is not to make new foods, but to find out what will work in terms of helping people change their diets and live healthier lives, especially people in lower socio-economic groups and poorer countries. These people need healthy foods to be cheaper and more accessible, not more expensive – which means tackling the politics of food, including the role of agriculture, food companies, governments and supermarkets.[763,764]

Functional foods also raise important health and safety issues. Modifying the nutritional content of food is different from selling supplements, because people may be less aware of what they are consuming, and because nutrients may typically harm some individuals whilst providing benefits for others. The difficulties in assessing safety are also complicated by the fact that both foods and supplements can interact with medicines, causing side-effects.[765] Benefits are also often difficult to quantify and a whole new raft of legislation is being developed in an attempt to regulate both health claims and safety in the European Union.[766,767] Some nutritionists argue that the functional foods approach leads to a misleading focus on single nutrients, instead of the healthy effects of plant-based diets in general.[768,769]

Promises that new GM crops will enhance nutrition have been made for many years. To date, these crops remain at an experimental stage and none have gained regulatory approval. There are technical problems, marketing and food safety challenges and economic uncertainty because alternative sources of nutrients are available. Nevertheless, a considerable amount of research effort is being directed at developing these crops. Enhanced levels of vitamins, minerals and omega-3 fatty acids are being engineered into both high-value crops, such as tomatoes and lettuce, and staples, such as rice, soya, sorghum and potatoes. Enthusiasts claim that these new crops will overcome public resistance to eating GM foods, by providing benefits directly to consumers, and will help people in poor countries who are nutrient-deficient.

However, GM crops may be able to cross breed with wild relatives and neighbouring crops. Additionally, once harvested, seeds can become mixed with non-GM crops. Thus, because GM introduces nutritional changes at the bottom of the food chain rather than in final, processed products, issues of traceability, liability and lack of reversibility arise. These issues may be particularly important for 'biofortified' staple crops, which could form a large proportion of people's diets, particularly in poor countries. There are also question marks over whether genetic modification can reliably produce the desired levels of nutrients in foods. For many other vitamins and other micronutrients, a deficiency is harmful to health, but too much may also be harmful, harm specific groups of people, or have unpredictable effects: this can make increasing levels in a staple crop unwise.[770]

So-called 'Golden Rice', which has been genetically-modified to produce enhanced levels of beta-carotene is one example of a 'biofortified' crop. GM Golden Rice has been promoted as a means of addressing vitamin A deficiency, which affects millions of people in poor countries, where it is a major cause of childhood blindness and also increases susceptibility to infection.[771] However, the promotion of 'Golden Rice' has been widely criticised on various grounds, including that:

- early versions produced too little beta-carotene to tackle vitamin A deficiency;[772] there remain doubts about bioavailability of vitamin A from the new version;[722] and no scientific study has yet proven the benefit of the technology to overcome vitamin A deficiency in humans[773];
- alternative ways to tackle Vitamin A deficiency exist that are immediately available and are being implemented now, including: encouraging breast feeding; helping people grow fruits and vegetables to give them a more varied diet; providing supplements or fortifying foods;[774]

tackling poor nutrition one nutrient at a time may distract from tackling poverty and malnutrition more broadly;

using GM-rice is not a “demand-led” approach and therefore may be socially or culturally unacceptable, not cost-effective, or undermine food security[775];

there may be unintended effects on health and the environment, including crossing with traditional and wild varieties of rice, which could have serious consequences because Asia is the centre of origin for rice.[722]

The Rockerfeller Foundation spent $100 million between 1990 and 2000 on developing GM 'Golden Rice' and has invested substantially more since. A deal made with AstraZeneca in 2000 to commercialise the rice was based on the product being given away to poorer farmers, who would be allowed to earn an annual $10,000 without paying royalties. At the same time, the company planned to develop the rice as a “functional food” in developed countries. Their general manager told the Financial Times: “*Golden rice contains the anti-oxidant beta-carotene, and anti-oxidants have been shown to play a role in the fight against cancer and heart disease*”.[400] However, two major clinical trials in the 1990s had already found that beta-carotene supplements unexpectedly increased risk of cancer in smokers and asbestos workers.[776,777,778,779,780] As further evidence of harm emerged, regulators issued warnings about beta-carotene supplements, which are widely sold as anti-oxidants (intended to reduce the risk of cancer). In 2003, the UK Food Standards Agency's Expert Group on Vitamins and Minerals set a Safe Upper Level for beta-carotene supplementation of 7mg/day for non-smokers and recommended that smokers or those exposed to asbestos should not take beta-carotene supplements.[781] In 2006, the US National Institutes of Health reviewed the evidence on beta-carotene and concluded: “*We found no evidence to recommend ß-carotene supplements for the general population and strong evidence to recommend that smokers avoid ß-carotene supplementation*”.[782]

Scientists in the US and at the Nestlé Research Centre, Switzerland stated in 2001: “*Currently, the goal of nutritional improvement of agriculture is to produce changes in crops and food that provide health benefits to all people. Few modifications to existing commodities that meet such a standard can be imagined because of the complex and heterogeneous makeup of humans. Recent mistakes made while attempting to improve the food supply highlight this conundrum. Beta-carotene was interpreted to be a highly beneficial ingredient, aiding in the protection against certain cancers, especially lung cancer. In response to this interpretation, a major shift in the carotenoid content of the food supply was underway when 2 large intervention trials…discovered that high intakes of beta-carotene as a supplement actually increased the incidence of lung cancer in smokers*”.[783] In 2000, a preliminary 'freedom-to-operate' review of intellectual property in relation to the components of Golden Rice identified numerous patents claimed in the belief that the anti-oxidant properties of beta-carotene would reduce the risk of cancer.[784] By 2001, these companies had all signed the required Material Transfer Agreements (MTAs) to give Golden Rice away for free to poorer farmers.

When the biotechnology industry first began promoting GM rice as a means to prevent blindness in poor children, the levels of beta-carotene in it were too low to contribute significantly to tackling vitamin A deficiency. A second generation of Golden Rice has now been developed which contains much higher levels.[785] However, recent claims that Golden Rice is cost-effective rest on unverified assumptions about bioavailability of vitamin A from the rice and the dose-response curve.[786] Not only are the benefits speculative, these studies exclude any consideration of possible harmful effects of increased beta-carotene levels in family members not suffering from Vitamin A deficiency, or other potential consumers of the rice. This may be a particular issue for smokers or those exposed to smoke from cooking stoves. The example of Golden Rice illustrates an important trade-off between delivering vitamin A to populations who are vitamin-deficient and potentially increasing mortality in other people who may consume such rice. This example suggests that bio-fortification of staple crops with vitamins and minerals is a risky health strategy because of the difficulties in weighing evidence of benefit and harm and recalling products should new evidence of harm emerge. The claimed advantage of bio-fortification relative to other methods – ease of distribution – may in reality be a disadvantage in situations where nutrients require careful targeting at nutrient-deficient populations to avoid harm to others.

The European Union's assessment process for GM foods is inadequate to consider such effects, relying, at most, on toxicology studies involving only 28-day feeding studies in rats.[787] Approval processes in poorer countries will generally be even more limited, due to the lack of resources to develop and to implement regulatory assessments and controls. The potential difficulties of future product recall, should this prove necessary to protect health, are exacerbated by the use of genetic-modification (GM), because of the potential of transfer of the trait to other crops, via gene flow or seed mixing, and because low-income farmers, rather than food or supplement manufacturers, would bear the brunt of any economic losses.

Jasanoff describes how the promotion of GM Golden Rice as the solution to vitamin A deficiency (VAD) involves creating a situation in which the expert controls the terms of the debate and creates an 'accountability gap', where the solution is presumed to be provided by unaccountable global institutions without civic engagement and democratic processes.[788] Thus, "*projects such as the development of GM Golden Rice are unfriendly to the flowering of bottom-up engagement in the politics of innovation*".

Botha and Viljoen note that millions of dollars have been committed to developing GM sorghum on the grounds that it has the potential to alleviate hunger in Africa.[722] However, they find that, on closer analysis, GM sorghum is faced with the same limitations as GM 'Golden Rice' in the context of combating vitamin A deficiency efficiently and sustainably. They conclude that it is questionable whether the cost of developing GM sorghum can be justified when compared to the cost of investing in sustainable agricultural practice in Africa.

Richards argues that one problem in devising a research strategy to support West African rice farmers is "the *bias of science towards the excitement of the unknown*".[789] He describes how the idea of selection and breeding for (low-yield but hardy) African rice was developed at the West African Rice Research Station to meet the food security needs of war-displaced farmers, by stressing conservation, screening and selection of the hardiest genotypes. This research proposal was characterised by EU assessors as old fashioned and of 'no scientific interest' because it did not involve GM. He argues that supporting the right to food requires the courage to use scientific knowledge to take the path of 'no scientific interest'. Developing seed as a magic bullet limits choice and control by famers, whereas possessing a range of varieties allows the mix to be determined by the user. Food security and the right to food can therefore be threatened if the pursuit of high yielding varieties is pursued to the exclusion of attempts to maintain a diverse range of seeds, through which the poor can exercise their rights to self-provisioning.

In addition, there is ongoing concern about the potential negative impacts of GM crops and industrial agriculture on biodiversity and the environment and about potential adverse effects on health, particularly from 'second-generation' crops designed to produce pharmaceuticals or other potentially harmful chemicals.[790,791,792,793,794,795] For example, the mechanisms of gene transfer to wild relatives are not understood in sufficient detail to enable the likelihood to be determined with confidence. Neither is there, in general, a good enough understanding of the ecology of wild relatives, and hence of how undesirable traits might spread in the environment.[796]

Two ecological effects from Monsanto's 'Roundup-Ready' GM plants (genetically modified to be resistant to the broad-spectrum herbicide glyphosate) have been the widespread emergence of glyphosate-resistant weeds, and the discovery of an unforeseen herbicidal residue in GM soybeans.[797] Monsanto scientists initially claimed that resistant weeds were unlikely to evolve but the company now advocates the use of additional herbicides, such as 2,4-D or atrazine, and other experts have recommended rotating crops with non-Roundup-Ready crops.

In China, some scientists are strong advocates of developing GM rice that is resistant to the stem borer pest, as a means to increase yields, but others fear that introducing GM rice could endanger the food supply and the environment, and undermine efforts to protect the endangered wild rice that is critical to maintaining biodiversity.[798] Concerns include that:

- GM is a short-term fix which distracts from protecting biodiversity, soils and water use;
- other rice pests are anyway becoming more important in Asia (the brown planthopper, rather than the stem borer);

alternatives particularly growing mixtures of rice varieties can also increase yields, and have been demonstrated to be effective against diseases such as rice blast;

strict management (using 'refuge' areas of non-GM crops for insects) is required to prevent the emergence of resistant pests, and this is impossible in practice;

cross-pollination and gene flow from GM rice to wild rice is inevitable, and this could threaten the gene pool of wild rice, which is critical to future food supplies;

short-term animal studies aren't enough to measure safety for a food eaten three times a day by a billion people.

The use of new plant breeding techniques, such as market-assisted selection, are also dependent on the availability of the genetic diversity of wild rice plants to identify and develop new traits.[799] This biodiversity could potentially be threatened by a decision to grow GM rice.

Based on field research in China, involving interviews with government officials, farmers, researchers and others, Keeley describes how rhetoric that China's 'biotechnology revolution' is unequivocally a good thing for poor farmers and that it has only positive environmental impacts, makes sense only when a lot of important assumptions are left out of the picture.[800] In fact, many in China are far from gung-ho about GM crops, and regulators express particular doubts about commercialising GM rice, because of China's role as the centre of diversity for rice.

Decisions about whether or not to plant GM crops are generally made on the basis of comparison with other industrial agricultural systems, and usually exclude comparisons with other options. Ortega and co-authors evaluated four different soybean production systems in Brazil that were divided into two main categories: biological models (organic and ecological farms) and industrial models (green-revolution chemical farms and herbicide with no-tillage farms) and found that the biological models showed better environmental, economic, and social performance indicators.[801] The omission of alternatives from decision-making may be important: a recent European model for the assessment of ecological and economic impacts at a farm-level of GM and non-GM maize crops found that organically managed crops got the highest evaluation, and, although GM systems including Bt and herbicide tolerant (HT) traits did slightly better than conventionally managed maize, their overall ecological assessment was still poor.[802] Organic far outperformed the other cropping systems in all the ecological indicators except soil biodiversity, where it was at least as good as the other systems. The economic differences were small, although organic was slightly poorer, due to lower production. In this model, the best economic value was expected with the GM systems, but they also had the highest variable costs, whereas organic benefited from low variable costs (an aspect that may be preferable for small-scale marginal farmers, who may have good reason to be risk-averse, as discussed in Section 5.2).

In developed countries, organic yields tend to be lower than yields from intensive farming. However, experiments suggest that organic, low-input or no-tillage farming can produce yields and financial returns that are comparable to industrial agriculture, with less environmental damage, provided suitable crop rotations and other methods are used to control pests and weeds and replenish nitrogen in the soil.[803,804,805,806] In a four-year study in Iowa, Liebman and co-authors found that corn and soybean yields were as high or higher in the low-input farming systems they studied as in the conventional one. Without subsidies, net returns were higher for the four-year rotation system than for the conventional system, but subsidies narrowed the gap in favour of intensive agriculture. Reduced tillage reduces yields but can also reduce soil erosion and fossil fuel consumption, sequestering carbon in the soil and lowering emission of greenhouse gases and, properly managed, can also be more profitable than conventional tillage.[807]

A recent study of the likely consequences of a future major shift towards organic agriculture in the UK found that food production losses would not be as great as some have supposed and would be partly compensated by a reduction of intensive chicken, egg and pig meat production, which would free up more grain for human consumption.[808,809] Organic fruit and vegetable yields would be comparable to intensive systems but grain output would fall by around 30%, and dairy production would also fall, with beef production rising by 68% and lamb by 55%. Benefits would include reductions in greenhouse gas emissions and water pollution, a reduction in intensive energy and fertiliser use, more wildlife, and a massive increase in rural employment, with the creation of 73% more farm jobs.

Altieri notes that millions of small farmers in developing countries produce the majority of staple crops needed to feed the planet's rural and urban populations and argues that: "*Small increases in yields on these small farms will have much more impact on food availability at the local and national levels, than the doubtful increases predicted for distant and corporate controlled large monocultures managed with high-tech solutions*".[666]

Given the real scientific and practical difficulties in modifying the genetic-make up of plants to better fit poor environments (see Section 5.3), it may prove more productive to spend more resources protecting the environment and managing existing land. There is no doubt that better environmental management of water resources, energy and soil could have a significant role to play in improving food security. For example, better agricultural drainage water management can help prevent problems with waterlogging and salinity;[810] better water and land management in rain-fed agriculture could significantly reduce poverty and increase productivity,[811] a participatory approach, involving activities such as tree-planting and forest regeneration, can help to combat desertification in Africa[812]; and benefits of strong, early action to reduce carbon dioxide emissions considerably outweigh the costs.[813] Instead of isolating agriculture as a production system, it is necessary to view it as an integrated multiple-use system and as an agro-ecosystem, providing services and interacting with other ecosytsems.[808]

Agro-ecological approaches do not stress boosting yields under optimal conditions as Green Revolution technologies do, but rather they aim to ensure sustainability of production under a whole range of soil and climatic conditions, especially under marginal conditions, whilst aiming to be more resource-efficient.[750] Such approaches typically utilise the knowledge and skills of farmers to understand and respond to the changing ecological dynamics of local agri-food systems, for example by using indigenous knowledge or participatory research (see Section 6.1.2). Thus, they focus on the food self-sufficiency of communities in particular regions, utilising techniques such as integrated pest management and conservation tillage.

The future role of small farms in food production and the global economy is complex and contested. However, small and medium-sized farms are often considered more efficient producers than large farms in low-income countries, although production may be constrained by population growth and other social and economic pressures and it is clear that multiple factors affect productivity.[815,816,817] Research into crop rotation, intercropping and other low-input methods therefore has potential to substantially benefit smallholder farmers in Africa and elsewhere.[818,819,820,821]

Developing these alternatives implies a different approach to innovation than that which underpins political commitments to the knowledge-based bio-economy. A leading example of this new approach is the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD).

IAASTD consists of a global assessment and five-sub-global assessments of the impacts of agricultural knowledge, science and technology on hunger, poverty, nutrition, human health, and environmental and social sustainability in relation to both the past and the future. The Assessment process was initiated in 2003 by the World Bank, in partnership with a group of stakeholder organisations, including the Global Environmental Facility (GEF), the UN agencies responsible for agriculture, development, environment and science (FAO, UNDP, UNEP, UNESCO), the World Bank, and the World Health Organisation (WHO) and representatives of governments, civil society, private sector and scientific institutions from around the world. It used a consultative 'bottom-up' process. The IAASTD global and sub-global assessments were peer-reviewed by governments and experts, and approved by a panel of 57 participating governments. Following publication, the UK became the 58th country to endorse the call for "A New Era of Agriculture."[822] An additional three governments (Australia, Canada and the United States) did not approve the full texts of the Executive Summary[823] and the Global Summary for Decision makers[824].

The IAASTD report highlights that the mounting crisis in food security is of a different complexity and potentially different magnitude than the one in the 1960s. The main challenge is to increase the productivity of agriculture in a sustainable manner, which must address the needs of small-scale

farms in diverse ecosystems, including increasing access to land and economic resources and empowering farmers to innovatively manage soils, water, biological resources, pests, disease vectors, genetic diversity, and conserve natural resources.

In relation to biotechnology, the IAASTD report notes that Intellectual Property rules determine what products become available and that, whilst this attracts investment in agriculture, it can also concentrate ownership of agricultural resources. Patents may drive up costs, restrict experimentation by the individual farmer or public researcher while also potentially undermining local practices that enhance food security and economic sustainability. The report notes particular concern that present Intellectual Property instruments may eventually inhibit seed-saving, exchange, sale and access to proprietary materials necessary for the independent research community to conduct analyses and long-term experimentation on impacts. It also notes that farmers face new liabilities as a result of GM crops: GM farmers may become liable if their crops contaminate neighbouring organic farms, and conventional farmers may become liable to GM seed producers if GM plants are detected in their crops.

The UNEP/UNCTAD report on Organic Agriculture and Food Security in Africa, also argues that an agro-ecological approach is more likely to succeed in meeting the needs of farmers around the world to produce food and other products, prevent climate change and protect natural resources and biodiversity (known as a 'multifunctional' approach).[825] The report includes analysis of 15 case studies in East Africa. It finds that, in developing countries, evidence shows that agricultural yields in organic systems do not fall, and at least remain stable when converting from systems that use relatively low amounts of synthetic inputs (many of which were by-passed by the earlier “green revolution”) such as those frequently found in Africa. Over time, yields increase as capital assets in systems improve, thus outperforming those in traditional systems and matching those in more conventional, input-intensive systems. Organic farming increases access to food on several levels. First, increased quantity of food produced per farm leads to household food security which results in all members of the household having access to enough food. Second, the production and selling of food surpluses at local markets means that farmers benefit from higher incomes, which increases their purchasing power. Third, fresh organic produce becomes available to more people in the wider community. Finally, organic farming enables new and different groups in a community to get involved in agricultural production and trade where previously they were excluded for financial or cultural reasons. The report concludes that organic agriculture can increase agricultural productivity and can raise incomes with low-cost, locally available and appropriate technologies, without causing environmental damage. Furthermore, the report finds that organic agriculture can build up natural resources, strengthen communities and improve human capacity, thus improving food security by addressing many different causal factors simultaneously.

One example of an alternative, multi-functional, approach to improving food security and nutrition, which aims to promote biodiversity at three levels – ecosystems, the species they contain and the genetic diversity within species – is being developed by the Food and Agriculture Organization of the United Nations (FAO) and the International Plant Genetic Resources Institute (IPGRI) under the umbrella of the Convention of Biological Diversity.[826] This approach – which considers wild or under-utilised species and the need to adapt nutrition and health interventions to a diversity of needs – recognises that biodiversity management plays a significant role: in the development of sustainable agriculture; strategies against malnutrition; and bringing socio-economic benefits.

In a series of three reports – on grains, vegetables and fruits – the US National Academies have highlighted that there is an overlooked food resource in sub-Saharan Africa that has vast potential: native food plants.[827,828,829] The authors note that during the colonial era indigenous crops in Africa were neglected and discarded, as the official focus shifted to valuable export crops, such as sugar cane, chocolate, coffee, and cotton, and other durable, transportable, and valuable crops.[830,831] An end result of these historical trends is that most of Africa's food now comes from a mere 20 or so species, almost all of foreign extraction. However, many 'lost crops' with high nutritional value and adapted to a wide variety of climates still exist and have the potential to help tackle Africa's food needs.

Ongoing efforts to create livable and sustainable cities have shown how the discipline of engineering can change to address environmental and health issues as issues of design and planning.[832,1026]

Sustained improvement in the nutrition status of children in developing countries requires fair social and economic development to help communities out of poverty and improve food security: including education for children and empowerment of women.[833,834] As Glover argues, tackling food security and malnutrition in a sustainable manner is not primarily an issue of technology, but requires a radical shift of attention towards the systems that will help farmers to cope with change and manage risks and uncertainty.[660]

The commitment to the knowledge-based bio-economy, outlined in the first part of this report, has instead led to a focus on agricultural biotechnology, particularly GM plants, underpinned by patents held by a small number of companies in the private sector. The accompanying shift in research priorities away from farms into laboratories means that the research system is poorly equipped to address farmers' needs. Further, this approach increases seed companies' control over the food system and the dependency of farmers on seeds developed by distant corporations. Members of the public also become dependent on the use of science within the regulatory system to prevent harm to health or the environment. More fundamentally, debates about the politics of food have been swept away amid promises that investments in the biosciences and biotechnology will inevitably deliver health, wealth and sustainability and at the same time meet global needs for feed, food and fuel. This means that political decisions about research priorities – and hence future pathways for food, agriculture and development – have been unaccountable. Unintended but foreseeable consequences (such as loss of food production capacity to agrofuels) have inevitably followed.

5.2 Good for the economy?

> "*If we go back to one of the motivating questions of this book – can science be a business? it would appear that the answer, based on the experience to date, would be no. The business of science in biotechnology has not yet been profitable, nor has it been particularly successful in turning scientific advances into drugs*". Professor Gary Pisano, Chair of the Technology and Operations Management Unit, Harvard Business School, 2006.[241]

> "*If Ventria's pharmaceutical rice were to escape into the commercial rice supply, the financial devastation to the US rice industry would likely be absolute. There is no tolerance, either regulatory or in public perception, for a human gene-based pharmaceutical to end up in the world's food supply*".[835] USA Rice federation, 2007.

> "*At least they* [the alchemists] *were doing it with their own venture capital*". Buchanan, Weiss and Fullerton (Penn State University and University of Washington Medical School), 2006.[326]

The biotechnology industry is not profitable: its survival depends on venture capitalists betting that they will make money from the biotech business in the future. Ernst and Young's Global Biotechnology Report for 2009 found:[836]

> Revenues of publicly traded biotech companies grew 12% to US$89.7 billion in 2008. The global industry's net loss improved 53%, from US$3 billion in 2007 to US$1.4 billion in 2008. The US industry reached aggregate profitability for the first time.
>
> Capital raised declined sharply in 2008. Companies in the Americas and Europe raised US$16 billion in 2008, a 46% decline from 2007. Initial Public Offering (IPO) funding fell 95% to US$116 million.
>
> Biotech venture financing remained relatively strong, falling only 19% from 2007's all-time record to about US$6 billion in 2008.
>
> Industry deal making remained brisk. The total value of mergers and acquisitions (M&As) involving US biotechs reached more than US$28.5 billion a record high when adjusting for megadeals that took place in prior years. In Europe, M&A transactions totaled US$5 billion.

Ernst & Young's analysis confirms that overall the biotech industry is still losing money. Pisano's 2006 analysis showed that profitability in the medical biotech industry has been flat for over 30 years and without the biggest biotech firm, Amgen, the industry has made steady losses throughout its history.[241]

Only a very small number of companies have been profitable, and between them Amgen and Genentech (the first biotech firm, founded in 1976, and now owned by the pharmaceutical company Roche) account for more than 50% of the cash generated by the sector. Further, because Pisano's analysis includes only publicly floated firms, the real situation is far worse. He concludes that "*it is virtually impossible to find other historical examples, at least at the industry level, for which such a large fraction of new entrants can be expected to endure such prolonged periods of losses and for which the vast majority may never become viable economic entities*". The underlying problem is that, whereas the science requires long-term cumulative learning, the biotech firms face market pressure to optimise short-term perceptions of value and to "*monetize IP*" through the system of creating spin-out companies, obtaining investment from venture capital and/or public equity, and trading IP via alliances with larger companies. Although it is possible that the sector just needs more time, Pisano argues that "*To date, predictions of future economic health for biotech have been consistently wrong*".

Since Ernst and Young's report, more recent figures suggest that financing for biotech companies has become substantially more difficult. In the second quarter of 2008, there was a dramatic fall in venture capital financing for biotech companies worldwide, as investors started to consider them too risky to invest in during the recession, or to transfer investment to clean energy companies.[837] By the end of 2008, 37% of biotech companies in Europe had less than one year of cash left and turned to their governments for rescue, lobbying through national industry associations and other interest groups.

In July 2001, a Boston Consultancy Group (BCG) report, *A Revolution in R&D Part II: The Impact of Genetics*, claimed that genetic information would deliver savings, in the best case, of more than $500 million and up to two years in developing each new drug.[838] The then senior vice president of GlaxoSmithKline (GSK), Peter Goodfellow (see Appendix A), warned delegates at a conference that the pharmaceutical industry was going to feel a backlash from US society, if people there appreciated that while US National Institutes of Health (NIH) spending on drug research had increased from $4.8 billion in 1980 to $20 billion in 2000, the number of new medical entities (NMEs) approved had gone down to 20 that year. Goodfellow proposed a number of solutions, starting with industry consolidation, with reference to the series of mergers that had brought about GSK, and including three technology solutions: genomics, genetics, and high-throughput chemistry. Leveraging scientific partnerships with publicly funded universities and research institutes was also highlighted at the conference as a way to address the problem.

However, despite massive investments in these technologies, the pharmaceutical industry's drug pipelines are increasingly empty and drug development has both slowed and become more costly. In 2005, biopharmaceutical R&D costs in North America reached a record $55.2 billion, more than double the amount spent in 1996, yet just 22 new drugs were approved by the US Food and Drug Administration (FDA) compared to the 53 new drugs approved in 1996.[839] Pharmaceutical companies are investing heavily in new biotech medicines (biologics) to attempt to address their empty pipelines: however, these are likely to be increasingly costly and targeted at smaller patient groups.[840,841] The industry is also shifting more into producing generic (off-patent) drugs, vaccines and household brands such as Ribena, Horlicks and Lucozade.[842] As recession bites, the industry has implemented cost-cutting strategies, and as a result of the biotech funding crisis, many smaller companies face potential bankruptcy as traditional sources of funding (debt markets, public offerings, private placements and convertible bonds) closed for these 'cash-burning' firms.[843] A shift to more use of generic (non-patented) drugs is expected to serve markets in poorer countries, cost-cutting health services in Europe, and the large population of people without health insurance in the USA.

As shown for example in Appendix A, substantial amounts of public money have been invested in public-private partnerships in an attempt to boost the knowledge-based bio-economy. A 'genetic revolution' in healthcare has been widely promoted in the absence of any analysis of the cost-effectiveness, impact on health, or impact on the NHS, of genetic screening in the general population. With the whole population potentially 'at risk' and eligible for preventive medication, the cost implications of genetic susceptibility testing have been described as *"staggering*".[844] A 2006 review found that conclusive evidence of favourable cost-effectiveness ratios for genetic testing is available only for few conditions: its author concludes that "*Based on current evidence, an era of healthcare consisting of gene technology built on widespread predictive testing is not desirable from*

a health economic viewpoint".[845] Although it is possible that some specific tests do prove useful and cost-effective in the future, this will depend on a variety of factors and does not imply that whole genome sequencing of the entire population would be of economic benefit, even if gene sequencing becomes much cheaper than it is today.[846]

Attempts to market 'genetic susceptibility' tests directly to consumers have fallen flat despite the enormous publicity given to this idea. The flag-ship genetic testing company DeCODE genetics, based in Iceland, declared bankruptcy in 2009. Its main rival, the market leader 23andMe, part-funded by Google, has sold only 30,000 gene tests over two years and been through two rounds of redundancies, despite being featured on the front page of Time magazine and the Oprah Winfrey show.[847]

Critics of the New Labour Government's commitment to the knowledge-based economy also point to the marginal growth in high-tech jobs (a slight rise in computer managers, software engineers and programmers) compared to a massive growth in low paid, routine and unskilled service work.[848,849] The knowledge-based bio-economy has fared worse than the knowledge-based economy in general. For example, over ten years, spin-out companies from bioscience departments within UK universities have generated only about 1,000 jobs; and BBSRC spin-out companies employ only 130 people.[850]

The European Commission's 2007 assessment of its biotechnology strategy, known as Bio4EU[28], is downbeat about what has actually been achieved in Europe in both medical and agricultural biotech. For example, it states that:

> The EU has a comparatively weak position in the development and marketing of biopharmaceuticals, with only one of the top ten products by sales produced in the EU (page 24).
>
> Recombinant vaccines produced using modern biotechnology have been successful, particularly against hepatitis B, and in veterinary medicines. However, vaccines play a minor role in the pharmaceutical market, representing about 1% of the worldwide market, and the veterinary market is also small.
>
> It is unclear whether modern biotechnology has significantly improved the R&D process for traditional drug discovery.
>
> New genetic tests have a lack of proven utility in clinical, social and ethical terms, and associated costs (page 41) and only a few pharmacogenetic tests have reached the market (page 45).
>
> Gene therapy and stem cell therapy face major technical challenges.
>
> The indirect contribution of modern biotechnology to economic growth by enabling a healthier population could not be discerned from the literature (page 47).
>
> GM crops have little economic significance because of low adoption rates (page 60);
>
> Molecular-marker assisted crop breeding (known as 'marker assisted selection' or MAS) may be profitable in the long-term, particularly for maize, however maize breeding is dominated by large companies and competition with the USA.
>
> No companies developing GM or cloned animals for food were identified in the EU and this would in any case raise animal welfare and ethical issues (pages 77 and 78).
>
> A number of concerns have been raised regarding the commercialisation of genetically tailored diets and nutrigenomics (nutritional genomics) and this field is still in its infancy (page 79).

The European Commission's 2007 Bio4EU report[851] claims (pages 6 and 7) that in 1995 modern biotechnology in the medicine and healthcare sector directly contributed to around 0.04% of the EU's gross value added (GVA) (a total of about 3.1 billion Euros, mainly in biopharmaceuticals, but including diagnostics and vaccines, Table 2.3); in the primary production and agro-food sector to 0.01% to 0.02% of the EU's GVA (a total of 3-5.6 billion Euros, of which 30% is in veterinary products, 28% in feed additives, 13% in food enzymes, 10% in diagnostics and 19% in plant, livestock and fish breeding, p. 80); and in the industrial biotechnology sector to around 0.08% of the EU's GVA. Overall, the report claims (p. 8) that modern biotechnology supports the generation of around 1.43-1.68% of the EU's GVA (which in 2005 was about 2,000 billion Euros[852]), or about 30

billion Euros, once downstream uses are included. This is a significant over-estimate because these calculations assume that in every application, 100% of the value added or turnover is due to the use of modern biotechnology (footnote 7, page 6), even though, in many applications, biotechnology will be just one of the supporting technologies in a production process (for example, the value of all detergents using biological enzymes was used, not just the value of the enzymes).

Even on this basis, the calculated 'added value' is much smaller than the projections made by the industry body EuropaBio in 1995. EuropaBio – cited in the UK Department of Trade and Industry's Genome Valley report (Table 13)[853] – claimed that the value of EU products using biotechnology was already 40 billion Ecu, and that by 2005 it would reach between 25bn and 250bn Euros, depending largely on 'consumer attitudes', with a base case scenario of 150bn Euros, assuming steady progress. The EC's 2002 Strategy report[181] also predicted major economic benefits, suggesting that by the year 2005 the European biotechnology market could be worth over EUR 100 billion and that, by the end of the decade, global markets could amount to over EUR 2 000 billion.

The reality would appear to be a poor return on the investment of 13.1 billion Euros of national governments' public investment over the four years 2002-2005, identified in the Biopolis report (Section 2.3).

The global value of the GM traits in crops and foods is estimated by the agricultural biotech industry to be US$7.5 billion, about 1% of the revenues of the pharmaceutical industry: so from an economic point of view the industry is relatively small.[258,854] Of the six companies involved in agricultural biotechnology, none has its headquarters in the UK, although two are based in the EU (the German companies Bayer and BASF undertake GM crop research at facilities in Belgium and Germany) and one multinational crop research facility is based in the UK (operated by the Swiss company, Syngenta).

Although sales of organic produce began falling in 2008 as recession took hold[855], the market is nevertheless much larger than that for GM crops, which are not grown commercially in Britain and in any case could only be sold as animal feed or biofuels. In January 2007, there was a total of 613,470 hectares of organically managed land in the UK, accounting for approximately 3.5% of the UK's total agricultural land area, whereas no GM crops were grown commercially. In France, the amount of land converted to organic production has been increasing rapidly[856] and, at the same time, there is overwhelming consumer rejection of GM foods[857].

Only two GM traits (herbicide tolerance and Bt insect resistance) have led to large sales of seeds globally. Four commodity GM crops: soya, maize, cotton and oil seed rape are grown on a commercial scale, covering approximately 2.4% of global agricultural and forestry land.[858] In 2008, GM maize (corn) had the biggest share of the market at $3.6 billion (48%); followed by soybean $2.8 billion (37%); cotton $0.9 billion (12%); and oil seed rape (canola), $0.2 billion (3%).[258] Through a series of mergers and acquisitions, by 2002 just six companies: Monsanto, Dow, and DuPont in the USA; BASF and Bayer in Germany; and Syngenta (Switzerland), owned 40% of US agricultural biotechnology patents on both key genes and transformation techniques[859] and through these can limit the ability of other firms to enter the market.[860] Therefore, any economic benefits of biotech seed sales are almost exclusively within the large corporate seed sector. There is evidence that, as a result of industry consolidation, the proportion of commercially-traded seed has grown, as farmers are less and less able to rely on the reuse and free exchange of seeds and must pay ever increasing prices for seeds, particularly in crops where GM seeds are prevalent (cotton, maize and soy).[239]

Reported R&D costs to develop a single GM crop with a specific trait are $50 million to $300 million.[861]

The US company Monsanto has 95% of the market in GM seeds. It is now collaborating with BASF in an attempt to retain its market dominance.[862] Each company is contributing $750 million to an R&D collaboration that over the next five years aims to discover and develop higher yield and drought-tolerant GM crops.[863] In 2009, BASF's chairman claimed that by 2020, BASF and Monsanto could be generating market value of well over €1 billion with plant biotechnology[864] – however BASF has already invested €1 billion in GM crop R&D over the past ten years (see Section 2.3) with no return to date on its investment. BASF received its first approval for commercial cultivation of a GM crop – a herbicide-tolerant soybean - from Brazil in February 2010.[865]

Tait and co-authors[866] note that Monsanto's strongly vision-driven approach, and its very early adoption of a combined agrochemical and biotechnology strategy, was possible because of its reliance on a single product, the herbicide glyphosate ('RoundUp'), which it sold linked to the sale of herbicide-tolerant ('RoundUp-Ready') GM seeds. For Monsanto, this strategy began to yield significant commercial rewards in the late 1990s with the rapid expansion of GM maize, soybean and cotton planted in North and South America. Between 1995 and 1999 Monsanto spent US $8bn-9bn buying or acquiring interests in biotechnology or seed companies around the world, including in Brazil and India.[398] In the US, Iowa's Attorney General has been investigating Monsanto's market practices to determine whether it violates antitrust laws amid concern from farmers about its monopoly position.[867]

Until 2008, Monsanto's profits had been rising rapidly, due to increased sales of 'RoundUp' - packaged with 'RoundUp-Ready' GM seeds – and of GM Bt maize (insect-resistant maize) for the industrial-scale production of biofuels (agro-fuels), subsidised by the US government.[868] However, analysts warned that future profits are likely to be hit because the cost of phosphate rock, a key raw material in RoundUp, that Monsanto mines, has surged ten-fold.[869,870] In 2009, the company's profits fell, due to stronger than expected competition in the herbicides market and it was forced to cut 900 jobs.[871] BASF also announced its dividend may fall.[872]

Other companies were slower to adopt Monsanto's strategy but are now also focused on selling an integrated package of GM seed and chemicals, concentrating on global commodity crops. For example, Bayer's 'LibertyLink' soybeans are genetically modified to be tolerant to its own herbicide 'Ignite', rather than to Monsanto's 'RoundUp' (glyphosate).[873] Bayer CropScience is currently already pursuing a total of 56 BioScience research projects involving six crops: at end 2009 it purchased a US company which has patented the largest collection of Bt genes in the industry (used in insect-resistant GM crops) and is also developing herbicide-tolerant crops.[874] In April 2009, the company announced that its Bioscience (Seeds and Traits) division would receive an increased share of Bayer Crop Science's R&D spend (up from 20% to 25%) and extend its activities in the research fields of stress tolerance and increasing yields.[875] It plans to invest some EUR 750 million in the development of new traits from 2008 to 2012.

Following the results of the Farm-Scale Evaluations, which identified likely adverse effects on farmland birds and other wildlife, and poor control of grass weeds, herbicide tolerant GM crops are not grown in Britain.[126] Soybeans and cotton are not suitable for the UK climate and the insects targeted by existing insect-resistant GM crops are not currently a significant problem in the UK.[253] Due to consumer rejection of GM foods, members of the British Retail Consortium, which includes all the major supermarkets, do not stock foods sourced from GM ingredients.[876] The market for GM crops in Europe is restricted to products which are not labeled for consumers: animal feed and some highly processed foods and biofuels.

It is worth noting that, even leaving aside the pros and cons of GM crops (discussed further below), the EU's Joint Research Centre (JRC) has concluded that the cost disadvantage of biofuels is so great with respect to conventional fuels (at least in the mix foreseen in the scenarios analysed), that even in the best of cases, they exceed the value of the external benefits that can be achieved.[877]

No GM crop yet has all the approvals needed for commercial cultivation in the UK.[878] Only one GM crop is grown commercially in the EU: Bt maize made by Monsanto (a GM corn resistant to corn borer using a gene encoding *Bacillus thuringiensis* (*Bt*) toxin). Spain is the only country growing significant quantities, which is used in animal feed.

Whilst some economic assessments of GM crops have shown on-farm benefits, derived from reducing production costs (weed control costs for herbicide-tolerant crops and pest control costs for Bt crops) these claimed net economic benefits for farmers have been highly variable, and are dependent on a number of assumptions made in the assessments.[889,890] In relation to herbicide tolerant crops, it is evident that a changed pattern of herbicide use is seen from one where a complex mixture is used to one where broad spectrum herbicide dominates. This has had advantages in terms of ease of application for large-scale intensive farmers in North and South America[879], leading to

some cost savings, but research in Europe suggests that for some GM crops this could be at the expense of adverse effects on farmland wildlife.[880] The emergence of herbicide resistance in weeds also threatens the long-term weed control effectiveness of the technology.[881] In relation to Bt insect resistant crops, the use of Bt maize and cotton appears to lead to some modest reductions in sprayed insecticide use, but these are small compared to the overall pesticide usage in these crops, and causality is difficult to establish.[882,662] Since Bt crops contain insecticide engineered into the crop, beneficial insects, farm animals and consumers remain exposed to the Bt toxin if they consume the crop as food.

Glover has reviewed published research on GM cotton, genetically-modified to produce the insecticide Bt, which is the only GM crop to have been commercialised widely in the developing world.[662] Reviewing studies conducted in China, India and South Africa, he finds that widespread assurances that GM crops have been demonstrated to be good for the poor are not well-supported by the evidence. In seasons where cotton bollworms cause a serious problem, the technology can help to prevent major crop losses, however, in other situations Bt cotton has performed poorly and significant question-marks remain over its future as pest-resistance emerges.

As pest-resistance develops and secondary pests emerge it may prove difficult to maintain the effectiveness of Bt toxin as a means of pest control. Bt-resistant populations of bollworm have now been identified in the US.[883] In China, initial economic benefits in terms of savings in insecticide use were lost as secondary pests emerged, requiring additional insecticide use.[884] Biodiversity measures in Bt fields do not seem to increase compared to non-GM fields because of the continuing use of insecticides on pests that are not sensitive to Bt.[885]

Existing GM crops have given variable yields, which are difficult to assess due to the multiple factors that may vary from year to year or farm to farm (such as soil, weather, irrigation, farm practices, pest pressures, farmer education, etc.). Methods of assessment of economic benefits differ widely, and – as with all crops – performance also varies considerably with location and time.[886] The environmental, institutional and social contexts all make a difference.[887] For example, one experiment found lower yields for glyphosate-resistant GM soybeans than conventional ones, but succeeded in narrowing the yield gap by applying fertiliser.[888] Most yield assessments have relied on farmer surveys, which are difficult to verify. Overall, studies do not find statistically significant increases in yield for most GM crops, with decreases in yields some studies, in particular for Bt soya.[889] Bt maize and cotton have shown yield increases in some situations (when there is a severe pest outbreak) but not others.[889,890] However, the methodology used in yield studies has been disputed by some researchers, because it fails to capture the dynamic nature of agricultural systems, the degree of ecosystem disruption, and the institutional conditions governing the use of pest control inputs.[891]

Companies such as Monsanto argue that the adoption of its technology across North America is a clear sign of benefits to farmers. On the other hand, agronomists at the University of Missouri Delta Research Center have identified that conventional soybean varieties are making a comeback, due to lower seed and weed-control costs, market price incentives and yields that rival Monsanto's Roundup Ready soybeans.[892]

In the UK and Europe, the future profitability of farming is more likely to be determined by national and EU policy decisions, particularly the Common Agricultural Policy (CAP), than by any small-scale cost-savings resulting from GM crops.[253] Globally, food prices and farm profitability are influenced by a wide range of factors, such as trade rules and oil prices, that have little connection with decisions on GM. Small-scale farmers are increasingly exposed to the risks of the global market, in which control of the commodities market by a small number of powerful players means that any price squeeze falls on the producers, who bear the bulk of the risk but little of the rewards.[753] Energy price rises, environmental degradation, conflicts and natural disasters all add to these risks.

Economic assessments have tended to make untested assumptions about the choices likely to be made by small-scale farmers in the Third World, where more than 2 billion people live on almost 500 million small-scale (less than 2 hectare) farms, including half the world's undernourished people and the majority of people living in absolute poverty.[893] In a survey of 334 farmers in Cuba, Guatemala and Mexico, Soleri *et al.* tested the assumptions that: (i) 'rational' farmers will choose GM crop

varieties because they will maximise profits, and; (ii) farmers are not risk adverse and prefer to maximise average profits, rather than minimise variance in profits or avoid years with very low profits. Their results did not support these assumptions: most farmers preferred farmer varieties for sowing and especially for eating, avoiding GM varieties. This preference was associated with being risk averse and with non-monetary preferences. The farmers made comments such as: "*How do we know it will work well? Seeds and other things do not work here the way they do in other places.*"; "*How do we really know it will be safe?*"; "*Commercial seed sources are unreliable, too risky for farmers. What if they don't produce any seed? Each farmer needs to have their own seed, and seed that is right for the location*"; and "*For us, maize is not a business, it is our sustenance*".

In addition, most of the research published on the economic impacts of GM crop introduction has considered a global market with no significant segmentation and has not looked at costs incurred to preserve the identity of GM and non-GM harvests and supply chains.[889] In a case study of GM herbicide-tolerant wheat, Johnson *et al.* found that producers and consumers of non-GM wheat would bear the extra costs of segregation and identity preservation, and that these were likely to be substantial and contribute to a small net loss of total economic welfare should GM wheat be commercialised.[894] Unmodified soya imported to the EU from Brazil to supply Europe's GM-free market is sold at a premium to cover additional costs of keeping it separate during transportation and storage.[895]

There has also been considerable effort placed in sourcing GM-free supplies and reformulating products. If GM crops are grown extensively in Europe, this would add considerably to the costs of producing non-GM foods. The costs to the organic sector of coexistence are considered to be higher than for the conventional sector because more stringent standards are put in place. [896]

As well as these obvious costs, there has also been public investment in developing testing systems and establishing specialist laboratories to test for the presence of GM ingredients and ensure labeling and traceability rules are being met.[897]

If segregation fails, substantial costs may be incurred. The US rice industry has already suffered lost markets, cancelled orders, import bans and restrictions as a result of contamination with a GM rice variety (LL601), owned by Bayer CropScience, which was not approved for human consumption.[898] In 2010, Bayer was ordered to pay $1.5 million in compensation to three US farmers for damages they incurred because of this contamination: about 500 similar cases are pending.[899] Contamination of Chinese rice with illegal GM seeds (from another variety, Bt63) has also occurred; the US company Prodigene was fined $250,000 in 2002 for contaminating a soybean crop with corn engineered to produce an experimental pig vaccine; and, in 2000, Aventis budgeted more than $1 billion to compensate producers and pay for the logistics of withdrawing maize that had become contaminated with a GM variety (known as 'StarLink') which had been approved only for use in animal feed.[835,900] Canada's entire $320-million flax seed industry was threatened when in 2009 it was found to be contaminated with an experimental GM variety called Triffid.[901] There have been many more GM contamination incidents around the world.[902] In many situations it is still unclear who will bear financial liability for cross-contamination of non-GM crops or co-mingling of seeds.[900]

Potential impacts on biodiversity have rarely been included in economic assessments. However, one study – of GM sugar beet in the EU – concluded that as soon as the average household's perceived loss of biodiversity caused by herbicide tolerant (HT) sugar beet exceeds 1 € per year, they would not benefit from the new technology.[903]

It remains unclear who will be liable for any environmental harm that might occur as a result of growing GM crops in Europe, as a result of the restricted scope of the new European Environmental Liability Directive, as well different interpretations of the legal loopholes available to companies in the different member states.[904] There will also be significant difficulties for organic or conventional non-GM farmers seeking to claim compensation for economic losses as a result of cross-contamination exceeding the threshold levels for crops to be sold as organic or GM-free.

In general, economic assessments have excluded potential harm to other markets, including both conventional GM-free and organic food.

Planting GM crops can affect organic markets due to the risk of cross-pollination, seed mixing, or contamination of machinery with GM crops. Smyth notes that the lost market for organic oil seed rape (canola), due to the planting of GM oil seed rape in Canada can be estimated at C$100,000 C$200,000, but "*this probably underestimates the opportunity cost of a market that many thought had significant potential for growth over this period*", and that Canada also lost access to the EU honey market, at an estimated cost of about C$5.3 million over a decade.[900]

Belcher *et al.* conclude that the relative ease of system-wide cross-pollination of farmland by GM crops indicates that significant external costs could be imposed on a typical farmer because of the inability to certify produce for sale in potentially lucrative GM-free markets.[905] Munro extends this analysis to consider whether planting patterns for GM and non-GM crops can allow all consumers to choose the type and quantity of foods they prefer and still maximize total profits for both GM and non-GM farmers.[906] His model suggests that even if GM crops occupy only 10% of farmland, over 60% could be denied to non-GM crops even if contamination spreads only as far as a single field around each farm. Thus, the presence of transgenic crops may eliminate or severely reduce the planting of organic varieties and other crops where some consumers have a preference for non-GM crops, so that co-existence of GM and non-GM crops may be impossible without strong regulation on planting patterns.

A 2007 study in Spain, based on in-depth interviews and participant observation, analyses the existing situation in Catalonia and Aragon, where the commercial cultivation of transgenic crops (Bt maize for animal feed) began in 1998.[907] The findings show that it difficult and expensive to segregate GM from organic and conventional production. As a result, the area devoted to organic maize was reduced by 75% in Aragon from 2004 (year in which the first analyses were carried out) to 2007 and by 5% in Catalonia between 2002 and 2005. The percentage in Catalonia is lower because the only available data come from the first years of the analyses, when the cultivation of GM maize was not as widespread as it is today.

Claims for future economic benefits from GM crops rest on the development of new traits and/or the use of existing traits in new crop varieties: either crops with health or nutritional benefits which consumers are persuaded to eat; or crops which produce non-food products such as industrial chemicals or pharmaceuticals[253], or are intended for use in industrial-scale biofuels (agrofuels). However, these new 'second generation' traits are expected to be much more difficult to develop than existing 'first generation' GM crops (see Section 5.3) and the use of crops for non-food purposes is likely to increase pressure on land use (See Section 5.1).

The role of 'nutrient enhanced' crops or functional foods in combating diet-related diseases is highly questionable: plenty of healthy foods (mainly plant-based foods such as fruits, vegetables and whole grains) already exist and are likely to remain a much more cost-effective means of tackling poor nutrition than premium-priced functional foods.[908,354] Further, the opportunity costs of investing in this strategy for health – rather than in population-based prevention strategies – could be considerable: the Strategy Unit estimates that the current costs of diet-related ill health to the NHS and society at large are probably in excess of £10bn a year; and that foregoing the health benefits that come with reaching dietary targets for salt, sugar, fruit and vegetables, and saturated fat costs Britain about £20bn a year.[909] If nothing is done to tackle the problem, the proportion of chronic disease including type 2 diabetes, stroke and chronic heart disease that is attributable to obesity will increase substantially. By 2050, the NHS costs attributable to overweight and obesity are projected to double to £10 billion per year and the wider costs to society and business are estimated to reach £49.9 billion per year (at today's prices).[910]

Second generation GM crops may also pose new threats to health or the environment and hence to existing industries;[911,912,913] and existing EU and US regulations may prove inadequate to prevent harm or economic losses resulting from contamination with these crops.[914] For example, the US rice industry strongly opposed the company Ventria Biocience's decision to grow GM rice in Kansas that

produces proteins found in human breast milk and saliva, on the grounds that there was "*no assurance or confidence that Ventria pharmaceutical rice can be kept separate from commercial food and feed rice*" and no prior risk analysis and risk assessment of the potential health affects that could occur when genetic material from the pharmaceutical rice is eventually found in commercial rice.[915] The USA Rice Federation warned that the decision to allow planting of this GM crop could be financially devastating to the industry.[835]

A comprehensive analysis of the costs and benefits of investing in GM crop research would include opportunity costs. In 2009, the BBSRC claimed that "*BBSRC institutes continue to produce excellent research underpinning UK priorities*" and cited evidence that John Innes Centre research has helped increase wheat production by £75m a year, and its impact on world wheat production could be as much as £4.6bn a year.[850] However, the BBSRC failed to report that most of this positive impact was achieved through a conventional breeding programme undertaken in the 1970s when the Plant Breeding Institute (PBI) was still involved in public good pre-breeding research and the BBSRC did not exist.[916] In 1998, Thirtle and co-authors showed that the returns to barley and wheat alone were sufficient to support the entire PBI budget and still give rates of return to applied research of between 14 and 25%.[917] In contrast, public investment in GM crop research in Britain has generated zero return.

5.3 Good science?

> "*The dated model of science, as a pyramid, with biochemistry and genetics at the base, leading to clinical advance at the apex, is wrong. It fails both as a description of clinical advance and, curiously, of how complicated biology is*." Jonathan Rees, University of Edinburgh, 2002.[918]

> "*There is a growing disparity at the heart of biomedicine. In some ways, the field is experiencing a golden age: the quantity of basic research is shooting off the charts and budgets are far higher than they were two decades ago. Yet the impact of this research is growing at a much more modest rate: new cures and therapies are ever more expensive to develop and worryingly thin on the ground*". Nature, 2008.[919]

> "*While reality remains reality, the consequences of the concepts used to describe nature can have a large impact on the direction of human understanding… A worry for those of us involved in plant physiology is to consider that we may have moved to something like a geocentric stage in examining the workings of higher plants. In our case, we are now dominated by a 'genocentric' view of evaluating plant growth, development, and responses to the environment*". Plant biologists Sinclair and Purcell, 2005.[920]

Although a wide variety of drivers, as described above, will impact on the ultimate role of genomics applications in society, a 2002 scenario workshop in the UK, involving scientists, social scientists, and people working in health policy and delivery, identified the functionality of genomics (how well do the applications of genomics work) as of the highest importance.[663]

In general, major scientific discoveries are by nature rare and hard to predict. It is much easier to claim that a new piece of research will bring major public benefit than it is to realise such claims. Contopoulos-Ioannidis *et al.* screened scientific publications in the top six basic science journals over the period 1979-1983 and found over a hundred articles where the authors suggested that their findings would have a major clinical application. Two decades later, the authors found that only five of these suggestions materialised into licensed clinical use and that only one had a major impact on current medical practice.[921]

The science journal Nature reports that, in research funding agencies, "*there is a growing perception that the enormous resources being put into biomedical research, and the huge strides made in understanding disease mechanisms, are not resulting in commensurate gains in new treatments, diagnostics and prevention*".[328]

Many governments have concluded that "translational" research is now needed to convert new biomedical discoveries into practical benefits for patients and this is being reflected in new structures for medical research funding (Sections 3.1.2 and 3.2.2).[922] Following the new agenda set by the US National Institutes of Health, the European Commission has earmarked much of its €6 billion health-research budget for the next 7 years for translational projects and the UK National Institute for Health Research has established 11 biomedical research centers devoted to translational research at a cost of £450 million over 5 years.[923] However, there are some problems with the model of translational research that has been adopted. One issue is whether it leads to the right research priorities for health: this is considered in Section 5.1 above. A second issue is whether the limits of science and biology are being adequately considered.

Although biomedical research has had some successes and also increased understanding, many treatments have failed due to unexpected side-effects and the complexity of disease progression and biology, or suffer from other ethical and/or practical limitations, such as the shortage of eggs for human cloning and the ethical implications of using them as the raw materials for new medicines.[924,925,926]

Martin and Morrison[927] consider genomic medicine under three broad headings:

The development of new gene-based diagnostics for common conditions;

The introduction of pharmacogenetics or so called 'personalised medicine';

The creation of novel biological therapies.

They conclude that technologies that are well entrenched in the clinic are: genetic testing for monogenic (single-gene) disorders; therapeutic proteins; and monoclonal antibodies.
The remaining technologies still face significant technical difficulties and will also have to overcome a number of commercial, clinical, ethical and regulatory difficulties.

Writing in the journal Science, Duyk notes that both public and private investment in medical research is predicated on the promise of a future impact on public health, but that the current research paradigm often confuses technical success with progress and fails to incorporate physiology and pharmacology (i.e. integrative, whole-organism, or organ system biology).[928] He notes the absence of expanding pipelines of medicines and states: "*We must acknowledge that we are falling woefully short of defining clear chains of causality that would effectively "link genetics to physiology" in a manner that could form the basis for robust, reliable models of complex biological processes*".

Similar problems arise in GM crop research, where the complexity of plant responses to environments has limited progress in developing traits such as salt-tolerance and drought-tolerance and nitrogen-fixation.

This section considers the prospects for genetic 'prediction and prevention' of disease and for the production of a new generation of GM crops. It suggests that complexity in biology, and interactions between biology and environments, may place fundamental limits on what can be delivered.

5.3.1 The genetic 'prediction and prevention' of disease?

"*Predicting disease occurrence many years in the future for persons who appear outwardly healthy is fraught with difficulty…We may have better technologies for extracting information out of raw materials, but we fall far short of our forebears in our ability to question the validity and relevance of the scientific enterprise*". Dr Robert Millikan, Director of the North Carolina Center for Genomics and Public Health, 2005.[929]

"…*it has been recognized that a reductionist approach is not sufficient for predicting factors affecting human health, yet current human health research has continued to focus heavily on the biochemical processes causing and modifying specific disease states in the individual, rather than critical analyses of the environmental determinants of health*". Scientists in the Environmental Systems Biology Group, US National Institutes of Health, 2007.[930]

"*The overall conclusion based on these arguments is that the predictive value provided by genetic screening tests for either disease susceptibility or normal variation will be too low to have widespread medical or social application*". Professor Andrew Wilkie, Oxford University. 2006.[931]

"*At* [Icelandic biotech company] *deCODE and elsewhere, the new genes linked to common diseases turned out to be rare or to have only small effects on individual risk*". Newsweek, 2010.[932]

"*While the importance of genetic data in understanding biology and etiology is unchallenged, we did not find evidence in this study of more than 19,000 women to incorporate the current body of known genetic markers into formal clinical tools for cardiovascular risk assessment*". Nina Paynter, Brigham and Women's Hospital, Boston, 2010.[933]

In Britain, the idea of a 'genetic revolution' in healthcare - involving a future in which individuals take a battery of genetic tests, at birth or later in life, to determine their individual 'genetic susceptibility' to disease – was strongly endorsed in the June 2003 White Paper 'Our inheritance, our future: Realising the potential of genetics in the NHS', and significant financial and political investment has been made in transforming the National Health Service to implement this approach (see Appendix A).[934] However, there remain many scientific critics of this strategy, who argue that it is likely to be of limited benefit to health.[935,936,937,938,939] Although the identification of rare genetic mutations can provide useful information to individuals, including people at risk of (relatively rare) familial forms of cancer, the evidence that screening people's genomes will prove useful to predict and prevent common diseases, such as heart disease or cancer, is extremely limited.

There is widespread recognition that identifying causal associations between genetic variants and common diseases may help identify biological pathways and disease mechanisms. However, it is less clear whether genetic variants will be of value in predicting individual risks of common, complex diseases, and the claim that genetic susceptibility screening will be good for health is strongly contested in the scientific literature.

Recent papers, whilst confirming statistical associations between some common genetic variations (polymorphisms) and common diseases, have shown very limited potential to benefit health by screening the genomes (genetic make-up) of individuals in the general population (as opposed to undertaking specific tests in a minority of high-risk families). For example:

- Nine genes showing replicated associations with type 2 diabetes explain only a very small proportion of the aggregation of this condition in families[940] and testing for these genes – plus another nine that have been discovered more recently - does not appear to improve prediction of type 2 diabetes compared to measuring existing risk factors (such as body mass index and fasting plasma glucose concentration).[941,942,943] A more recent paper has confirmed these findings.[944]
- Of 32 candidate breast cancer susceptibility genes, all may be false, because the odds ratios from statistical meta-analyses (studies combining all previous research) are reducing over time and converging to showing a negligible risk.[945,946,947] Seven common genetic variants (known as single-nucleotide polymorphisms or SNPs) that have recently been associated with breast cancer risk do not improve prediction of breast cancer compared to the National Cancer Institute's existing Breast Cancer Risk Assessment Tool (based on ages at menarche and first live birth, family history of breast cancer and history of breast biopsy examinations).[948]
- No region of the human genome has a uniformly large impact on hypertension and susceptibility genes for hypertension may be very difficult to detect.[949] Recent studies have found some new genetic variants with individually small effects, but with only partial overlap between study findings.[950]
- An overview of meta-analyses of genetic associations for heart attack or coronary artery disease, concluded that even with large-scale evidence from statistical meta-analyses, significant associations may be subject to bias.[951] Genetic variants associated with increased

risk of early-onset heart attacks explain only about 2.8% of the observed differences between individuals.[952]

A study of nine common genetic variants (polymorphisms) associated with cholesterol levels found that use of the genotype did not improve clinical risk prediction in 5000 subjects.[953]

The much-hyped 'fat gene' (the FTO gene), combined with other known genetic factors, explains less than 1% of the differences in Body Mass Index (BMI) observed between individuals. Only about 6% of observed differences in cholesterol levels in the general population and 1% the observed differences in blood pressure have been explained by the genetic factors so far identified.[954,955,956,957,958]

In general, common genetic differences are not more but less predictive than most other types of test, and no common genetic variants exist either singly or in combination - that meet medical screening criteria for the general population.[959] Whilst some scientists argue that predictions will improve in future, when hundreds or even thousands of genetic variations are combined to calculate an individual's risk[960], others argue that these claims are unrealistic and that even combining multiple genetic variants cannot be expected to give useful or reliable predictions of most diseases in most people.[961,962,931]

In addition, confirmed genetic links, such as the link between the FTO gene and increased risk of obesity, are not useful to tailor medical advice, because encouraging a healthy diet is good for everyone.[963] The FTO gene and other genes that have been associated with obesity to date also appear to affect appetite, rather than metabolism.[964] Hence, their existence does not imply that some people can eat more than others whilst remaining thin, or that efforts to eat less and exercise more should only be targeted at a minority of the population based on their genetic make-up.

Scientists from the US National Cancer Institute and the University of Helsinki have questioned whether searching for common inherited genetic variants that increase susceptibility to cancer is worth the resources being spent.[965] They note that:

Evidence from biology, migration studies, and twin studies suggests that common cancer susceptibility genes are unlikely;

Even if susceptibility genes were identified, further large, expensive studies would be needed to show the clinical benefit of targeting the proposed intervention at those individuals with the genetic variant(s).

Early expectations for highly predictive tests were based on the common disease-common variant hypothesis (CD-CV), which states that the genetic component in the causation of common diseases is likely to arise from a relatively small number of genes. This now appears unlikely to be correct, except in special cases.[966] To be meaningful, multiple genes and gene-gene interactions need to be included in calculations of genetic risk and for these risk profiles to be useful, interventions must be proven more effective for individuals with certain genotypes.[967] These and other limitations of genetic 'prediction and prevention' are not unexpected, but result from the underlying complexity of biology, and the role of chance and multiple environmental factors in disease.[968,969,970] As Sarkar notes, as the Human Genome Project proceeded there were expected to be increasing controversies over claims of the genetic origin of complex traits, including diseases and behaviours, and: "*The reason for this is that most of these controversies are ultimately not generated by inadequate data…Rather the controversies usually arise from more difficult methodological and interpretive issues*", such as whether 'heritability' (calculated from twin studies) truly shows a genetic basis for anything.[971]

In November 2008, the journal Nature published an article called "*The case of the missing heritability*", which stated: "*When scientists opened up the human genome, they expected to find the genetic components of common traits and diseases. But they were nowhere to be seen*".[387] It reports that "…*even when dozens of genes have been linked to a trait, both the individual and cumulative effects are disappointingly small and nowhere near enough to explain earlier estimates of heritability*". In April 2009, the New York Times also reported that genes show limited value in predicting diseases and highlighted the growing debate between geneticists about where to find the 'missing heritability'.[972]

In general, twin studies exaggerate the importance of shared genetic factors in explaining why diseases run in families, because the classical method of analysing twin data assumes that there are no gene-gene or gene-environment interactions; no confounders; and that behaviours, such as appetite, have no element of choice but are entirely predetermined by a person's genes and their environment.[973,974] Heritability varies with environmental conditions, so there are significant differences between populations in natural environments and those in the controlled, constant environments for which quantitative genetic theory has been developed.[975] The information about genetic risk that can be given to individuals and their families depends on the assumptions made about how multiple genes and environment work together: yet these theoretical underpinnings are still lacking.[976]

The usefulness of genetic information as a means to 'personalise' medical advice is therefore seriously questionable, because special conditions must be satisfied to achieve high clinical utility.[973] Although these conditions may be met for some diseases in some people, it seems highly unlikely that most common genetic variants – either singly, or in combination – will satisfy medical screening criteria for the general population.[974]

There has recently been a shift to developing more complex computer algorithms to try to improve predictions: but the predictive value of these algorithms is also very limited, suggesting that even an optimistic view of a role in medicine would be restricted to testing relatives of people who have developed certain conditions at a young age.[977] Complex systems – like the weather – are not highly predictable far in advance, so there are likely to be inherent limits to disease predictability, even if algorithms can be improved.

In policy documents, there has been a shift to using the new term 'stratified medicine' to mean prescribing drugs based on the results of genetic tests (known as 'pharmacogenetic' tests). However, 'germline' pharmacogenetic tests have in general also shown low clinical utility. A 2006 review considered gene testing in relation to eleven different enzymes known to effect response to numerous different groups of drugs. It concluded that a case for routine genetic testing before drug administration could be made only for very few drugs.[978] Genes clearly play an important role in the metabolism of some medicines and a few cases will be relatively clear-cut. However, most reactions to medicines are complex, there are difficulties in reproducing findings, and many tests have limited predictive value and uncertain or limited clinical utility.[979,980,981] Multiple biological pathways are likely to be involved in drug metabolism and many other factors are also important, including exposure to other medicines, supplements, toxins, allergens and infections; the patient's diet, smoking and drinking habits; and their age, size and sex.

There is no doubt that genetic variations can make a significant difference to the concentration of a medicine in a patient's blood, but there is significant complexity and the extent to which drug response is heritable is poorly known.[982] A wide variation in response is only likely to be important if the drug has a 'narrow therapeutic range'. Such drugs are only safe and effective at a particular concentration and can be dangerous or ineffective if the concentration is unexpectedly higher or lower, even by a small amount. However, even in such cases, it may be difficult to calculate correct doses in advance using genetic test results because of the complexity involved. The anti-coagulant drug warfarin has been one of the most extensively studied, because clear genetic effects on drug response have been identified and internal bleeding is a serious side effect in many patients: however, a recent review concluded that there was not sufficient evidence to support the use of pharmacogenetics to guide warfarin therapy, because the highest quality study found no significant difference in health outcomes.[983] Studies continue and it is possible that this or other tests might prove useful in the future. However, in general, it remains unclear why 'germline' pharmacogenetic testing would be medically justified, except prior to prescribing a few specific drugs.

Pharmacogenetics is proving its importance in the field of cancer, but these tests involve looking for changes in gene expression that occur in a cancer when a patient has already become ill. The National Institute of Clinical Excellence (NICE) has issued appraisal guidance the use of the biological cancer drugs trastuzumab (Herceptin) and cetuximab (Erbitux) in this way.[165] However, use of these 'genetically-tailored' drugs does not involve testing the genetic make-up that a person is born

with, and is not relevant to the plan for 'early health' described in Section 4.2 and Appendix A: 'somatic' testing (of mutations or gene expression in the cancer) can only be performed once someone has developed cancer.

This does not mean that genetics and genomics has no value in medicine, or that there is no useful research which could be conducted in these areas. For example, genetic services in the NHS play a valuable role in diagnosing rare genetic disorders. Some women from the minority of very high risk families choose to take tests for mutations in the BRCA1 and BRCA2 genes that are thought to account for about 5% of cases of breast cancer, which have relatively high predictive value. New services, also involving 'cascade screening' (testing family members) may be useful to identify other groups of people, such as those at high risk of an unexpected heart attack at a young age.[984] Some new pharmacogenetic tests may be developed in the future, particularly tests of the changes in gene expression that occur when someone develops cancer. However, none of these applications implies a need to sequence the genomes of large numbers of healthy people or to transform the health service to create a new system geared towards the 'prediction and prevention' of disease.

Studying the genetics of complex diseases can sometimes provide clues about the mechanisms of these diseases by identifying new biological pathways. Improved understanding of biology is valuable in itself and can perhaps leading to new insights and treatments in the future. However, as new research reveals ever increasing complexity – including complex interactions between genetic and 'epigenetic' factors (chemical changes other than the DNA sequence itself)[985] – it is important that theoretical understanding and R&D priorities keep pace with these developments. Although many critics raised such issues in the run-up to the Human Genome Project, recognition of complexity is only now beginning to re-appear in innovation strategies. For example, the Technology Strategy Board (TSB) stated in September 2009 that: "*the complete causal pathway of common multifactorial diseases is likely to differ between individuals, and this inherent variability means that accurately predicting risk at an individual level maybe difficult to achieve*".[161]

5.3.2 A new generation of GM crops?

"*Development of first generation GM (genetically modified) crops, concentrating on input traits such as herbicide, insect pest and disease resistance, was based on early scientific research and relatively simple technology that could be implemented fairly rapidly. However, most companies have not profited greatly from this early technology and they see second-generation GM crop technology as being much more difficult to achieve*". Professor Joyce Tait and co-authors, Policy Influences on Technology for Agriculture (PITA), 2002.[866]

"*GM may be less helpful in enhancing quantitative traits that depend on the action of many genes, each of which has a relatively small impact on the trait. Examples include complex phenomena such as the dependence of crop yield on environmental conditions*". Strategy Unit, 2003.[253]

"*In conclusion, if achievements made to date in developing salt-tolerant plants through conventional breeding or genetic engineering are compared, it is not difficult to infer that conventional breeding has been relatively successful in improving the yield potential, disease resistance, and abiotic stress tolerance of most crops, but undoubtedly, at the expense of little resources and with little or no knowledge of underlying biochemical pathways of stress tolerance. In contrast, genetic engineering has resulted into relatively little success particularly in terms of enhanced crop stress tolerance despite the fact that large sums of resources have been utilised in generating transgenic lines of different crops*…" Muhammad Ashraf and Nudrat Aisha Akram, University of Agriculture, Pakistan, 2009.[986]

"*The management and agronomy of crops are typically more important as drivers of yield than genetics. They also make crop production more sustainable*." Agricultural scientists, John Porter and Bernd Wollenweber, Denmark, 2010.[987]

It can also be argued that agricultural biotechnology may be failing to deliver partly because technical difficulties in plant genetic modification limit what can be achieved, due to the underlying complexity of biological systems.

The first GM plants were produced in 1984, yet only two traits (herbicide resistance and insect tolerance) are in commercial production. As noted in Section 5.1.2 a major difference between the 'Green Revolution' and the 'Gene Revolution' is that the beneficial traits – such as high yield and salt and drought tolerance – claimed for future GM crops do not yet exist. Claims that GM crops will benefit the poor therefore rest largely on assumptions that a new generation of products will be developed if sufficient investment is made.

Tait and co-authors note that second generation GM crops, involving output traits such as altered nutritional properties are much more difficult to achieve than first generation GM crops, which concentrated on relatively simple input traits such as herbicide, insect pest and disease resistance.[866]

Much of the current focus of research within Europe (see Section 3.3.5) is on plants with 'enhanced' nutritional value, or on plants to produce industrial products, including pharmaceuticals.

A 2006 review by the Office of Technology Assessment at the German Parliament (TAB)[517] found that :

> The production of GM functional foods (with supposedly 'improved' nutritional status) was still at the proof of concept stage. There were technical problems, marketing and food safety challenges and economic uncertainty because alternative sources were available.
>
> No drug produced from a plant was yet approved for use and that cost benefits would only be gained with open air growing which may prove unrealistic because of safety concerns.
>
> Plant-made industrial products such as oils and starches had not met expectations in terms of yield and side effects were common. Alternative methods of production were progressing more quickly.

The TAB report found that by 2006, eleven GM plants with modified output traits had been licensed in various countries, although nine were irrelevant for the purposes of the report (five tomatoes with longer shelf life, a carnation with longer shelf life and two with blue flowers, a tobacco with reduced nicotine content). The two remaining varieties, a rapeseed with high lauric acid content (Laurical), which was licensed in the USA as long ago as 1994, and a soy bean with increased oleic acid content (licensed in the USA since 1997) had both had been unsuccessful on the US market, and are accordingly not grown to any effective extent. In the EU, only the three carnations had been licensed since 1997/98. The licensing pipeline contained (since 1997) 21 applications, including one 'plant made industrial' GM plant, a potato with modified starch composition. This BASF potato (called Amflora) was approved for commercial cultivation in the EU in March 2010. The potato is designed for use in commercial starch production primarily for the paper industry, and the potato pulp is expected to be used in animal feed. However, the largest German and second largest world-wide potato starch producer immediately announced it would not cultivate the crop.[988] Some EU member states objected to the approval (made by the Commission), with particular concerns raised about the inclusion of an antibiotic resistant marker gene.[989]

The TAB report concludes that: "*The relevant documents typically focus on scenarios for the use of possible products from GMP* [genetically modified plants] *modified for output traits, describing scenarios for production and cultivation which have little contact with reality, and completely ignore regulatory aspects and realistic coexistence scenarios*".

Graffe and co-authors provide an updated (2009) biotech industry view of GM plants currently under development, based on two surveys of the global R&D pipeline.[990] The primary survey was backward looking, drawing upon published records to reconstruct the histories of 558 product quality innovations, 243 of which reached initial field trials (mainly in the US). Consistent with the TAB report, the survey found that only 5 of these products had been commercialised: one involved altered oils or fatty acids (presumably one of the products described in the TAB report as being unsuccessful on the US market); one involved reduced non-nutrients, allergens or toxins (presumably the reduced-nicotine tobacco included in the TAB report); two involved altered ripening, freshness or shelf-life (both GM tomatoes); and one involved aesthetics or convenience (a GM carnation).

A second forward looking survey reported by Graffe and co-authors collected predictions from agricultural biotech companies and industry analysts about future product commercialization. It identified 28 quality innovations expected by 2010 (of which 17 involved altered nutrient content), and a further 21 by 2015 (of which 13 involved altered nutrient content). Other than altered nutrients, expected properties were extended shelf-life and fibre quality (for pulping or animal feed digestibility), plus a blue rose. The commercialisation dates are estimated by the organisations developing the products and/or by the authors. Whilst the authors speculate that increased regulation may have been the cause of slowed innovation, other potential causes are the difficulties in modifying complex traits, and the complexities of evaluating benefits and harms (safety and 'food claims') for nutrient-altered crops.

The EU's Joint Research Council (JRC) also published a report on the global pipeline of GM crops in 2009.[991] It lists crops that are already in the pipeline and may be marketed worldwide in the short-term (2-3 years) to medium term (7-8 years from 2008). The pipeline was compiled for the seven crops for which GM crops already exist or may be marketed in the near future (soybean, maize, rapeseed, cotton, sugarbeet, potatoes and rice). The report predicts that by 2015 insect resistance and herbicide tolerance traits will still be dominant (probably including many 'stacked' traits conferring resistance to multiple herbicides), but that new commercial traits will also be available involving altered crop composition (altered oil and starch content and nutrient profiles). Salt-tolerant and drought-tolerant GM rice are predicted to be commercialised in India after 2015 (Table 12), but the developer is unnamed and the predictions are based on single gene modifications, which are unlikely to be realistic (see below).

The JRC report does not account for potential delays in approvals resulting from concerns about impacts on health or the environment, or broader social concerns, in countries such as India or China. In 2010, the Indian Government put a decision to commercialise Bt brinjal (aubergine) on hold, following massive public protest.[992,993] The Indian Environment Minister announced that he would hold a series of public consultations before finalising his decision on release of Bt brinjal, the first GM food crop to come up for consideration by the government (GM cotton is already grown in India). Issues raised included the lack of labeling laws in India, the impossibility of monitoring any health effects, and conflicts-of-interest on the Genetic Engineering Approval Committee.[994] India is the centre of origin for brinjal, so there are also concerns that growing Bt Brinjal could lead to the loss of original varieties by transgenic cross-pollination.[995] There is also no liability law in the event of contamination of non-Bt brinjal by the GM variety.

There is a long history of claims that GM technology will deliver crops of significant benefit in 'feeding the world', particularly salt-tolerant and drought-tolerant crops and nitrogen-fixing crops.

The US Office of Technology Assessment (OTA) report, published in 1981[176], argued (page 162) that "*If the genes can be identified, the possibility of actually transferring those for salt tolerance into plants makes the adaptation of plants to high salt, semiarid regions with high mineral toxicities or deficiencies a more feasible prospect* [than with traditional breeding]" and stated "*Such techniques could be applied to agricultural programs in less developed countries, where, commonly, supplies of fertilisers and lime are scarce, the potential for irrigation is small, and adequate support for technological innovation is limited. In addition, the United States itself contains marginal land that could be exploited for forest products and biomass. The semiarid lands of the Southwest, impoverished land in the Lake States, and reclaimed mining lands could become cost-effective areas for production*". The 1981 OTA report also noted that "*geneticists are looking into the possibility that the genes for nitrogen fixation present in certain bacteria (called "nif genes") can be transferred to the major crops*" in order to reduce dependency on the nitrogen fertilisers needed for industrialised agriculture. The report stated (page 163): "*Reducing the amount of chemically fixed nitrogen fertiliser and the cost of the natural gas previously used in the chemical process would be the largest benefit of successfully fixing nitrogen in crops. Environmental benefits, from the smaller amount of fertiliser runoff into water systems, would accrue as well. But is it difficult to predict when these will become reality. Experts in the field disagree: some feel the breakthrough is imminent; others feel that it might take several decades to achieve*".

Nearly three decades later, the Royal Society's 2009 report on science and global agriculture has revisited some of these ideas. The report argues for £50 to £100 million per year of additional government spending on agricultural research, including research on a new generation of GM crops (a total of £2 billion over ten years).[259]

The Royal Society report (page 34) describes three approaches to engineering nitrogen-fixation into non-legume crops, all of which are described as unlikely to deliver anything (at best) for ten to 15 years. It also notes (page 28) that "*Several GM lines have been developed with drought and other stress tolerances, but they remain to be tested in the field*" and "*In addition, several targeted genetic approaches to salt tolerance involving GM have shown promise*". The report endorses spending more public funding, via the research councils on such "*long-term high-risk approaches*" (Recommendation 4). However, it does not assess the reasons why these supposedly traits have not yet been delivered, or the opportunity costs associated with continuing to invest in areas where the prospects of success may be rather limited.

Godfray and co-authors argue that a "*multifaceted and linked global strategy is needed to ensure sustainable and equitable food security*".[996] The authors – who are all involved in the UK Foresight 'Global Food and Farming Futures' project[997] – recognise the complexity of the challenge, and discuss a wide variety of factors of importance to food security, including the role of markets, transport and infrastructure, the importance of reducing waste and the role of changing diets. They also advocate investment in developing a new generation of GM crops, whilst recognising "*the need for this technology to gain greater public acceptance and trust before it can be considered as one amongst a set of technologies which may contribute to improved global food security*". Based on the claims made in the Royal Society report and a book by GM crop scientist John Gressel, they list predicted timescales for the development of new GM crops shown in Table 4.

Table 4: Godfray et al (2010): Predictions of new GM crops

Time scale	Target crop trait	Target crops
Current	Tolerance to broad-spectrum herbicide	Maize, soybean, oilseed rape
	Resistance to chewing insect pests (Bt crops)	Maize, soybean, oilseed rape
Short-term (5-10 years)	Nutritional bio-fortification	Staple cereal crops, sweet potato
	Resistance to fungus and virus pathogens	Potato, wheat, rice, banana, fruits, vegetables
	Resistance to sucking insect pests	Rice, fruits, vegetables
	Improved processing and storage	Wheat, potato, fruits, vegetables
	Drought tolerance	Staple cereal and tuber crops
Medium-term (10-20 years)	Salinity tolerance	Staple cereal and tuber crops
	Increased nitrogen-use efficiency	
	High-temperature tolerance	
Long-term (>20 years)	Apomixis (where plants produce seeds without the need for fertilization)	Staple cereal and tuber crops
	Nitrogen fixation	
	Denitrification inhibitor production	
	Conversion to perennial habitat	
	Increased photosynthetic efficiency	

However, the paper does not discuss the basis for these estimates, or the likely costs, or any of the potential downsides discussed elsewhere in this report, although it acknowledges that intellectual property "*is a major governance challenge*". Nor does it make any comparison with the costs and benefits of alternative approaches, such as traditional plant breeding; marker-assisted selection (MAS) (which uses genetic knowledge to assist conventional plant breeding);[998] or agro-ecological approaches, which have shown potential to increase yields and bring other benefits to small-scale farmers in poor countries[825].

Complex traits which involve many genes and complex interactions between plant physiology and the environment are still poorly understood. For example, Flowers notes that after ten years of research using transgenic plants to alter salt tolerance, the value of this approach has yet to be established in the field. He comments that: "*It is surprising that, in spite of the complexity of salt tolerance, there are commonly claims in the literature that the transfer of a single or a few genes can increase the tolerance of plants to saline conditions*".[999] Similarly, the understanding of the physiology of plant yield in water-limiting conditions is described by Tuberosa and Salvi as "*rudimentary*" and they note that: "*despite all the recent technological breakthroughs, the overall contribution of genomics-assisted breeding to the release of drought-resilient cultivars has so far been marginal*".[1000]

Dozens of different physiological traits (such as plant leaf area, rooting depth and chemical responses to sunlight and water) affect a plant's response to drought conditions.[1001] Selection for grain yield under water-stressed conditions has been hampered by low heritability, polygenic (multiple gene) control, epistasis (gene-gene interactions), and significant gene-environment interaction. Cattivelli *et al.* report that, in the last decade, many differently genetically engineered plants have been proposed and tested for improved performance under drought. However, tests usually apply 'shock' treatments to these experimental plants while for most crops drought tends to develop slowly as the soil dries. Tests have also usually only assessed survival, not yield potential. Single gene effects are likely to be small because of the complex nature of drought tolerance and, notably, effects may depend on genetic background, with, in one example, only one of four genes for root length having an effect when transferred from one rice variety to another. Cattivelli *et al.* argue that only field trials under real stress conditions would allow for definite conclusions to be drawn.

Sinclair and Purcell question the current focus of research on identifying genes that might be relevant in plant development and growth and argue that much of this 'genocentric research' "*appears to be organised and executed without regard to the practical needs of enhancing plant performance under applied conditions*".[920] The genocentric view has caused a preponderance of plant physiological research to focus on genes and DNA as the ultimate description of plant life. However, in reality, the analogy of the genetic code as a blueprint to describe plant development and growth is misleading. They note that, although empirical plant breeding coupled with improved plant husbandry has resulted in greatly increased crop yields, there has been little success in increasing potential crop yield that can be directly attributable to either classical plant physiology or genocentric research, and "*it has not been easy to 'convince' plants in targeted physiological studies to set aside the successes of evolution and function in the manner desired in agriculture*".

Sinclair and Purcell claim that there is a widening disconnect between the reality of plant performance in the cropping environment and research priorities. While improved plant performance under water-limited conditions would be hugely beneficial, much of the actual research reflects serious misunderstandings about the fundamental limitations of water in the agricultural environment and what is needed to increase crop yields. The four main problems are:

> Drought survival is not important for agriculture, because yield losses are rarely as a result of failure to survive drought: a better focus would be on improved exploitation of the available water before crops are subjected to severe drought.
>
> Continued growth under water-deficit conditions (via 'osmotic adjustment') is not generally a desirable trait because, as soil water supply becomes low, plants need to stop plant growth to minimise further water loss and a worsening of the soil water-deficit.
>
> Dynamic interactions between plants and environment mean that yields for a given trait will depend on local conditions and be highly variable: however, a trait that offers a mean

increase in yield over a number of years but suffers yield loss in a few years will not be of use for growers.

Gene activity as a consequence of drying over a few hours or days in laboratory experiments may well be quite different from that expressed by plants in a cropping environment.

Sinclair and Purcell explain that yield is an emergent trait responding to a number of genes and confounding factors in the plant and surrounding environment. They argue that this means that superior physiological performance of a trait at a lower level diminishes at each higher level of complexity leading to crop yield. For example, photosynthesis was extensively studied as a trait that might be enhanced to increase crop yield. However, although genetic variability in leaf photosynthetic activity was identified and found to be heritable, no yield benefits were found. One reason is that nitrogen for increased seed growth must also be accumulated and stored in the plant for eventual use in generating seed yield. Calculations showed that, depending on assumptions about the physiological impact on plant nitrogen accumulation associated with the increase in photosynthetic activity, grain yield could either increase by 6% or decrease by 6%. The authors conclude that: "*It is not surprising that many years of intensive investigation of increasing photosynthetic capacity have not resulted in increased crop yields*". They examine the few rare cases where crop improvement has resulted from fundamental physiological research and argue that it is understanding of interactions within plants and between plants and dynamic environments that can provide the key link between gene activity and crop yield, requiring a balance between the fundamental and the practical, including consideration of the extent to which growers will be economically benefited by having crops with specific traits.

Ashraf and Akram report that conventional plant breeders have succeeded to some extent in producing salt-tolerant lines/cultivars of some crops through conventional breeding, using very limited resources.[986] Success has been limited mainly by the low magnitude of genetic variation in the gene pools of most important crops. Considerably greater resources have been invested in trying to produce salt-tolerant GM crops, however this approach has not been successful. The main reason is that in most cases only a single gene has been transformed, although it is now widely known that salt tolerance trait is multigenic in nature and a multitude of physiological, biochemical and molecular processes are involved in the mechanism of salt tolerance. The authors conclude that conventional breeding, whilst limited, has been relatively successful compared to transgenics.

Similar problems plague claims that the 'next-generation' of industrial-scale biofuels (agrofuels) will provide a technical solution to the growing problems caused by diverting food crops and land to fuel production.[360] Second-generation agrofuels are being promoted as the answer to these concerns amid claims that fuel will be provided from a range of biological materials currently regarded as waste; carbon savings will be far greater than when using food crops; and food supplies can be reserved for feeding the world's growing population. The ultimate aim is to develop genetically modified micro-organisms (GMMs) that can digest cellulose and produce ethanol, but, so far, the GMMs appear to be struggling to produce the high yields obtained from ethanol production using sugar or grain crops. Little funding has been allocated for examination of the environmental or plant health issues connected to the development of GM micro-organisms that contain potentially harmful traits. Nor is there any research into whether these traits could be passed on to naturally occurring micro-organisms, or whether they could be released into the environment.

The EU's Joint Research Centre (JRC) has noted that unpredictable technology breakthroughs are needed to make the cellulose-to-ethanol process (which best uses straw and wet biomass) competitive. The JRC concludes that it is unlikely that second generation biofuels will be competitive with first generation by 2020 (the date the EU has set for a binding minimum target for biofuels use of 10% in all member states), and that they will anyway use largely imported biomass. Their economic analysis indicates that second generation biofuels will be much more expensive than first generation biofuels, with costs dominated by investment cost of the plant.[877] However, EU science and innovation policy, which remains driven by the idea of biotechnology as a driver for growth and sustainability, appears unable to adjust to these assessments of technical, scientific and economic claims. A new generation of 'sustainable biorefineries' is now being described by the EC as "*the back-bone of the knowledge-based bioeconomy*".[1002] The EC issued a 55 million euro call for R&D proposals on biorefineries under the FP7 research programme in 2008.[1003]

5.4 Winning support from the public?

> "*Once the pursuit of science becomes heavily geared to profit, which the public feels it is not sharing in any major way, scientists may be compromised. They may be perceived as ... not working merely for the public good*." Lord Winston, 2005.[1004]

> "*If the promise of tangible clinical benefits is used to counter an intuitive moral reservation about a given technology, we may be creating a circumstance where loss of public trust is inevitable*". Timothy Caulfield, Director of the Health Law Institute, University of Alberta, 2005.[367]

Another important question is the extent to which there is public support for the knowledge-based economy and the approach to science and technology it is seeking to promote.

The 2008 DIUS/RCUK 'Public Attitudes to Science Survey' showed that public trust in scientists continues to be strongly influenced by their perceived independence from government and big business. It also indicates a demand for more consultation on scientific issues with 75% of those surveyed wanting to hear about potential new areas of science and technology before decisions are made.[1005]

It is beyond the scope of this report to analyse the numerous studies and reports of public attitudes to GM crops in the UK and Europe. However, most analyses have raised issues of public trust in political, regulatory and scientific institutions.[1006,1007,1008,1009,1010]

Whilst the public have generally been supportive of investments in the medical applications of the biosciences, including genetics and genomics, a number of studies indicate concerns about issues such as lack of regulation and consent (see Appendix A). Focus group research in the UK has shown that members of the public instinctively distrust data-sharing of medical information with the private sector and believe that such data will inevitably be used for marketing purposes.[1011] There is a general suspicion of all vested interests, not just commercial ones, and 'people with an axe to grind' are seen as including patient groups and scientists themselves.[1012] Legislation adopted in the US in 2007 that allows babies' DNA blood spots to be stored and used for genetic research without consent has recently become controversial as people have become aware that their babies' DNA is being stored.[1013]

The EU and Government's commitment to the 'knowledge-based bio-economy' has not been widely discussed or debated. However, two studies in the EU and UK, discussed below, revealed considerable scepticism about the 'knowledge-based economy' and mistrust about how research investment decisions are made.

5.4.1 Public opinion and the Lisbon Strategy

> "*Apart from the fact that virtually no one had heard of the* [Lisbon] *strategy, the initial reactions of the participants showed …that attitudes on the subject are extremely variable. They tend to be positive in some countries, at least for some population categories, but often negative, sceptical or reserved for the majority of other persons questioned.*". Bureau of European Policy Advisors, 2005.[1014]

In 2005, the European Commission's Bureau of European Policy Advisors published a qualitative study of the attitudes of citizens of the European Union towards the renewed Lisbon Strategy.[1014] This was a new plan to implement European Ministers' commitment to making Europe "*the most competitive and dynamic knowledge-based economy in the world*", which recognised that after five years the Lisbon Strategy had not delivered the predicted growth and therefore proposed increased investment in research (see Annex IV, p100 of the report).

The study was based on group discussions involving three groups of citizens in each of the 25 EU countries in May or June 2005: (i) a group of average citizens: men and women, aged between 25 to 60 years, of middle-level socio-professional categories of salaried employees; (ii) a group of people in socio-economic difficulties in the same age group; (iii) a group of managers in small and medium-sized enterprises (SMEs): either owners of their own firm or salaried top managers.

The study found that there is a very general consensus that recognises the crucial nature of the development of research and innovation activities and a belief that Europe potentially has all the qualities and competences necessary, due to its high level of education and culture. Opinions were, however, more balanced as regards Europe's true capacity for competitiveness in this area. Regarding economic growth the researchers observed reservations about "growth for growth's sake" and its perverse effects in social and societal terms – or the idea of a kind of natural limit to growth for countries having already attained a high level of development and prosperity. Participants were generally pessimistic about the economy and Europe's competitiveness and tended to pin responsibility on the State (seen as guilty of mismanagement), the political class, the very wealthy and profit-making businesses. Some respondents questioned the legitimacy of competitiveness, or at least the pursuit of competitiveness "at all costs", which seemed to them to characterise the current trend at the expense of quality of life of persons and "human values".

Virtually no one who took part in the study had heard of the Lisbon Strategy, although they were not surprised by its content. Re-launching a plan for growth based on Europe's recognised assets was generally supported but there were some fears of a policy aiming at competitiveness and productivity "at all costs" and people were doubtful about the credibility of a recovery plan for a Europe that has failed over the course of the last five years. The report states that: "*Responsibility for the mediocre situation was mainly placed with political leaders or governments and their erroneous policy choices and their mismanagement of public money*".

5.4.2 Science Horizons in the UK

The UK Government's Science and Innovation Investment Framework (para 1.36) recognises that: "*In pushing forward the boundaries of science and breaking new ground in technological progress, the public needs to have confidence in the ethical and regulatory framework within which these advancements are being made*".[41] The Framework therefore made an important commitment to more public engagement in science.

In September 2007, the UK Government published the reports of the three strands of its Science Horizons project (a deliberative panel, facilitated public events and small group discussions).[1015] The project's primary aims were: to discover views about the issues raised by possible future directions for science and technology, from a broad set of participants, to inform policy and decision-making on the direction of research and the regulation of science and technology, and to help identify priorities for further public engagement on areas of science and technology.

There was a widespread view amongst participants that the deliberative process ought to be used more and that this would be healthy for public life and policy. However, people needed reassurance that their views really would be taken seriously and would inform policy discussions.

The summary report of the Science Horizons project[1016] states that the discussions about science and technology *"brought to the surface numerous deep seated social concerns and policy themes*". These included anxieties about privacy and surveillance, erosion of the human dimension in services and relationship building, future employment, trustworthiness of authorities, safety, fair access to technology and the potential for technologies to be misused. The concern that technology is being developed by industry and/or government in order to make profits, rather than in response to societal needs was "*a fairly common theme*" and some people expressed feeling a lack of control over the direction in which science technology is heading. Trust in expert authorities in the abstract tended to be low and there was "*pervasive anxiety*" about potential abuse of technologies. It is also "*widely assumed that policy-makers in government and big business are not candid with citizens*".

The report of the Deliberative Panel[1017] revealed a "*striking trust deficit*" and some people saw expert priorities for research investments as inevitably not the same as those of the average citizen.

5.5 Summary of research priorities

Successive governments and the European Commission have chosen to promote biotechnology and genetic research as a major driver of growth in a new knowledge-based economy. This has involved major investments in human genetic databases and biobanks – linking DNA and personal medical information – and a significant shift in the focus of agricultural research to create genetically modified (GM) plants. These investments have delivered neither the claimed economic benefits nor significant benefits to health or the environment.

Companies support strategies for investment in science and technology that will expand markets or increase control, because their aim is to compete successfully with other companies and maximise their growth. In the context of the knowledge-based bio-economy, they have argued that strong intellectual property protection, weak regulation, and policies which ignore 'irrational' public objections and use education to create informed consumers are the key to delivering the promise of biotechnology (Section 1).

This type of approach will not deliver genuine solutions because it always leads to a narrow 'techno-fix' approach (for example, engineering supposedly 'healthier' foods, rather than changing the food production system); and because most of the consequences fall outside the competence of those developing the technology, so that undesired effects tend to be greater than desired ones. A striking example is the 2008 food crisis, in which millions of people were pushed into poverty due to increased food prices. One of the many complex causes was the use of land and crops for biofuels on an industrial scale (agro-fuels): intended to be a new, sustainable source of fuel for cars and trucks.

Further, the assumptions which underpin the knowledge-based bio-economy ignore key drivers of success or failure for particular innovation strategies. These include the fundamental issue of whether science and technology can actually deliver on the promises made, as well as broader social issues, such as how to best tackle the underlying causes of hunger or obesity, and the reasons why members of the public may not perceive particular technologies as of benefit to them.

The evidence in this report suggests that unrealistic promises have distorted research priorities and led to political 'entrapment' in biotech innovation strategies. Driven partly by the need to secure funding, some scientists have claimed that they will be able eliminate cancer and crime with genetic research and DNA databases; and both feed the world and fuel it with GM crops: without considering the unintended consequences or requiring policy-makers to tackle pervasive inequality and social disadvantage. Distorted research priorities can indirectly claim lives, contribute to disease and hunger, and waste public money: preventing investment in genuine solutions to overcome the current economic, social and environmental crises.

Decisions about the knowledge-based economy and Europe's Lisbon Strategy have been neither transparent nor democratic, and most citizens remain unaware of the commitments that have been made. When the issues are discussed, people are often sceptical of the claimed social and economic benefits; and concerned about the influence of commercial companies and the increased level of surveillance and control. They have lost trust in decision-makers and tend not to believe that science is being conducted for the public good, or that economic growth should be pursued regardless of the human or environmental costs.

6. How Could Things Change?

6.1 A new approach making decisions more accountable

> "*At the beginning of the 21st century, we face a choice. We can either pretend that the many issues our civilization faces can be dealt with one at a time by a technical approach, or we can recognize that all these issues are symptoms of the same thing: the technical approach making everything perform more by undermining everything else. If we get to the root of the problem, beginning with university reform, the 21st century could be an age when technical civilisation avoids collapse by choosing life instead of power, thus ensuring a future for our children*." William Vanderburg, University of Toronto, June 2006.[1018]

> "*When we have been feeding the public exuberant promises of enormous return on investment, from personalised medicine to near-immortality, it is wrong to evade accountability for how their money is spent. And, arguably the stakes are higher now than they have ever been – many of the proposed fixes for complex diseases require greater resources, for potentially smaller return than ever before*". Buchanan, Weiss and Fullerton (Penn State University and University of Washington Medical School), 2006[326]

> "*Science and technology used to be seen as outside politics, but this view has become obsolete… Decision-making in these contexts cannot be left to the 'experts' but must involve politicians and citizens*". Anthony Giddens, The Third Way, 1998.[16]

> "*The challenge is (1) to involve a broad cross-section of people in decision making about research priorities and (2) to allow all interested people to be engaged in research themselves, at some level. To meet this challenge, social movements need to put research on their agendas*". Brian Martin, 'Information Liberation', 1998.[331]

Giddens argued in 1998 that public-private partnerships could "*give private enterprise a larger role in activities which governments once provided for, while ensuring that the public interest remains paramount*".[16] In this report we suggest that public-private partnerships in bioscience have not in general served the public interest, partly because corporate objectives may align poorly with people's health needs and with environmental sustainability, and partly because – contrary to Giddens' claim – decision-making has been left to a narrow circle of 'experts', often with vested interests in a particular approach, and civil society has been excluded.

The system of specialisation and bureaucratisation of universities and other institutions created to support the knowledge-based economy also drives a technical approach to solving problems that can side-step underlying causes, create undesired effects and block real solutions.

The model of science as a business which underlies the knowledge-based economy has also failed as an engine for economic growth. Much of the financial risk of research and innovation has fallen to the taxpayer, yet research decisions are made behind closed-doors with no democratic accountability, and without even cursory scientific diligence to check the claims made by a narrow circle of enthusiasts. 'Optimism bias' – underestimating costs and exaggerating benefits – based on unrealistic techno-visions, is the norm.

The overall effect of the policies adopted to promote the knowledge-based bio-economy has been to weaken accountability for significant investments in research and development, which are determined neither by free markets, nor by democratic institutions.

This section considers how research might better meet people's needs for health and a sustainable environment.

The analysis in this report suggests that issues that need to be addressed include:

- Who defines the public interest?
- What mechanisms and institutions are needed to attempt to deliver public benefit from science and technology?
- How can 'blue skies' research and the 'non-instrumental' roles of science be safeguarded, including the ability to advance knowledge and understanding and to assess and debate techno-scientific claims?
- Who should bear the financial risk of research and innovation?
- How should research priorities be decided?

There are no simple answers to these questions, but an increasingly widely held view is that they can only be addressed by opening up decisions on research priorities, and on the political agenda of science and innovation, to much broader debate by society.

For example, in health research, Lehoux *et al.* argue that direct and active cooperation between users and designers enhances innovations, and that a new kind of policy-orientated research should be initiated based on a core set of values: relevance, usability and sustainability.[1019] In farming research, Joly argues that the current issue is to broaden knowledge production and open debate on[234]:

- How to prioritise research and development and balance innovation and risk
- How to manage a collective exploration process
- How to make links between research and development choices and evolution of the production system
- What type of research is needed for more remote stakeholders as well as immediate users.

.

Alternative approaches to innovation and the idea of 'upstream engagement' in science are discussed further below.

6.1.1 Alternative approaches to innovation

> "*Policymakers tend to be more inclined than economists to take economic and institutional change into account, but they often understand change in limited ways; they are particularly prone to technological determinism, especially in terms of the allegedly major impacts of 'critical technologies', such as information and communication technology (ICT), biotechnology or nanotechnology*." Professor of Innovation Keith Smith, 2005.[1020]

> "*Everyone now agrees that the kind of linear model, where you put technology and science in one end and product and services come out the other, is not a good representation of what happens*". Lord Sainsbury, 2007.[1021]

> "*GM technology as it is currently developed does not foster wider innovation in the rural economy. In fact GM has a negative inventive potential in as much as it promotes standardized farming practices…This 'command and control' vision of GM technologies is diametrically opposed to the kinds of localised and site specific innovation required to support environmentally sustainable rural livelihoods*." Robert Doubleday, University of Cambridge, 2008.[854]

Lord Sainsbury's 2007 review of the UK Government's science and innovation policies recognises that innovation is not a simple linear process in which research comes first, followed by development and then production and marketing.[52] The report also shows a broadening of focus from biotechnology and IT to a much wider range of sectors, including energy, creative industries, computer games, business and financial services, computer services and education. However, it continues to advocate very similar policies to those pursued whilst Sainsbury was science minister, including: a new leadership role for the 'business-driven' Technology Strategy Board; and more knowledge transfer

(including more spin-out companies, patents, and links between commercial companies and universities). The report also advocates increased 'user-driven' R&D spending by the Ministry of Defence.

The Sainsbury report makes the familiar argument that the developing world is taking over manufacturing (due to much lower labour costs) and that Britain needs to compete with emerging economies in China and India but at the same time resist calls for protectionism (except in Intellectual Property). This implies the need for a 'race to the top', leading to a focus on high-value goods and 'knowledge-intensive' services and industries. However, it notes that the UK still has an unimpressive record in industrial research; that privatisation has reduced R&D in the utilities and communications sectors; and there has been a decline in graduates in key subjects such as chemistry and engineering.

Concerns about the current approach to innovation have been echoed elsewhere, for example, the European Science Foundation has recently argued that science needs to renew its relationship with society.[1022] It notes that citizens in Europe and in the developed world have been losing trust in science as a source and factor in the solution to their problems and, in turn, asking for opportunity to express their views about scientific efforts and achievements. In addition, seeing the aversion of the customers towards certain products (e.g., GMOs) and technologies, industry has also started to raise questions about the assumption that properly funded research will inevitably lead to products that will be accepted by the market.

In the health and medical sector, Nightingale and Martin argue that the 'biotech revolution' model of technological change is unsupported by the empirical evidence.[665] Instead, biotechnology is following a well-established, historical pattern of slow and incremental technology diffusion. Consequently, "*many expectations are wildly optimistic and over-estimate the speed and extent of the impact of biotechnology, suggesting that the assumptions underpinning much contemporary policy-making need to be rethought*". They argue that: "*A key factor is the need for innovators and their sponsors to create high expectations to get access to the very considerable resources (money, people, and intellectual property) required to develop new medical technologies*", which rests on the creation of high hopes and the promotion of the idea of a biotechnology revolution.

Daniel Sarewitz, co-director of the Consortium for Science, Policy and Outcomes at Arizona State University, argues that the AIDS story provides a clear message for policy-makers seeking to address urgent problems with new technologies: look for what already works, and make it work better.[1023] Sarewitz contrasts the successful development of drugs to treat HIV infection (anti-retroviral therapy) with the failure of HIV vaccines. He argues that the reason the drug path has succeeded is simple: when the AIDS crisis began in the early 1980s, chemicals already existed that could slow the disease, and the state of the science was sufficient for drug companies to identify them and make step-by-step improvements in treatment. In contrast HIV vaccine research "*has been carried out mostly by academics whose main motive is to advance knowledge and careers*". Private sector involvement has generally been limited to biotech firms looking for a "*game-changing new product*"; and most of the big drug companies have stayed away, seeing little opportunity for profit and lots of risk. Sarewitz concludes that basic research should be aggressively pursued as part of a portfolio of public investment in innovation, but the chances of success should be understood as both unpredictable and long-term.

Thus, 'blue skies' research should not be neglected, but neither should its potential to solve immediate practical problems be over-sold. For example, the Human Genome Project and subsequent research has transformed scientific understanding of the complexity of biological systems, and increased understanding of the biological mechanisms of disease. Yet, this does not mean that germline gene sequencing will transform medicine or provide reliable, useful or cost-effective predictions of disease risk for most people: or, that transforming medicine in this way is necessarily a good idea. Nor has sequencing the human genome delivered the promised bonanza of new drugs. Perhaps if the 'non-instrumental' roles of science, such as improving understanding, were more valued by society, scientists would be under less pressure to 'over-promise' that revolutionary developments and commercial applications will inevitably flow from their research.

Martin and Morrison[927] argue that, in order for effective public policy to be developed, two things need to change; firstly, a more realistic set of expectations about the speed and scale of innovation needs to be adopted; and secondly, a different model, which views biomedical innovation as a slow and incremental process, should be used to inform public discussion and policy-making.

As a response to the problems of 'entrapment' that he identifies (in which political commitments are 'dug in', leading to neglect of externalities and throwing 'good money after bad'), Walker advocates the use of an 'implementation analysis' and an 'extrication analysis' to test the robustness of particular innovation strategies from an early stage in the decision-making process.[436]

An innovation system in which political commitments are 'dug in' in contrasts with one in which many diverse alternatives are being pursued. Stirling notes that some of the most creative innovations are seen to arise through the cross-fertilisation of disparate disciplines or traditions and argues in favour of an innovation system that encourages diversity.[1024] A culture in which diverse systems are maintained in parallel might be expected to provide an environment which is more conducive to radical and genuinely beneficial innovations. Stirling therefore argues that diversity is a major factor in the fostering of innovation and growth, an important strategy for hedging against intractable uncertainty and ignorance, the principal means to mitigate the effects of 'lock-in' and a potentially effective response to some fundamental problems of social choice.

McKelvey and Bohlin point out that decision-making has to be made under conditions of uncertainty about 'what will work' as well as about 'what will raise capital and what will sell'.[1025] If uncertainty seems wide-spread, then the best course of action may be to invest in a set of diverse possible directions of technological development. If uncertainty seems limited, then the best course of action may be to focus and prioritise on the major technological areas. However, both tactics require a continuing assessment of technologies and markets, including major areas of unknown outcomes. They note that: "*Certainly, biotechnology as an area of concern for basic science, small entrepreneurial firms and huge pharmaceutical companies has been one which holds out enormous promise - yet has also absorbed large amounts of resources with apparently few results in terms of direct industrial development*".

One approach to dealing with policy-making in the face of considerable uncertainty has been proposed by the Foresight obesity project[1026], which developed an initial strategy to tackle obesity based on a diversity of cross-disciplinary research over long timescales. The project advocated a 'practice-based evidence' approach, involving monitoring the strategy over different timescales and modifying it as it becomes clearer which actions are the most effective.[1027] This would involve scientists being more fully involved in assessment and re-focusing of strategies and taking more responsibility for the wider implications of their research. The Foresight obesity project also adopted a 'problem-led', rather than a 'technology-driven' approach, in which the biosciences may play a role but biotechnological innovations are not seen as the ultimate objective. The report argues that to address the 'obesogenic environment' (in which it is easy to eat too much and exercise too little), changes in transport infrastructure and urban design may be necessary. Such changes can be more difficult and costly than targeting intervention at the group, family or individual. However, they are more likely to affect multiple pathways within the obesity system in a sustainable way. Creating demand for such change requires a different way of thinking and may rely on aligning the benefits with those arising from broader social and economic goals such as reducing energy consumption, pollution, direct and indirect health costs, traffic congestion and crime rates.

In contrast to a more 'technology-led' approach, the Foresight obesity report was relatively downbeat about the future contribution of technological solutions. For example, it noted that better medicines were likely to be developed but the relatively high costs, possible risks and lack of societal acceptability mean the use of medicines alone is not a long-term sustainable solution. Similarly, the report recognised that the expected development of devices to monitor and provide feedback on energy intake and energy expenditure, along with biomarkers of health, such as blood pressure, and blood glucose in real time, would not necessarily mean that people would act on this information. Instead, the report identified five core principles for tackling obesity:

1. A system-wide approach, redefining the nation's health as a societal and economic issue
2. Higher priority for the prevention of health problems, with clearer leadership, accountability, strategy and management structures
3. Engagement of stakeholders within and outside Government
4. Long-term, sustained interventions
5. Ongoing evaluation and a focus on continuous improvement.

This approach implies a need to break down some of the divisions between different academic and scientific disciplines and between science and society. Vanderburg describes the distinction between knowledge embedded in experience and culture – knowing derived from everyday life and experience – and knowledge separated from it by technological specialisation.[1028,1029] He argues that there are three limitations of the current knowledge system[1030]:

(i) it imposes an 'end-of-pipe' (or techno-fix) approach to dealing with the undesired consequences of decision-making, rarely getting to the root of any problem;
(ii) individual practitioners of a speciality are trapped in a 'triple abstraction', leading to a poor ratio of desired to undesired effects of their decision-making: because a specialist has no idea whether any gains in desired outputs are realised in part or in whole at the expense of something else;
(iii) it bars the road to genuine solutions to many difficulties faced by contemporary civilisation.

Vanderburg concludes: "*Hence the present intellectual and professional division of labour and the knowledge infrastructure built on it together prevent genuine solutions from emerging when these represent a non-cumulative development*".

As an alternative, Francis *et al.* argue that agro-ecology provides an integrative alternative to the conventional division of research into specialised disciplines and that: "*Given the complexity of challenges in agriculture and food, one objective is to commit more energy to transdisciplinary approaches that enable us to look at the whole picture in a systematic way*".[327] They describe the co-ordinated education strategy being developed by the Nordic Agroecology Program, which "*uses a systems approach to address production, economic, environmental, and social challenges that must be solved to produce food and maintain a liveable environment*". Courses give students the unique learning opportunities of working directly with clients on the farm and in the food system over a period of time and are designed to prepare students to face uncertainty, complexity, and change in the future. They consider this approach to innovation through 'discovery learning' to be an important preparation for future researchers to contribute to responsible and meaningful development.

Similarly, Thompson and co-authors argue that the existing systems of agricultural science struggle to deliver integrated solutions to sustainability that address issues of uncertainty, diversity and complexity.[753] They highlight the contrast between a molecular biology approach and a 'holistic' approach to agricultural science, including agro-ecology, conservation biology and landscape ecology, characterised as a science of integration; involving inter-disciplinarity and synthesis, and cross-sectoral and cross-scale research and analyses. They argue that dynamic and diverse agri-food systems require policies and actions that not only contribute to social objectives, like poverty reduction, but also achieve continually modified understandings of the evolving ecological, economic, social and political conditions and provide flexibility for adapting to surprises. They question the assumption is that progress is achieved through the transfer of knowledge, ideas, models, practices and technologies from the 'developed' world to the 'developing' world, or from 'modern' science to 'backward' farming settings and argue that there may be multiple routes to improving the relationship between complex food system and poor people in developing countries, and that poor rural people often have relevant agricultural knowledge.

Divisions between government departments may also need to be bridged or broken down in order to provide integrated solutions to problems. In a study of health research in Canada, Lehoux *et al.* argue that these departmental divisions are one reason why innovation processes are not sufficiently informed by down-stream concerns.[1007] The innovation branch of government supports national innovation and commercialisation activities in order to promote economic growth, whilst the adoption of innovations is largely constrained by the health policy branch, which seeks to increase evidence-

based decision-making and set priorities given available resources. These branches of government tend to pull in opposite directions and, whilst the innovation branch tends to intervene early and mostly upstream, the health policy branch intervenes through regulation and evaluation just before innovations are ready to enter the market. Patients, clinicians and decision-makers often struggle with the local adoption of innovations because of ethical, clinical, economic or organisational problems and the innovation process is inefficient because of investment of time and resources in technologies that lack clinical relevance or are likely to be misused. Rather than limiting downstream evaluation, they argue that there is a need for clear and strong incentives for innovators to provide more desirable innovations; and appropriate feedback from health services and policy research about the level of fit (or misfit) between potential innovations and their likely real-world use.

The various approaches described above have a number of characteristics that differ substantially from the commitment to the knowledge-based bio-economy and biotechnology as a key technology platform for growth. These characteristics include:

- Being problem-based, rather than technology-led (and seeing problems as social and political, not just technical);
- Investing in diverse alternative approaches rather than a single 'magic bullet' solution or approach;
- Recognising the complexity of health and agricultural systems (which include social, economic, political and environmental factors, as well as biological ones);
- Acknowledging uncertainties and ignorance and involving practice-based ('on the ground') learning, evaluation, adaption and policy feedback, rather than a prior commitment to a long-term technological 'vision';
- Valuing science's role in informing strategies and policies, not just its potential to generate or market new technologies and products;
- Drawing on diverse disciplines, involving cross-departmental policies and participatory research, and developing a closer relationship between science and society;
- Openly recognising conflicts between different interests and investment priorities and the need for policy trade-offs, necessitating political decisions;
- Recognising governance and regulation as part of the system that influences who bears the costs and risks, or reaps the benefits, of innovation;
- Advocating approaches that examine and decide these trade-offs in a fair, democratic and transparent way;
- Viewing economic benefits as being rooted in society – for example, supporting rural economies and livelihoods – rather than in terms of gains for venture capitalists or city traders, or growth in particular industrial sectors such as food manufacture or pharmaceuticals.

6.1.2 Upstream engagement and participatory research

> "*Collective collaborations, in which intermediary groups strive to produce general guidelines, grounded in good science, vetted by both medical and patient representatives, and forged behind firewalls that minimise for-profit market influences, seem the more promising route for the future. History suggests that this work will be difficult and frustrating. But it offers the best hope for fully realising the benefits of collaboration between doctor and patient…*".[1031] Tomes, 2007.

> "*Contrary to the standard take on the issue, we have …seen that ordinary citizens rationally focus on important questions that scientific experts ignore or neglect. Practical discourse assists in revealing the systematic connections between the scientists' technical data and the particular social situation, the societal system and the way of life*". Frank Fischer, 2005.[1032]

> "*Public values and perceptions of research priorities may diverge considerably from commercial and professional priorities. Contentious issues have been raised in areas such as GM crops and weapons research. It is not unimaginable to think that greater public involvement in policy decisions may have an impact on the balance of scientific research that is carried out…Under the more interactive model of public engagement, organisations will not only have to listen but also be seen to listen, or risk engendering more scepticism*". The Wellcome Trust and the Prime Minister's Strategy Unit, 2003.[1033]

Many authors have concluded that to address the dislocation of science from the public, there needs to be more civil society engagement with setting the research agenda and science and innovation policies.[1034, 1035, 1036, 1037, 1038, 1039, 1040, 1041, 1042, 1043, 1044]

Participation is generally seen as furthering two aims – more democratic decisions and better ones. However, it is not a panacea and the notion of upstream engagement is a contested concept giving rise to its own dilemmas and tensions.[1045] Participation, whether upstream or not, is influenced by power dynamics and can either open up or close down debate.[1046]

The role of 'participatory' or 'co-operative' research - research which involves users and citizens directly - has also been emphasised by some. This includes a wide variety of projects, such as 'participatory plant breeding' and other research involving farmers,[753,755] and the engagement of workers in investigating occupational and environmental causes of disease.[1047] Such approaches can help to avoid situations where technologies and practices are found to be inappropriate for practical use on farms or in healthcare, or where the concerns of people affected 'on the ground' are sidelined or ignored. Inevitably, such methods introduce their own challenges, such as the difficulties of including all forms of knowledge in situations where there are inevitably divisions and hierarchies, differences in interpretation, and unequal power relations.[1048] However, they allow alternative forms of (unpatentable) knowledge – such as farmers' knowledge – to be valued, in a more 'bottom-up' approach to supporting local agricultural economies or improved health services. Innovation is then more a means to overcome obstacles, based on social relations and co-operation, and involves different knowledge types (not just bioscience).[1049]

The idea of 'cognitive justice' moves beyond 'participation' as a means to seek citizens' or consumers' approval for scientific projects, to visualize a body of knowledge that citizens, especially in subsistence cultures, have access to as consumers, critics, practitioners and philosophers.[1050] It sees citizens as inventors of knowledge, not merely consumers of it.

In 2008, the UK Department for Innovation, Universities and Skills (DIUS) launched a consultation on its 'Vision for Science and Society', following a survey which found that only 21% of the public agree that 'the public is sufficiently involved in decisions about science and technology'.[59,1051] However, the consultation was heavily criticised by researchers on science and innovation policy who argued that a radical revision of the relationship between science and society is required, which reviews past experiences properly and reflects in a fundamental way on how to support more democratically and technically robust science and technology policies.[1052] In GeneWatch's view, the most serious omissions from the listed areas for action were the actions policy-makers need to take to better understand, evaluate and communicate the limitations of techno-scientific claims, and to make more democratic, transparent and accountable decisions about research funding priorities.[1053]

Whilst there has been a shift towards more upstream engagement in science, this has tended to exclude debates about research priorities and what taxpayers' money should be spent on.

Although some scientists will have concerns about public interference in the research agenda, the evidence in this report shows that the Haldane Principle (which is often cited to state that scientists rather than politicians should determine how research funds are spent) does not reflect reality because the entire system of research funding is now shaped by institutional commitments to the knowledge-based bio-economy. Public engagement is meaningless unless it is allowed to influence research priorities, with the aim of helping to direct research investments in a way that meets societal

needs. There is no evidence that scientific excellence would suffer as a result. For example, the Scottish Government's decision to take on board public concerns about growing GM crops has not had any adverse effects on Scotland's reputation for world-leading research in science.[1054] Scotland's research is still cited by other researchers around the world more often than any other country in comparison to its GDP and areas of strength include biological sciences, environment, and health and medical research.[1055]

The European Commission-funded project 'Participatory science and scientific participation: The role of civil society organisations (CSOs) in decision-making about novel developments in biotechnologies' (PSx2) involved people from CSOs (including GeneWatch UK) and academics in a study about participation in science.[1056] Based on evidence gathered from interviews in ten European countries it found that, contrary to popular perception, CSOs that were engaged in debates about the development of agricultural biotechnology are not anti-science, but felt that current policy-making frameworks are disproportionately orientated towards the co-operation between science and industry, leaving other actors either under-represented or not represented at all. Although the original intention of the project was to focus on 'good practice' in participation, it found that CSOs believe themselves to be operating within a structure that fundamentally denies them opportunities for meaningful participation.

The people who were interviewed in the PSx2 project believed that there is a need to re-examine the way science feeds innovation so that the whole process is more transparent and equitable. The main CSO recommendations to improve participation in science at the invited (or institutional) level were:

- EU as well as research and political institutions should endow CSOs with real forums and opportunities to express their opinion and to influence the process in an open debate.
- The opportunities for participation should exist from the very beginning of the process, when research projects are authorised or funded.
- Broaden the focus of debate to include social and political implications, rather than merely technical, safety and economic issues.
- Promote transparency in science policy. The public should be informed of what are the ultimate goals of publicly funded research, what interests are at stake and what risks are involved.
- Emphasise the need for a precautionary approach that takes into account unacknowledged and longer-term uncertainties in the science and the possible long term risks and consequences, by a transparent, alternative and multidisciplinary expertise.
- Guarantee public debate, but also that the conclusions of these debates are taken into account.
- Open up the innovation process in order to ensure that everyone, particularly significant stakeholders such as farmers (who work full time and long hours) have enough time and opportunity to consider the implications of new products and to express their opinions on important issues.
- Counter-expertise is regarded as the best way to expose the fact that government appointed experts may be biased towards the interests of the industry. However there cannot be counter expertise without funding. Financing counter-expertise is regarded as a way to gain better objectivity on the problem linked to research objectives and technical applications.
- General issues, like the adoption of very innovative technologies, could be submitted to more direct democracy (such as a referendum).

Additionally, at a broader (societal) level, recommendations were made to:

- Promote research that fits the needs of local farmers, like organic agriculture as an alternative, sustainable, and economically viable form of agricultural development.
- Promote cooperation between CSOs and scientific institutions in research projects, such as PICRI (Partenariat Instituts Citoyens pour la Recherche et l'Innovation).
- Diffuse information and improve scientific education at all levels, organizing conferences and creating adequate spaces for a dialogue with civil society.

The report concludes that participation at the regulatory stage of the science and innovation process can only occur if civil society has been on board ever since the agenda setting stage. It argues that it

is not legitimately possible to expect CSOs or wider society to participate if they have not been consulted or involved at early stages, simply because the products of the innovation process that are to be regulated come to be perceived as totally alien and unsafe. On the contrary, if these products result from both a combined effort and a shared path, all the actors involved will be 'responsible' for the outcomes that they can legitimately perceive as 'belonging' to them. The report concludes that, although this wider involvement would inevitably slow down the innovation process, it may uncover problems before huge investments are made and also lead to more creativity in innovation because of broader range of experience drawn upon. The report also highlighted ten principles of effective participation (Box V)

Box V: Ten principles of effective participation

Funding for scientific research should be allocated according to 'public interest' and the needs of the final user.

Early participation of civil society, at a meta level, when the terms of the innovation process are non-technical.

Everyone could, and should, be able to participate at some level and in some capacity and this would necessarily include Civil Society Organisations as 'stakeholders'.

Participation must be on an equal footing to address unequal power relations.

Two way exchange of information, open mindedness and genuine engagement, by the scientific institutions, between themselves and citizens.

Debates about science should involve different opinions/viewpoints and a plurality of expertise and recognition of other types of knowledge that take into account minority opinions.

Openness and transparency are crucial in the development and practice of publicly funded scientific research and its regulation.

Easily accessible and non-technical information is required. The public needs to be given the opportunity to acquire a good understanding of the technical issues.

Participation in science requires consideration of specific interests and ways of life e.g. women's perspectives and specific requirements and farmer's needs and timetables.

Public participation in science requires evidence that public concerns have been listened to and taken into account.

7. Conclusions and Recommendations

> "*The biggest fallacy…is simply to presume that the 'output' of scientific research, no matter what the circumstances, is always and everywhere generic 'knowledge', indifferent to the uses to which it might be put…A more threatening aspect of this sort of 'new economics of science' resides in the possibility that the commercialisation of science actually changes what we get at the end of the process*…"
> Economists Philip Mirowski and Robert van Horn, 2005.[1057]

> "*It's not done to kill the goose that lays the golden eggs, nor to bite the hand that feeds you - nor, in my own profession, to criticise the research programme of the Wellcome Trust, an enormously rich charity that paid much of the bill to read the message written in human DNA. Not done, perhaps: but a pack of renegade biologists has turned on that source of nutrition to claim that what it is doing is welcome, but plain wrong… We thought it* [genetic research] *was going to change our lives but that has turned out to be a false dawn.*" Geneticist Steve Jones, 2009.[384]

> "*Our scientific institutions, regulatory bodies, innovation policies and intellectual property regimes are a long stretch from being fit for effective problem-solving. Far from being a carte blanche for GM foods, it means putting them on hold pending deep-rooted institutional reform*".[1058] Tom MacMillan, Food Ethics Council, 2008.

> "*…if science is to fulfil its promise of global problem-solving, then there is no other course than to repoliticise it: not through capture by a narrow range of wealthy special interests, but by opening up science's hidden normative presumptions to authentic and inclusive public debate*". Sheila Jasanoff, 2005.[788]

The existing system of investment in research in health and agriculture has wasted billions in taxpayers' money and delivered nothing in terms of a viable new 'bio-economy'. It has also exacted a high price in human lives due to wasted opportunity costs by acting as a distraction from more immediate, lower-cost alternatives. This is partly because ensuring that existing treatments and a varied, balanced diet reach everybody would save a lot more lives than any possible technological developments; and partly because the system distorts the research agenda away from human needs as well as from the broader development of scientific knowledge and understanding. The problem is not that commercial interests should not play a role in funding and helping to drive (at least some) R&D investment, or that technology (including biotechnology) has no positive applications, but that the system of policies and incentives created to drive the 'knowledge-based bio-economy' is deeply flawed.

The technical, commercial and economic failure of the bio-economy has generally been attributed to unfavourable policies – particularly 'over-regulation' and weak IP protection – and public 'ignorance', rather than the underlying R&D strategy and its failure to appreciate the complexities of biology, society, markets, agriculture and the environment. This results in an agenda that is self-perpetuating, as there is no mechanism to re-appraise existing policies or to stop throwing good money after bad.

In common with most people, scientists are concerned about the extent to which their funding may be cut as a result of the global economic crisis and the resulting burden of public debt. As venture capital dries up, their jobs will depend on whether governments see science as a strategic investment or a wasteful expense that should be cut. This report suggests that investments in biological sciences and biotechnology would benefit from a more self-critical approach, combined with greater public scrutiny and oversight of scientific and technical assumptions. Unsubstantiated claims made about future developments and benefits need to be re-evaluated in the light of past experience, and a more realistic appraisal is needed of how to tackle urgent real-world problems, such as hunger and obesity.

There is an urgent need to re-assess what has been delivered by the major political and financial investments made in the bio-economy over the past three decades, and to review whether current funding structures, institutions and review mechanisms are fit-for-purpose to deliver genuine solutions to the problems that we face.

Review of the research funding system should lead to a major overhaul, including significant reforms to improve the scientific and technical advice available to the UK Government and to the European Union; reform the patents system; and re-structure funding institutions. Objectives should include:

- More democratic decisions about research funding priorities and a more diverse research agenda;
- Greater accountability and scrutiny of major research investment decisions: including economic assessments and appraisals, scrutiny of scientific and technical assumptions, and active steps to prevent political 'entrapment' in research agendas based on false assumptions and misleading claims;
- A role for public engagement in setting research questions and priorities, including consideration of a variety of alternative approaches to addressing problems, and greater democratic accountability for science policy decisions;
- More public engagement in research itself, involving closer co-operation between universities, communities and civil society organisations;
- More funding for research which does not necessarily benefit large corporations but may deliver other benefits including economic ones (for example, public health research, and research into improving agro-ecological farming methods);
- Funding for 'counter-expertise' and multi-disciplinary research which can identify long-term scientific uncertainties and regulatory gaps;
- Ensuring a thriving scientific culture that can analyse, critique and develop the theoretical concepts that often underlie decision-making, and which are key to developing new understandings;
- A commitment to taking public opinions into account in decisions about science and innovation, including methods to ensure full consideration of the broader social, environmental and economic issues associated with adopting particular approaches and technologies.

APPENDIX A

Appendix A is available online at:
http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/UK_Biobank_fin_1.pdf

1 Proctor RN (1995) Cancer Wars: How politics shapes what we know and don't know about cancer. Basic Books.

2 Rose H (1994) Love, power and knowledge. Polity Press, Cambridge.

3 Lang T, Heasman M (2004) Food wars: the global battle for mouths, minds and markets. London, Earthscan.

4 Harrison A, New B (2002). Public interest, private decisions: health-related research in the UK. The King's Fund.

5 Scientists for Global Responsibility (2005) Soldiers in the laboratory: Military involvement in science and technology and some alternatives. January 2005. http://www.sgr.org.uk/ArmsControl/MilitaryInfluence.html

6 StateWatch (2006) Arming Big Brother: The EU's security research programme. TNI briefing series No. 2006/I. http://www.statewatch.org/news/2006/apr/bigbrother.pdf

7 Blair T(2006) Our nation's future: science. Speech to the Royal Society of Oxford. 3rd November 2007. http://www.number10.gov.uk/output/Page10342.asp

8 Amos J (2007) EU money geared to smart future. *BBC Online*. 7th Feb 2007.

9 OECD(1996) The knowledge-based economy. OCDE/GD(96)102. Paris 1996. http://www.oecd.org/dataoecd/51/8/1913021.pdf

10 http://www.oecd.org/document/58/0,3343,en_2649_34483_1889402_1_1_1_1,00.html

11 Blair T (2006) Britain's path to the future - lit by the brilliant light of science. Speech to the Royal Society in Oxford. 3rd November 2006. http://www.pm.gov.uk/output/Page10337.asp

12 Wilkie T (1991) British science and politics since 1945. Blackwell.

13 Krimsky S (2003) Science in the private interest: Has the lure of profits corrupted biomedical research? Rowman & Littlefield.

14 Andersson J (2007) Socializing capital, capitalizing the social: Contemporary social democracy and the knowledge economy. Centre for European Studies Working Paper http://www.ces.fas.harvard.edu/publications/docs/pdfs/Andersson.pdf

15 Peters M (2001) Education, enterprise culture and the entrepreneurial self. *Journal of Educational Enquiry*, 2(2), 58-71. http://www.literacy.unisa.edu.au/jee/Papers/JEEVol2No2/200144.pdf

16 Giddens A (1998) The Third Way: The renewal of social democracy. Polity Press, Cambridge.

17 http://www.britishcouncil.org/gost/rop.htm

18 HM Treasury (2007) Lisbon strategy for jobs and growth: UK national reform programme, update on progress. September 2007. Http://www.hm-treasury.gov.uk/media/B/9/lisbon_nationalreformprogramme210907.pdf

19 http://www.cst.gov.uk/cst/about/history.shtml

20 DTI(1998) Allocation of the science research budget 1999/00 to 2001/02. http://www.berr.gov.uk/files/file14535.pdf

21 HM Treasury (1998) University Challenge Unlocking Britain's Commercial Potential. Press Release. 17th March 1998. http://archive.treasury.gov.uk/budget/1998/hmt15.htm

22 DTI(1999) UK competitiveness indicators. Http://www.dtistats.net/competitiveness5/Past%20Indicators/UKPC1999.pdf

23 http://www.dti.gov.uk/science/knowledge-transfer/schemes/Science_Enterprise_Challenge/page12138.html

24 http://www.hm-treasury.gov.uk/newsroom_and_speeches/press/1999/press_63_99.cfm

25 Baker J (1999) Creating knowledge creating wealth: Realising the economic potential of public sector research establishments. A report by John Baker to the Minister for Science and the Financial Secretary to the Treasury. August 1999. http://www.hm-treasury.gov.uk./documents/enterprise_and_productivity/research_and_enterprise/ent_sme_baker.cfm

26 DTI (2000) Excellence and Opportunity: A science and innovation Policy for the 21st Century. 26th July. http://www.berr.gov.uk/files/file11990.pdf

27 Council for Science and Technology (2000) Technology Matters. http://www.berr.gov.uk/files/file14964.pdf

http://www.hmtreasury.gov.uk/spending_review/spending_review_2000/associated_documents/spend_sr00_ad_ccrcontents.cfm

28 http://www.hefce.ac.uk/Research/SRIF

30 http://www.hefce.ac.uk/reachout/heif/heif.asp

31 DTI(2001) Opportunity for all in a world of change. 13th February 2001. Http://www.dfes.gov.uk/pns/DisplayPN.cgi?pn_id=2001_0085

32 http://www.scotland.gov.uk/Resource/Doc/158401/0042918.pdf

33 HM Treasury (2002) Cross-Cutting Review of Science and Research. http://www.hm-treasury.gov.uk/media/E/7/science_crosscutter.pdf

34 Roberts G (2002) SET for success: the supply of people with science, technology, engineering and mathematics skills. http://www.hm-treasury.gov.uk/documents/enterprise_and_productivity/research_and_enterprise/ent_res_roberts.cfm

35 DTI(2000) Excellence and opportunity: a science and innovation policy for the 21st century. Http://www.rcuk.ac.uk/aboutrcuk/history/rcuklaunch

36 HM Treasury (2002) Investing in Innovation: A Strategy for Science, Engineering and Technology. http://www.hm-treasury.gov.uk/spending_review/spend_sr02/spend_sr02_science.cfm

37 NAO(2002) Delivering the commercialisation of public sector science. Report By The Comptroller and Auditor General. HC 580 Session 2001-2002: 8 February 2002. http://www.nao.org.uk/publications/nao_reports/01-02/0102580.pdf

38 Lambert Review of Business-University Collaboration. Http://www.hm-treasury.gov.uk/consultations_and_legislation/lambert/consult_lambert_index.cfm

39 DTI(2003) Competing in the global economy: the innovation challenge. December 2003. Http://www.berr.gov.uk/files/file12093.pdf

40 Sainsbury D (2003) Learning Skills Council speech. 9th June 2003. http://www.dti.gov.uk/ministers/speeches/sainsbury090703.html

41 HM Treasury, DTI, DfES (2004) Science and innovation investment framework 2004-2014. Http://www.hm-treasury.gov.uk/spending_review/spend_sr04/associated_documents/spending_sr04_science.cfm

42 Sainsbury D (2004) Technology Strategy Information Day Speech. 26th April 2004. http://www.dti.gov.uk/ministers/speeches/sainsbury260404.html

43 OGC (2004) Capturing Innovation : Nurturing Suppliers' Ideas in the Public Sector. May 2004. http://www.ogc.gov.uk/documents/capturing_innovation.pdf

44 http://healthtech.globalwatchonline.com/epicentric_portal/site/KTN

45 Scottish Executive (2006) Progress report on "A Science Strategy for Scotland 2001". Http://www.scotland.gov.uk/Publications/2006/02/23092427/0

46 http://www.scotland.gov.uk/Topics/Business-Industry/science/16607

47 HM Treasury, DTI, DfES, DoH (2006) Science and innovation framework 2004-2014: next steps. March 2006. http://www.hm-treasury.gov.uk./media/7/8/bud06_science_332v1.pdf

48 Research Council Economic Impact Group (2006) Increasing the economic impact of Research Councils. 14th July 2006. http://www.dti.gov.uk/files/file32802.pdf

49 Leitch S (2006) Prosperity for all in the global economy – world class skills. December 2006. http://www.hm-treasury.gov.uk./media/6/4/leitch_finalreport051206.pdf

50 GSIF(2006) A strategy for international engagement in research and development. October 2006. http://www.berr.gov.uk/files/file34726.pdf

51 Gowers Review of Intellectual Property. HM Treasury. December 2006. http://www.hm-treasury.gov.uk/independent_reviews/gowers_review_intellectual_property/gowersreview_index.cfm

52 Lord Sainsbury of Turville (2007) A review of Government's science and innovation policies. October 2007. HMSO. http://www.hm-treasury.gov.uk/independent_reviews/sainsbury_review/sainsbury_index.cfm

53 Treasury (2007) £1bn strategy to drive business innovation and success. Press Release. 5th October 2007. http://www.hm-treasury.gov.uk/newsroom_and_speeches/press/2007/press_102_07.cfm

54 Darling A (2007) 2007 Pre-Budget Report and Comprehensive Spending Review statement to the House of Commons. 9 October 2007. http://www.hm-treasury.gov.uk/2007_pbr_speech.htm

55 http://www.hm-treasury.gov.uk/d/pbr_csr07_annexd4_168.pdf

56 http://www.scotland.gov.uk/Topics/Business-Industry/science/16607/Sframework

57 BERR(2008) Enterprise: unlocking the UK's talent. 12 March 2008. http://www.berr.gov.uk/whatwedo/enterprise/enterprisesmes/enterprise-framework/index.html

58 DIUS(2008) Innovation Nation. http://www.dius.gov.uk/publications/innovation-nation.html

59 DIUS(2008) A vision for science and society. July 2008. http://interactive.dius.gov.uk/scienceandsociety/site/

60 Lord Drayson (2009) Foundation for Science and Technology Lecture. Royal Society, 4th February 2009. http://www.dius.gov.uk/news_and_speeches/speeches/lord_drayson/fst.aspx

61 Rt Hon John Denham MP (2009) Staying ahead: investing in research in the downturn. Royal Academy of Engineering, 19th February 2009. http://www.dius.gov.uk/news_and_speeches/speeches/john_denham/rae.aspx

62 Lord Mandelson (2009) Speech to CBI manufacturing dinner. 5th February 2009. http://www.berr.gov.uk/aboutus/ministerialteam/Speeches/page50022.html

63 Prime Minister Gordon Brown (2009) Romanes Lecture. Sheldonian Theatre, Oxford, 27th February 2009. http://www.number10.gov.uk/Page18472

64 Henderson M (2009) Funding for science to get business focus, says Lord Mandelson. The Times. 10th June 2009. http://www.timesonline.co.uk/tol/news/uk/science/article6471800.ece

65 University budget cuts revealed. BBC Online. 1st February 2010. http://news.bbc.co.uk/1/hi/education/8491729.stm

66 http://www.dti.gov.uk/ministers/speeches/sainsbury261005.html

67 Speech by the chancellor of the exchequer, Gordon Brown MP at the Smith Institute. 15th April 1997. http://www.hm-treasury.gov.uk/speech_chex_150499.htm

68 Speech by the Chancellor of the Exchequer, Gordon Brown MP at the UK-US Enterprise Conference. 2nd July 1999. http://www.hm-treasury.gov.uk/speech_chex_020799.htm

69 Anderson R, Brown I, Dowty, T, Inglesant P, Heath W, Sasse A (2009) The database state. The Joseph Rowntree Reform Trust Ltd. http://www.jrrt.org.uk/uploads/Database%20State.pdf

70 Rodriguez V, Montalvo C (2007) Innovation policies from the European Union: Methods for classification. *Bulletin of Science, Technology & Society*, **27**(6), 467-481.

71 Sandholz W (1992) Hi-Tech Europe: The politics of international co-operation. University of California Press. http://www.escholarship.org/editions/view?docId=ft609nb394;brand=ucpress

72 Korres GM (2007) Industrial and innovation policy in Europe: The effects on growth and sustainability. *Bulletin of Science, Technology & Society*, **27**(2), 104-117.

73 http://cordis.europa.eu/itt/itt-en/special96/introduction.htm

74 http://ec.europa.eu/enterprise/innovation/consultation/eu_landmarks.htm

75 http://ec.europa.eu/enterprise/innovation/documents_en.htm

76 http://ec.europa.eu/growthandjobs/areas/fiche05_en.htm

77 http://ec.europa.eu/growthandjobs/areas/fiche06_en.htm

78 Dearing A (2007) Enabling Europe to innovate. *Science*, **315**, 344-347.

79 http://cordis.europa.eu/itt/itt-en/02-3/policy01.htm

80 http://ec.europa.eu/invest-in-research/action/2006_ahogroup_en.htm

81 http://ec.europa.eu/invest-in-research/pdf/download_en/aho_report.pdf

82 European Commission (2005) New perspectives on the knowledge-based bio-economy. Conference report.

83 OECD (2005) The bioeconomy to 2030: designing a policy agenda. Paris: OECD. http://www.oecd.org/findDocument/0,3354,en_2649_36831301_1_119829_1_1_1,00.html

84 Sainsbury D (2001) Speech to the Biotechnica Business Forum. 28th November 2002. http://www.dti.gov.uk/ministers/archived/sainsbury281102.html

85 Spinks A (1980) Biotechnology. Report of a Joint Working Party of the Advisory Council for Applied Research and Development, the Advisory Board for the Research Councils and the Royal Society. HMSO.

86 Birch, K. (2008) Alliance-driven governance: applying a global commodity chains approach to the UK biotechnology industry. *Economic Geography*. [Forthcoming] http://eprints.gla.ac.uk/3784/01/Birch33RepositoryPaper.pdf

87 Thirtle C, Palladino P, Piesse J (1997) On the organisation of agricultural research in the United Kingdom, 19451994: A quantitative description and appraisal of recent reforms. Research Policy, **26**, 557-576.

88 Accelerating into a new age. RTD Info 27. September 2000. Http://ec.europa.eu/research/rtdinfo/en/27/genome01.html

89 http://genome.wellcome.ac.uk/doc_WTD022307.html

90 http://genome.wellcome.ac.uk/doc_WTD022310.html

91 http://www.prnewswire.co.uk/cgi/news/release?id=18755

92 http://www.prnewswire.co.uk/cgi/news/release?id=13224

93 http://www.foresight.gov.uk/first_phase/1994-1999/index.html

94 Steering group of the technology Foresight programme (1995). Progress through partnership. http://www.foresight.gov.uk/first_phase/1994-1999/dl/General_Publications/Report%20from%20the%20Steering%20Group%20of%20the%20Foresight%20Programme/Report_from_the_Steering_Group_1995.pdf

95 Foresight (1995) Progress through partnership: 4 Health & life sciences. 2nd August 1995. http://www.foresight.gov.uk/first_phase/1994-1999/dl/Health_%20Life%20Sciences/Health_and_life_Sciences_1994-99.pdf

96 Foresight (1995) Progress through partnership: 11 Agriculture, natural resources and environment. http://www.foresight.gov.uk/first_phase/1994-1999/dl/Agriculture_Natural_Resources_Environment/Agriculture_Natural_Resources_Environment_1994-99.pdf

97 UK biotech companies to become British industrial success story, says Arthur Andersen. Press Release. http://www.prnewswire.co.uk/cgi/news/release?id=31208

98 Rowan D (1997) Money in genes. The Guardian. 27th November 1997. http://www.guardian.co.uk/science/1997/nov/27/genetics

99 Forum : Promises, promises - From extra cash to better access to the Net, all three parties claim to be on the side of science. Here's how they measure up in New Scientist 's 1997 election call. New Scientist. 26 April 1997. http://www.newscientist.com/article/mg15420796.700.html

100 Culyer A (1994) Supporting research and development in the NHS. A report to the Minister for Health by a Research and Development Task Force chaired by Professor Anthony Culyer. London: HMSO. September 1994.

101 Modern Public Services for Britain: Investing in Reform. Comprehensive Spending Review: New Public Spending Plans 1999-2002. Presented to Parliament by the Chancellor of the Exchequer by Command of Her Majesty, July 1998. Cm4011. http://www.archive.official-documents.co.uk/document/cm40/4011/4011.htm

102 Brown G (1998). Statement by the Chancellor of the Exchequer on the Comprehensive Spending Review - 14 July 1998. http://www.hm-treasury.gov.uk/Spending_Review/spend_csr98/spend_csr98_statement.cfm

103 HM Treasury (1998) Financing of High Technology Businesses. A report to the Paymaster General. November 1998. http://archive.treasury.gov.uk/pub/html/docs/fhtb.pdf

104 Office of Science and Technology (1999) The Advisory and Regulatory Framework for Biotechnology: Report from the Government's Review. May 1999. http://www.berr.gov.uk/files/file14498.pdf

105 Sainsbury (1999) Biotechnology Clusters. Report of a team led by Lord Sainsbury. August 1999. http://www.berr.gov.uk/files/file28706.pdf

106 Genome Valley: the economic potential and strategic importance of biotechnology in the UK. http://www.berr.gov.uk/files/file28709.pdf

107 http://www.mrctechnology.org/history.htm

108 White House, Press Release, 26th June 2000. http://www.genome.gov/10001356

109 NHS(2000) The NHS Plan. July 2000. Cm 4818-I. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4002960

110 Foresight (2000) Healthcare 2020. Foresight Healthcare Panel. December 2000. http://www.foresight.gov.uk/first_phase/1999-2002/dl/Healthcare/Reports/Healthcare_2020/Healthcare_2020_Dec_2000.pdf

111 Research and development for a first class service. R&D funding in the new NHS. Department of Health. March 2000.

112 House of Lords Science and Technology Committee, Human Genetic Databases: Challenges and Opportunities, 4th Report, Session 2000-0. http://www.publications.parliament.uk/pa/ld200001/ldselect/ldsctech/57/5701.htm .

113 Blair T (2002) Speech to the Royal Society. 23rd May 2002. http://politics.guardian.co.uk/speeches/story/0,11126,721029,00.html

114 http://www.defra.gov.uk/environment/gm/crops/debate/index.htm

115 Pharmaceutical Industry Competitiveness Task Force Final report. March 2001. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4058390.pdf

116 http://www.advisorybodies.doh.gov.uk/pictf/publications.htm

117 HM Treasury (2002) Investing in Innovation: A Strategy for Science, Engineering and Technology. http://www.hm-treasury.gov.uk/spending_review/spend_sr02/spend_sr02_science.cfm

118 DTI(2001) Opportunity for all in a world of change. 13th February 2001. http://www.dfes.gov.uk/pns/DisplayPN.cgi?pn_id=2001_0085

119 Brooks R (2007) How this government is blowing £12.4bn on useless IT for the NHS. Private Eye (1179). March 2007.

120 Wanless D (2002) Securing our future health: taking a long-term view. Final Report. April 2002. http://www.hm-treasury.gov.uk/Consultations_and_Legislation/wanless/consult_wanless_index.cfm

121 WAG(2002) A Health and Social Care Research and Development Strategic Framework for Wales. February 2002. http://wales.gov.uk/topics/health/research/word/publications/rdstrategy/?lang=en

122 Department of Health (2003) Our inheritance, our future: realising the potential of genetics in the NHS, June 2003, Cm 5791-II (London, The Stationary Office). http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4006538

123 BIGT (2003) Bioscience 2015 Improving National Health, Increasing National Wealth. http://www.bioindustry.org/bigtreport/index2.html

124 Academy of Medical Sciences (2003) Strengthening clinical research. 6 October 2003. http://www.acmedsci.ac.uk/p99puid22.html

125 http://www.gmsciencedebate.org.uk/report/default.htm

126 http://www.defra.gov.uk/environment/gm/fse/index.htm

127 http://www.defra.gov.uk/corporate/ministers/statements/mb040309.htm

128 http://www.sciencewise.org.uk/index.php

129 http://www.berr.gov.uk/files/file28434.pdf

130 Better health through partnership: a programme for action: final report. Healthcare Industries Task Force. Department of Health. November 2004. http://www.advisorybodies.doh.gov.uk/hitf/hitf_final_report_nov2004.pdf

131 http://www.ukcrc.org

132 Research for patient benefit working party Final report. April 2004. http://www.dh.gov.uk/en/Policyandguidance/Researchanddevelopment/A-Z/DH_4082668

133 Choosing health: making healthy choices easier. Department of Health. The Stationery Office Limited. November 2004.

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4094550

134 Derek Wanless. Securing good health for the whole population: final report. HMSO. February 2004. ISBN: 0-947819-98-3. http://www.hm-treasury.gov.uk/consultations_and_legislation/wanless/consult_wanless03_index.cfm

135 AEBC(2005) What shapes the research agenda? in agricultural biotechnology. April 2005. http://www.berr.gov.uk/files/file27181.pdf

136 DTI, DEFRA, BBSRC (2005) Government response to the AEBC report: What shapes the research agenda? in agricultural biotechnology. December 2005. http://www.berr.gov.uk/files/file21560.pdf

137 National R&D Costing Initiative Working Group (2005) Guidance to Facilitating the Conduct of Commercially-funded Research in the National Health Service (Secondary Care). http://www.rdforum.nhs.uk/docs/commercial_research_guidance_2005.pdf

138 Clinical research in the UK; towards a single system that reliably delivers distinctive quality and rapid access at reasonable cost. http://www.ukcrn.org.uk/index/library/reports/mainColumnParagraphs/01/document/McKinsey%20Report.pdf

139 Treasury (2005) Improving the nation's health, increasing the nation's wealth: A new deal for medical research. Press Release. 2nd December 2005. http://www.hm-treasury.gov.uk/newsroom_and_speeches/press/2005/press_100_05.cfm

140 Department of Health (2006) Best research for best health. 25th January 2006. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4127127

141 http://www.nihr.ac.uk/about.aspx

142 Cooksey D (2006) A review of UK health research funding. December 2006. http://www.hm-treasury.gov.uk/pre_budget_report/prebud_pbr06/other_docs/prebud_pbr06_odcooksey.cfm

143 Academy of Medical Sciences (2006) Personal data for public good: using health information in medical research. http://www.acmedsci.ac.uk/p48prid5.html

144 BBSRC(2007) High-level food research strategy 2007-2012. http://www.bbsrc.ac.uk/organisation/policies/reviews/scientific_areas/0707_food_research.pdf

145 DoH(2007) Delivering high quality care for all. Press Release. 4 October 2007. http://www.gnn.gov.uk/environment/fullDetail.asp?ReleaseID=319602&NewsAreaID=2&NavigatedFromDepartment=False

146 Darzi (2007) Our NHS, our future. Interim Report. 4 October 2007. http://www.ournhs.nhs.uk/?p=40

147 http://www.advisorybodies.doh.gov.uk/hitf/mmtsg.htm

148 Darzi (2008) High quality care for all. June 2008. http://www.ournhs.nhs.uk/2008/06/30/high-quality-care-for-all-nsr-final-report-launched/

149 OSCHR(2008) Chairman's First Progress Report. November 2008. http://www.nihr.ac.uk/files/pdfs/OSCHR_Progress_Report_18.11.08.pdf

150 Time running out for biotech. Pharmafocus. 8th June 2009. http://www.pharmafocus.com/cda/focusH/1,2109,21-0-0-JUN_2009-focus_news_detail-0-492834,00.html

151 BIGT(2009) The review and refresh of bioscience 2015. A report to Government by the Bioscience and Innovation Team. January 2009. http://www.bioindustry.org/biodocuments/BIGTR2/BIGT_Review_and_Refresh.pdf

152 Further information is available on: http://www.genewatch.org/sub-563487

153 Ghosh P (2009) Ministers' £1 billion UK science plea. BBC Online 17th March 2009. http://news.bbc.co.uk/1/low/sci/tech/7946371.stm

154 http://www.dius.gov.uk/ols

155 UK's OLS “to make a real difference to pharma/biotech”. Pharma Times. 7th April 2009. http://www.pharmatimes.com/UKNews/article.aspx?id=15631

156 Department of Business Innovation and Skills (2009) Life Sciences Blueprint: A Statement by the Office for Life Sciences. July 2009. http://www.dius.gov.uk/innovation/business_support/~/media/publications/O/ols-blueprint

157 Department of Health (2009) NHS 2010-2015. From good to great. Preventative, people-centred, productive. December 2009. http://www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_109887.pdf

158 http://www.cso.scot.nhs.uk/SuppScience/sahsc.htm

159 http://www.wales.nhs.uk/documents/NISCHR-Launch.pdf

160 House of Lords Science and Technology Committee (2009) Genomic Medicine, 2nd Report of Session 2008-09. HL Paper 107-I. July 2009.

161 Technology Strategy Board (2009) Biosciences Technology Strategy 2009-2012. September 2009. http://www.innovateuk.org/_assets/pdf/Corporate-Publications/BioSciencesTechnologyStrategyFinal.pdf

162 Technology Strategy Board (2009) Medicines and Healthcare Strategy 2009-2012. October 2009. http://www.innovateuk.org/_assets/pdf/Corporate-Publications/MedicinesHealthcareStrategy.pdf

163 NHS Connecting for Health (2009) Summary of responses to the consultation on additional uses of patient data. 27th November 2009. http://www.dh.gov.uk/en/Consultations/Responsestoconsultations/DH_109310

164 http://www.food.gov.uk/gmfoods/gm/gmdialogue/

165 Department of Health (2009) Government response to the House of Lords Science and Technology Committee inquiry into genomic medicine. December 2009. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_110005.pdf

166 Office for Life Sciences (2010) Life sciences 2010: Delivering the blueprint. http://www.dius.gov.uk/innovation/business_support/~/media/publications/O/OLS-Blueprint-Progress

167 Academy of Medical Sciences (2010) Reaping the rewards: a vision for UK medical sciences. January 2010. http://www.acmedsci.ac.uk/download.php?file=/images/publicationDownload/Reapingt.pdf

168 Barling D, Henderson R (2000) Safety first? A map of public sector research into GM food and food crops in the UK. Centre for Food Policy. Thames Valley University. Discussion paper 12. October 2000.

169 Poste G, Fears R (1999) Joining up for the genome. Times Higher Education Supplement, 19th February 1999. http://www.timeshighereducation.co.uk/story.asp?storyCode=145155&sectioncode=26

170 Wallace HM (2005) The development of UK Biobank: Excluding scientific controversy from ethical debate. *Critical Public Health*, **15**(4), 323-333.

171 Wynne, B. (2001) Creating public alienation: expert cultures of risk and ethics on GMOs. *Science as Culture*, **10**, 445-481.

172 GM crops needed in Britain, says minister. The Independent, 19th June 2008. http://www.independent.co.uk/news/uk/politics/gm-crops-needed-in-britain-says-minister-849991.html

173 Lean G(2008) Celtic revolt against Westminster over GM crops. *The Independent*. 28 September 2008. Http://www.independent.co.uk/environment/green-living/celtic-revolt-against-westminster-over-gm-crops-944768.html

174 http://www.scottish.parliament.uk/s3/committees/justice/correspondence/20090302CSfJtoBACoroners and JusticeLCM.pdf

175 http://ec.europa.eu/biotechnology/index_en.htm

176 US Office of Technology Assessment (1981) Impacts of applied genetics: Micro-organisms, plants and animals. April 1981. Http://www.fas.org/ota/reports/8115.pdf

177 Watson JD, Cook-Deegan RM (1991) Origins of the human genome project. *FASEB Journal*, **5**(1), 8-11.

178 EC(1991) Promoting the competitive environment for the industrial activities based on biotechnology within the Community. Brussels, 19 April 1991. SEC(91) 629 Final. http://aei.pitt.edu/5970/01/003168_1.pdf

179 McNally R, Wheale P (1998) The consequences of modern genetic engineering: patents, 'nomads' and the 'bio-industrial complex'. In: Wheale, Schomberg & Glasner (Eds) The social management of genetic engineering. Ashgate. ISBN 1 85972 686 0.

180 Commission of the European Communities (2001), Towards a Strategic Vision of Life Sciences and Biotechnology: Consultation Document, 4 September 2001.

181 EC(2002) Life Sciences and Biotechnology: A Strategy for Europe. COM(2002) 7. http://ec.europa.eu/biotechnology/pdf/com2002-27_en.pdf

182 http://ec.europa.eu/biotechnology/index_en.htm

183 http://ec.europa.eu/enterprise/phabiocom/docs/cbag_2004_report_2005-01-21_final_version.pdf

184 http://ec.europa.eu/enterprise/phabiocom/docs/cbag_2006_final_version.pdf

185 http://ec.europa.eu/enterprise/phabiocom/comp_biotech_commit.htm

186 http://ec.europa.eu/enterprise/phabiocom/docs/cbag_members_20060106.pdf

187 IPTS(2007) The Biotechnology for Europe Study (BIO4EU): Consequences, opportunities and challenges of modern biotechnology for Europe. http://bio4eu.jrc.es/index.html

188 EC(2007) Communication from the Commission to the Council, the European Parliament, the European Economic and Social Committee and the Committee of the Regions, on the mid-term review of the Strategy on Life Sciences and Biotechnology. Brussels, 10.4.2007. COM(2007) 175 final. http://ec.europa.eu/biotechnology/docs/com_2007_175_en.pdf

189 EU (2007) En-route to the knowledge-based bioeconomy. 30 May 2007. http://www.bio-economy.net/reports/files/koln_paper.pdf

190 http://cordis.europa.eu/fp7/kbbe/about-kbbe_en.html

191 Thacker E (2006) The Global Genome: Biotechnology, politics and culture. MIT Press.

192 Scott P (2003) The ethical implications of the new research paradigm. *Science and Engineering Ethics*, **9**(1), 7384.

193 Godin B (2006) The knowledge-based economy: conceptual framework or buzzword? Journal of *Technology Transfer*, **31**, 17-30.

194 BioPolis (2007) Inventory and analysis of national public policies that stimulate biotechnology research, its exploitation and commercialisation by industry in Europe in the period 20022005.http://ec.europa.eu/research/biosociety/pdf/biopolis-finalreport_en.pdf

195 Amerikaner, Japaner und Europäer haben die Jagd eröffnet: Supermarkt der gene.Der Spiegel, 44/93. 1st November 1993. http://service.spiegel.de/digas/find?DID=13692693

196 http://ec.europa.eu/dgs/policy_advisers/docs/PatentWorkshopSumm.pdf

197 The International Expert Group on Biotechnology, Innovation and Intellectual Property (2008) Toward a new era of Intellectual Property: from confrontation to negotiation. Montreal, Canada. September 2008.

198 Cutler T (2008) Venturous Australia - building strength in innovation. Review of the National Innovation System. Canberra, Australia. September, 2008. http://www.innovation.gov.au/innovationreview/Pages/home.aspx

199 OECD (2005) Proposal for a major Project on the Bioeconomy in 2030: A Policy Agenda. Organisation for Economic Co-operation and Development. http://www.insme.org/documenti/THE%20BIOECONOMY%20IN%202030_project.pdf

200 Darhos P, Braithwaite J (2002) Information feudalism: Who owns the knowledge economy? Earthscan.

201 Jenkins R, Henderson M(2008) Medical research is 'hindered by out-of-date laws'. The Times, 5th July 2008. http://www.timesonline.co.uk/tol/news/uk/science/article4272828.ece

202 Food Ethics Council (2004) Just Knowledge? Governing research on food and farming. http://www.foodethicscouncil.org/files/justknowledge.pdf .

203 Commission on Intellectual Property Rights, Innovation and Public Health (2006) Public health, innovation and intellectual property rights. April 2006.

204 Blind K, Edler J, Frietsch R, Schmoch U (2003) Erfindungen kontra Patente. Karlsruhe: Fraunhofer-Institut fur Systemtechnik und Innovationsforschung [Summary in English].

205 Patent inspectors strike over quality fears. 10th May 2006. http://news.zdnet.co.uk/itmanagement/0,1000000308,39268138,00.htm

206 Fearn H (2009) Pursuit of IP is 'a distraction'. Time Higher Education. 16th May 2009. http://www.timeshighereducation.co.uk/story.asp?storycode=406559

207 Tofano D, Wiechers IR, Cook-Deegan R (2006) Edwin Southern, DNA blotting, and microarray technology: A case study of the shifting role of patents in academic molecular biology. Genomics, Society and Policy, 2(2), 50-61. http://www.hss.ed.ac.uk/genomics/vol2no2/documents/DTGSPVol2No22006.pdf

208 Renault CS (2006) Academic capilatism and university incentives for faculty entrepreneurship. *Journal of Technology Transfer*, **31**, 227-239.

209 Guena A, Nesta L (2003) University patenting and its effects on academic research. http://www.druid.dk/conferences/summer2003/Papers/GEUNA_NESTA.pdf

210 http://www.ipr-helpdesk.org/documents/GracePeriodinventionLaw_0000004514_00.xml.html#N2001F

211 http://www.innovation.gov.uk/lambertagreements/index.asp?lvl1=1&lvl2=1&lvl3=0&lvl4=0

212 The Corner House (2004) Who owns the knowledge economy? Political organising behind TRIPS. http://www.thecornerhouse.org.uk/pdf/briefing/32trips.pdf

213 Albright M (2004) Profits pending: How life patents represent the biggest swindle of the 21st century. Common Courage Press, Canada.

214 McNally R, Wheale P (1998) The consequences of modern genetic engineering: patents, 'nomads' and the 'bio-industrial complex'. In: Wheale P, von Schomberg R, Glasner P (Eds) The social management of genetic engineering. Ashgate Publishing.

215 Jackson A, Mullan N (2008) Vita Nullius. *Soundings*. December 2007. http://www.lwbooks.co.uk/journals/soundings/current.html

216 Commission on Intellectual Property Rights, Innovation and Public Health (2006). Public Health, Innovation, and Intellectual Property Rights. http://www.who.int/intellectualproperty/en/

217Tansey G (2008) For good or for greed? The Ecologist, November 2008.

218 Barton JH (2002) Patents, genomics, research, and diagnostics. *Academic Medicine*, **77**, 1339-1347.

219 Harry D (2005) Acts of Self-Determination and Self-Defense: Indigenous Peoples' Responses to Biocolonialism. In: Krimsky S, Shorett P (Eds) Rights and Liberties in the Biotech Age: Why We Need a Genetic Bill of Rights. Lanham, Rowman & Littlefield.

220 Kaye J (2007) Patents and translational research in genomics. *Nature Biotechnology*, **25**(7), 739-741.

221 Caulfield T, Einsiedel E, Merz JF, Nicol D (2006) Trust, patents and public perceptions: the governance of controversial biotechnology research. *Nature Biotechnology*, 24, 1091-1095.

222 Andrews L, Paradise J, Holbrook T, Bochneak D (2006) When patents threaten science. *Science*, **314**, 1395-1396.

223 UK-IPO (2008) Technology report on genomic medicine. A response to the call for evidence of the House of Lords Select Committee on Genomic Medicine. April 2008.

224 UK court rules HGS gene patent invalid lawyers. Reuters, 9th February 2010. http://www.reuters.com/article/idUSLDE6181IV20100209

225 Calvert J (2007) Patenting genomic objects: genes, genomes, function and information. *Science as Culture*, **16**(2), 207-223.

226 Thomas SM, Hopkins MM, Brady M (2002) Shares in the human genome the future of patenting DNA. *Nature Biotechnology*, 20, 1185-1188.

227 Ioannidis JPA (2005) Why most published research findings are false. *PloS Medicine*, **2**(8), e124.

228 Ioannidis JPA (2006) Commentary: Grading the credibility of molecular evidence for complex diseases. *International Journal of Molecular Epidemiology*, **35**, 572-577.

229 Wallace HM, Mayer S (2007) Scientific Research Agendas: Controlled and Shaped by the Scope of Patentability. In: Waelde C, MacQueen H (Eds), Intellectual Property: the many faces of the public domain. Edward Elgar Publishing.

230 Mayer S (2006) Declaration of patent applications as financial interests: a survey of practice among authors of papers on molecular biology in Nature. *Journal of Medical Ethics*, **32**, 658-661.

231 Lebovitz RM (2007) The duty to disclose patent rights. *Northwestern Journal of Technology and Intellectual Property*, **6**(1), 36-45.

232 Oguamanam C (2007) Tension on the farm fields: The death of traditional agriculture? *Bulletin of Science, Technology & Society*, **27**(4), 260-273.

233 Hughes D (2008) Seed companies are big but not special. In: GM foods: the wrong debate? *Food Ethics*, **3**(3), 14.

234 Joly PB (2005) Resilient farming in a complex world = new issues for the governance of science and innovation, *Australian Journal of Experimental Agriculture*, **45**, 617-626.

235 Aoki K (2008) Seed wars. Carolina Academic Press. Durham, North Carolina.

236 Tansey G, Rajotte T [Eds] (2008) The future control of food: a guide to international negotiations and rules on Intellectual Property, biodiversity and food security. Earthscan, London.

237 Shiva V (2001) Biopiracy: the theft of knowledge and security. In: Tokar B [Ed] (2001) Redesigning life? Zed Books.

238 Oldham P, Cutter AM (2006) Mapping global status and trends in patent activity for biological and genetic material. *Genomics, Society and Policy*, **2**(2), 62-91.

239 Then C, Tippe R (2009) The future of seeds and food: under growing threat of patents and market concentration. No Patents on Seeds Coalition. April 2009. http://www.no-patents-on-seeds.org/index.php?option=com_content&task=view&id=91&Itemid=42

240 Commission on Intellectual Property Rights (2002) Integrating Intellectual Property Rights and Development Policy. London: Department for International Development

241 Pisano GP (2006) Science Business: The promise, the reality, and the future of biotech. Harvard Business School Press.

242 Richter B, Neises G (2009) 'Human' insulin versus animal insulin in people with diabetes mellitus (Review). The Cochrane Collaboration. Published by JohnWiley & Sons, Ltd. http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003816/pdf_fs.html

243 Laurance J (2009) Firm that led the way in DNA testing goes bust. The Independent. 18th November 2009. http://www.independent.co.uk/life-style/health-and-families/health-news/firm-that-led-the-way-in-dna-testing-goes-bust-1822413.html

244 Abate T (2002) Do gene patents wrap research in red tape? San Francisco Chronicle. 25th March 2002. http://www.gene-watch.org/programs/patents/red-tape.html

245 Ray T (2008) Whole genome sequencing poses 'serious challenge' to US patent system, HHS finds. 10th December 2008. Pharmacogenomics Reporter. http://www.genomeweb.com/dxpgx/whole-genome-sequencing-poses-%E2%80%98serious-challenge%E2%80%99-us-patent-system-hhs-finds-0

246 Cook-Deegan R, Chandrasekharan S, Angrist M (2009) the dangers of diagnostic monopolies. *Nature*, **458**, 405-406.

247 Gaisser S, Hopkins MM, Liddell K, Zika E, Ibarreta D (2009) The phantom menace of gene patents. *Nature*, **458**, 407-408.

248 Atkinson Roberts P (2004) Malaria Vaccine Initiative: Intellectual Property Rights and Vaccines in Developing Countries. WHO Meeting, April 19-20, 2004. http://www.who.int/intellectualproperty/events/en/Patricia.Roberts.pdf

249 Shapiro C(2000) Navigating the patent thicket: cross licences, patent pools, and standard setting. In: Jaffe B, Lerner J, Stern S (Eds). Innovation policy and the economy. MIT Press, 2000.

http://faculty.haas.berkeley.edu/shapiro/thicket.pdf

250 Editorial (2002) How many lawyers doe sit take…New Scientist. 18 May 2002. http://www.newscientist.com/article/mg17423430.100-how-many-lawyers-does-it-take-.html

251 D'Este P, Senker J, Costa J (2007) Biopolis National Report: United Kingdom. http://ec.europa.eu/research/biosociety/pdf/biopolis_unitedkingdom_en.pdf

252 http://ec.europa.eu/biotechnology/docs/com_2007_175_en.pdf

253 Strategy Unit (2003) Field work: weighing up the costs and benefits of GM crops. Cabinet Office, July 2003. http://www.cabinetoffice.gov.uk/strategy/~/media/assets/www.cabinetoffice.gov.uk/strategy/gm_crop_report%20pdf.ashx

254 Lean G (2007) GM: the secret files. The Independent. 28th October 2007. http://www.independent.co.uk/environment/green-living/gm-the-secret-files-395453.html

255 European Commission, DG Research (2004) Plants for the Future. http://www.epsoweb.org/Catalog/TP/Plants%20for%20the%20future-Dec04.pdf

256 Blake A (2009) BASF halts GM potato research in UK. Farmers Weekly, 8th July 2009. http://www.fwi.co.uk/Articles/2009/07/08/116528/BASF-halts-GM-potato-research-in-UK.htm

257 Laget, P & Cantley, M (2001) European Responses to Biotechnology: Research, Regulation, and Dialogue. Issues in Science and Technology Online. Summer 2001http://issues.org/17.4/laget.htm

258 Fernandez RA (2009) Biotech crops' global value reaches $7.5 billion. Philstar. 6th April 2009. http://www.philstar.com/Article.aspx?articleId=455280&publicationSubCategoryId=77

259 Royal Society (2009) Reaping the benefits: Science and the sustainable intensification of agriculture. October 2009.

260 Vecchio RP (2006) Journal reviewer ratings: Issues of particularistic bias, agreement, and predictive validity within the manuscript review process. *Bulletin of Science, Technology and Society*, **26**(3), 228-242.

261 http://www.rae.ac.uk/aboutus .

262 Gilbert N (2009) Good grades, but who gets the cash? *Nature*, **457**,1-122.

263 http://www.hefce.ac.uk/research/funding/QRFunding/

264 http://www.rae.ac.uk/aboutus/panels.asp

265 Smith A (2006) RAE changes threaten research reputation, warn VCs. *The Guardian*. 10th November 2006. http://education.guardian.co.uk/RAE/story/0,,1943776,00.html

266 Experts still needed [Editorial]. *Nature*, **447**, 7.

267 HEFCE (2007) Strategic Plan 2006-11. Updated April 2007. http://www.hefce.ac.uk/pubs/hefce/2007/07%5F09/07_09.pdf

268 Kaptchuk TJ (2003) Effect of interpretative bias on research evidence. *British Medical* Journal **326**: 1453-1455.

269 Patsopoulos NA, Analatos AA, Ioannidis JPA (2006) Origin and funding of the most frequently cited papers in medicine: database analysis. *British Medical Journal*, **322**(7549), 1061-1063.

270 Caulfield T(2007), Profit and the Production of the Knowledge: The Impact of Industry on Representations of Research Results, *Harvard Health Policy Review*, **8**, 68-77.

271 Krimsky S (2003) Science in the private interest: Has the lure of profits corrupted biomedical research? Rowman & Littlefield (Maryland).

272 Stelfox H, Chua G, O'Rourke K, Detsky A (1998) Conflict of interest in the debate over calcium-channel antagonists. *New England Journal of Medicine*, **2**, 101-106.

273 Bhandari M, Busse JW, Jackowski D, et al. (2004), Association between industry funding and statistically significant pro-industry findings in medical and surgical randomized trials. Canadian Medical Association Journal, **170**(4), 477-80.

274 Mohit Bhandari, Jason W. Busse, Dianne Jackowski,, et al., “Association between industry funding and statistically significant pro-industry findings in medical and surgical randomized trials” CMAJ 2004;170(4):477-80.

275 Friedman L, Richter E (2004), Relationship between conflicts of interest and research results, *Journal of General Internal Medicine*, **19**, 5156.

276 Lexchin J, Bero LA, Djulbegovic B, Clark O (2003) Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *British Medical Journal*, **326**, 1167-1170.

277 Hartmann M, Knoth H, Schulz D, Knoth S (2003) Industry sponsored studies in oncology vs studies sponsored by nonprofit organisations. *British Journal of Cancer*, **89**, 1405-1408.

278 Curtis P (2007) Researchers see bias in private-funded studies. *The Guardian*. 9th January 2007.

279 Katan MB (2007) (2007) Does Industry Sponsorship Undermine the Integrity of Nutrition Research? PLoS Med 4(1): e6 doi:10.1371/journal.pmed.0040006

280 Barnett A (2003) Revealed: how drug firms 'hoodwink' medical journals. *The Observer*, 7th December 2003. http://www.guardian.co.uk/society/2003/dec/07/health.businessofresearch

281 Gøtzsche PC, Hróbjartsson A, Johansen HK, Haahr MT, Douglas G. Altman DG, Chan A-W (2007), Ghost authorship in industry-initiated randomised trials, PLoS Medicine, **4**, 47-51.

282 Flanagin A, Carey L, Fonterosa P, Phillips SG, Pace BP et al. (1998) Prevalence of articles with honorary authors and ghost authors in peer-reviewed medical journals. *Journal of the American Medical Association*, **280**, 222-224.

283 Wager E (2007) Authors, Ghosts, Damned Lies, and Statisticians. PLoS Med 4(1): e34. doi:10.1371/journal.pmed.0040034

284 Lexchin J, Light DW (2006) Commercial influence and the content of medical journals. *British Medical Journal,* **332**, 1444-14447.

285 Ramsey S, Scoggins J (2008) Commentary: Practicing on the Tip of an Information Iceberg? Evidence of Underpublication of Registered Clinical Trials in Oncology. Oncologist. 2008 Sep 15. [Epub ahead of print].

286 Goldacre B (2008) Missing in action: the trials that did not make the news. *The Guardian*, 20th September 2008. http://www.guardian.co.uk/commentisfree/2008/sep/20/medicalresearch.cancer

287 House of Commons Health Committee (2005) The influence of the pharmaceutical industry. Fourth report of Session 2004-05. http://www.publications.parliament.uk/pa/cm200405/cmselect/cmhealth/42/42.pdf

288 MacLeod D (2005) Firms push scientists to tailor research results. The Guardian. 22nd March 2005.

289 Cart J (2005) U.S. Scientists Say They Are Told to Alter Findings. Los Angeles Times. 10th February, 2005.

290 Sainsbury, D(2004) Universities in the knowledge economy. Speech to the University of Surrey, 22nd November 2004. http://www.dti.gov.uk/ministers/speeches/sainsbury221104.html

291 Stivers R (2006) The need for a "shadow" university. *Bulletin of Science, Technology & Society*, **26**(3),217-227.

292 Castelfranchi C (2007) Six critical remarks on science and the construction of the knowledge society. *Journal of Science Communication*, **6**(4), 1-3. http://jcom.sissa.it/archive/06/04/Jcom0604(2007)C01/Jcom0604(2007)C03/Jcom0604(2007)C03.pdf

293 Smith L (2009) Robot scientist 'Adam' solves genetic problems. The Times. 3rd April 2009. http://www.timesonline.co.uk/tol/news/uk/science/article6024880.ece

294 Becher T, Trowler PR(2001) Academic tribes and territories: Intellectual inquiry and the culture of disciplines. Open University Press, 2001. http://www.mcgraw-hill.co.uk/openup/chapters/0335206271.pdf

295 OECD (2003) Turning science into business: Patenting and licensing at public research organizations.

296 http://www.ktnetworks.co.uk/epicentric_portal/site/KTN/?mode=0

297 http://ec.europa.eu/education/policies/educ/bologna/bologna_en.html

298 http://www.bologna-bergen2005.no/Docs/00-Main_doc/990719BOLOGNA_DECLARATION.PDF

299 EC(2007) Communication from the Commission to the Council, the European Parliament, The European Economic And Social Committee and the Committee of the Regions. Improving knowledge transfer between research institutions and industry across Europe: embracing open innovation Implementing the Lisbon agenda. Brussels, 4.4.2007

COM(2007) 182 final. http://eur-lex.europa.eu/LexUriServ/site/en/com/2007/com2007_0182en01.pdf

300 Ganache I (2006) "Commercial revolution" of science: the complex reality and experience of genetic and genomic scientists. *Genomics, Society and Policy*, **2**(3), 96-114.

301 http://www.libraryhouse.net/publications/download/Gatsby-v8lowres.pdf

302 http://www.libraryhouse.net/publications/download/MTSO_report_Mar2007.pdf

303 http://www.foundation.org.uk/events/pdf/20071114_Sainsbury.pdf

304 http://www.dius.gov.uk/speeches/pearson_britishventure.html

305 Smith G, Akram MS, Redpath K, Bains W (2009) Wasting cash the decline of the British biotech sector. Nature Biotechnology, 27(6), 531-537.

306 Rutovitz J, Mayer S (2002) Genetically modified and cloned animals. All in a good cause? GeneWatch UK. April 2002. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/GMAnimalsA4.pdf

307 EFSA (2008) Scientific Opinion of the Scientific Committee. Food Safety, Animal Health and Welfare and Environmental Impact of Animals derived from Cloning by Somatic Cell Nucleus Transfer (SCNT) and their Offspring and Products Obtained from those Animals. Adopted on 15 July 2008. *The EFSA Journal*, 767, 1-49.

308 Fransman M (2001) Designing Dolly: interactions between economics, technology and science and the evolution of hybrid institutions. *Research Policy*, **30**, 263-273.

309 Ward S (2003) Dolly creators begin mass slaughter. *The Scotsman*, 15th July 2003.

310 Foley S (2003) Dolly the Sheep company sacks workers in struggle for survival. The Independent. 19th June 2003. http://www.independent.co.uk/news/business/news/dolly-the-sheep-company-sacks-workers-in-struggle-for-survival-541198.html

311 http://www.isis-innovation.com/about/news/gnostics.html .

312 http://www.g-nostics.com/index.php?option=com_content&task=view&id=12&Itemid=26

313 Doyle C (2004) DNA test can identify 'the smokers' gene'. The Telegraph. 3rd December 2004. http://www.telegraph.co.uk/news/uknews/1478004/DNA-test-can-identify-'the-smoker's-gene'.html

314 'DNA test' to help smokers quit. 2nd December 2004. BBC Online. http://news.bbc.co.uk/1/hi/health/4061137.stm

315 Three reasons not to but the NicoTest genetic test. GeneWatch UK. December 2004. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Nicotest_brief_final.pdf

316 Letter from Oxford University to GeneWatch UK. 18th March 2005. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/UofOxford_1.pdf

317 Letter from Cancer Research Technology to GeneWatch UK. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/CRT.pdf

318 http://www.nicotest.com

319 http://www.uknscc.org/2007_UKNSCC/presentations/lisa_miles.html

320 Hall WD, Gartner CE, Carter A (2008) The genetics of nicotine addiction liability: ethical and social policy implications. *Addiction*,**103**, 350-359.

321 Gartner CE, Barendregt JJ, Hall WD (2009) Multiple genetic tests for susceptibility to smoking do not outperform simple family history. *Addiction*, **104**, 118-126.

322 www.vbc-genomics.com

323 GeneWatch UK evidence to the MHRA regarding genetic tests sold by the UK company Genetic Health. August 2007. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/MHRA_GWevidence_fin.doc

324 GeneWatch UK evidence to the MHRA regarding genetic tests sold by the UK company Genetic Health. Appendix A. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/AppendixA.pdf

325 Fujimura JH (1988) The molecular biological bandwagon in cancer research: where social worlds meet. *Social Problems*, **35**(3), 261-283.

326 Buchanan AV, Weiss KM, Fullerton SM (2006) On stones, wands and promises. *International Journal of Epidemiology*, **35**, 593-596.

327 Francis CA, Lieblein G, Breland TA, Salomonsson L, Geber U, Sriskandarajah N, Langer V (2008) Transdisciplinary research for a sustainable agriculture and food sector. *Agronomy Journal*, **100**(3), 771-776.

328 Butler D (2008) Crossing the Valley of Death. *Nature*, **453**, 840-842.

329 Duyk G (2003) Attrition and translation. *Science*, **302**, 603-605.

330 BBSRC (2009) Future directions in research relating to food security. A consultation by the Biotechnology and Biological Sciences Research Council (BBSRC) on behalf of the Research Councils.

331 Martin B (1998) Information liberation: Challenging the corruptions of information power. Freedom Press. London. (Chapter 7).

332 Doward J (2004). Tobacco giant funds 'bad gene' hunt. *The Observer*. 30 May 2004.

333 Proctor RN(1995) Cancer Wars. New York, Basic Books.

334 Lichtenstein P, Holm NV, Verkasalo PK, Iliadou A, Kaprio J, Koskenvuo M, Pukkala E, Skytthe A, Hemminki K (2000) Environmental and heritable factors in the causation of cancer analyses of cohorts of twins from Sweden, Denmark, and Finland. *New England Journal of Medicine*, **343**(2), 78-85.

335 Braun MM, Caporaso NE, Page WF, Hoover RN (1995) A cohort study of twins and cancer. *Cancer Epidemiology Biomarkers and Pre*vention, **4**(5),469-73.

336 Wallace HM (2009) Genetic screening for susceptibility to disease. In: Encyclopedia of Life Sciences. John Wiley & Sons Ltd., Chichester. http://www.els.net/[Doi: 10.1002/9780470015902.a0021790]

337 Wallace HM (2009) Big Tobacco and the human genome: driving the scientific bandwagon? *Genomics, Society and Policy*, **5**(1), 1-54. http://www.gspjournal.com/

338 Marcy TW, Stefanek M, Thompson KM (2002) Genetic Testing for Lung Cancer Risk: If Physicians Can Do It, Should They? *Journal of General Internal Medicine*, **17**, 946-951.

339 Hall, W, Madden, P, Lynskey, M (2002) The Genetics of Tobacco Use: Methods, Findings and Policy Implications. *Tobacco Control*; **11**, 119-124.

340 Caporaso, N, Hayes, RB, Dosemeci, M, Hoover, R, Ayesh, R, Hetzel, M, Idle, J (1989), Lung Cancer Risk, Occupational Exposure, and the Debrisoquine Metabolic Phenotype, *Cancer Research*, **49**, 3675-3679.

341 Vineis P, Ahsan H, Parker M (2004) Genetic screening and occupational and environmental exposures. *Occup Environ Med*, **62**, 657-662.

342 Idle JR. Pharmacogenetics in the new patterns of healthcare delivery. *Pharmacogenetics* 1995; **5**:347-350.

343 http://www.liv.ac.uk/pharmacogenetics/professional_perspective.htm

344 Pearce N (1996) Traditional epidemiology, modern epidemiology, and public health. American *Journal of Public Health*, **86**(5), 678-683.

345 Davies K (2001) The Sequence: Inside the race for the Human Genome. Weidenfeld & Nicholson, London.

346 Weelcome Trust (2009) Lung cancer and melanoma cancer genomes are revealed. Press Release. 17th December 2009. http://www.wellcome.ac.uk/News/Media-office/Press-releases/2009/WTX058047.htm

347 Chase DS, Tawn EJ, Parker L, Jonas P, Parker CO, Burn J (1998) *The North Cumbria Community Genetics Project*, **35**, 413-416.

348 Whong-Barr M, Haimes E (2004) Levels and styles of participation in genetic databases. In: Tutton R, Corrigan O (eds) Genetic databases: socio-ethical issues in the collection and use of DNA. Routledge.

349 The North Cumbria Community Genetics Project (2000) Report 1996-2000. September 2000.

350 National Radiological Protection Board (1999) Genetic Heterogeneity in the Population and its Implications for Radiation Risk Doc. NRPB 10 (3) 1999. Chilton, Oxon: NRPB

351 Gilham I, Rowland, T (2001), Predictive Medicine: Potential benefits from the integration of diagnostics and pharmaceuticals, International Journal of Medical Marketing, 2, 18-22.

352 Sykes R (2000) New medicines, the practice of medicine, and public policy. Nuffield Trust, 2000. Lodon, The Stationary Office.

353 GeneWatch UK (2009) Is 'early health' good health? April 2009. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Data_mining_brief_fin.doc

354 Wallace HM (2006). Your diet tailored to your genes: preventing diseases or misleading marketing? GeneWatch UK. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Nutrigenomics.pdf

355 Cannon G(2004) Out of the box. *Public Health Nutrition*, 7(1), 3-6.

356 http://www.ilsi.org/AboutILSI

357 http://www.ilsi.org/NR/rdonlyres/39EDBCDE-0F3A-4A94-B467-13E4169A1A76/0/Assembly_of_Members.pdf

358 Dye L, Blundell J (2002) Functional foods: psychological and behavioural functions. *British Journal of Nutrition*, **88**, Suppl.2, S187-S211.

359 ILSI (2002) Concepts of functional foods. ILSI Europe Concise Monograph Series. http://europe.ilsi.org/file/ILSIFuncFoods.pdf

360 GeneWatch UK(2009) Agrofuels and the use of genetic modification. July 2009.

361 Nelkin D (1994) Promotional metaphors and their popular appeal. *Public Understanding of Science*, **3**, 25-31.

362 Resberger B (2009) Science journalism: Too close for comfort. *Nature*, **459**, 1055-1056.

363 Guthrie J (2007) Business and boffins have a volatile chemistry. Financial Times, 29th November 2007. http://www.ft.com/cms/s/0/63e00206-9e1e-11dc-9f68-0000779fd2ac.html?nclick_check=1

364 Blackman S (2009) Promises, promises. The Scientist, **23**(11), 28. http://www.the-scientist.com/article/display/56082/

365 Bubela TM, Caulfield TA (2004) Do the print media “hype” genetic research? A comparison of newspaper stories and peer-reviewed research papers. *Canadian Medical Association Journal*, **170**(9), 1399-1407.

366 Caulfield T (2004) The commercialisation of medical and scientific reporting. *PloS Medicine*, **1**(3), e38.

367 Caulfield T (2005) Popular media, biotechnology, and the 'cycle of hype'. Houston Journal of Health Law & Policy, 52, 213-223. http://www.law.uh.edu/hjhlp/Issues%5CVol_52%5CCaulfield.pdf

368 Petersen A (2001) Biofantasies: genetics and medicine in the print news media. Social *Science and Medicine*, **52**, 1255-1268.

369 Ooi ES, Chapman S (2003) An analysis of newspaper reports of cancer breakthroughs: hope or hype? *Medical Journal of Australia*, **179**, 639-643.

370 Woloshin, S, Schwarz, LM (2002) Press Releases: Translating Research Into News, *JAMA*, 287 (21), 2856-2858.

371 Cheerleader or watchdog? *Nature*, **459**, 1033.

372 Murcott T (2009) Science journalism: Toppling the priesthood. *Nature*, **459**, 1054-1055.

373 Bosman J (2006) Reporters Find Science Journals Harder to Trust, but Not Easy to Verify. The New York Times. 13th February 2006.

374 Tatsioni A, Bonitis NG, Ioannidis JPA (2007) Persistence of contradicted claims in the literature. *Journal of the American Medical Association*, **298**, 2517-2526.

375 Paz-Elizur, T, Krupsky, M, Blumenstein, S, Elinger, D, Schechtman, E, Livneh, Z. DNA repair activity for oxidative damage and risk of lung cancer. *J Natl Cancer Inst* 2003; **95**(17): 1312-19.

376 JNCI. Press Release. DNA repair activity may be associated with risk of lung cancer. 2003 Sept 3. Available on: URL: http://jncicancerspectrum.oupjournals.org/cgi/content/full/jnci;95/17/1257-a . Accessed: 2008 Oct 31.

377 Reuters Health Information. Lower levels of DNA-repair enzyme associated with lung cancer risk. 2003 Sept 3.

378 Hawkes, N. Test will show which smokers face lung cancer death. *The Times* 2003 Sept 3.

379 Demetriou, D. Gene link to lung cancer could lead to early blood test. *The Independent* 2003 Sept 3.

380 Anon. Smokers' death test. *The Sun* 2003 Sept 3.

381 Anon. The battles to come. *The Economist* 2003 Sept 5.

382 Doward J (2004). Tobacco giant funds 'bad gene' hunt. *The Observer*. 30 May 2004. http://www.guardian.co.uk/society/2004/may/30/health.smoking

383 Li H, Hao X, Zhang W, Wei Q, Chen K (2008) The hOGG1 Ser326Cys polymorphism and lung cancer risk analysis: a meta-analysis. *Cancer Epidemiology, Biomarkers and Prevention*, **17**, 1739-1745.

384 Jones S (2009) One gene will not reveal all life's secrets. The Telegraph, 20th April 2009. http://www.telegraph.co.uk/scienceandtechnology/science/stevejones_viewfromthelab/5189941/One-gene-will-not-reveal-all-lifes-secrets.html

385 Alleyne R, Devlin K (2009) Genetic research in a “blind alley” in search for cures for common diseases. The Telegraph, 20th April 2009. http://www.telegraph.co.uk/health/healthnews/5189873/Genetic-research-in-a-blind-alley-in-search-for-cures-for-common-diseases.html

386 Gannon F (2007) Hope, hype and hypocrisy. *EMBO Reports*, **8**, 12, 1087. http://www.nature.com/embor/journal/v8/n12/full/7401129.html

387 Maher B (2008) The case of the missing heritability. *Nature*, 456 (6), 18-21.

388 Duncan DE (2010) From hope to reality in personalized medicine. Technology Review. 5th February 2010. http://www.technologyreview.com/biomedicine/24481/

389 Burne J (2003) Genetics: hope or hype? *The Times*. 5th May 2003. http://www.timesonline.co.uk/tol/life_and_style/health/article878156.ece

390 Moss L (2010) Half-hour test to check for killer diseases. The Scotsman. 16th February 2010. http://thescotsman.scotsman.com/news/Halfhour-DNA-test-to-check.6074299.jp

391 EPSO, EuropaBio, ESA, COPA, Cogeca (2007) 'Plants for the Future' invites Europe to reap fruits of knowledge-based bio-economy. Press Release. 25th June 2007. http://www.epsoweb.org/Catalog/TP/Launch_25June07/PR-Launch_SRA_EN.pdf

392 Butelli E, Titta L, Giorgio M, Mock H-P, Matros A, Peterek S, Schijlen EGWM, Hall RD, Bovy AG, Luo J, Martin C (2008) Enrichment of tomato fruit with health-promoting anthocyanins by expression of select transcription factors. *Nature Biotechnology* 26, 1301 – 1308.

393 John Innes Centre (2008) Purple tomatoes may keep cancer at bay. Press Release. October 2008. http://www.jic.ac.uk/corporate/media-and-public/current-releases/081026martin.htm

394 http://www.fsascience.net/archives/2008/10

395 NHS Choices (2008) Purple tomatoes 'beat cancer'. Monday October 27th 2008. http://www.nhs.uk/news/2008/10October/Pages/Purpletomatoes.aspx

396 http://info.cancerresearchuk.org/news/archive/cancernews/2008-10-27-purple-gm-tomato-high-in-antioxidants

397 Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C (2008) Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. *Cochrane Database of Systematic Reviews*, Issue 2. Art. No.: CD007176. DOI: 10.1002/14651858.CD007176. http://www.cochrane.org/reviews/en/ab007176.html

398 Glover, D (2008) Made by Monsanto: the corporate shaping of GM crops as a technology for the poor. STEPS Working Paper 11. STEPS Centre, Brighton. http://www.steps-centre.org/PDFs/GM%20Crops%20web%20final_small.pdf

399 http://en.wikipedia.org/wiki/File:TIME_cover_july_31_2000.jpg

400 Gugliotta G (2000) New vitamin A-rich rice strain termed nutrition breakthrough. The Washington Post. 14th January 2000.

401 Wron M, Tait N (2000) Third world to be given free GM rice. The Financial Times, 16th May 2000.

402 Jha A (2009) Return of GM crops: Ministers back moves to grow crops in UK. The Guardian. 17th September 2007. http://www.guardian.co.uk/science/2007/sep/17/gmcrops.politicalnews1

403 Poulter S (2007) Scientist who claimed GM crops could solve Third World hunger admits he got it wrong. Daily Mail, 18th December 2007. http://www.dailymail.co.uk/sciencetech/article-503339/Scientist-claimed-GM-crops-solve-Third-World-hunger-admits-got-wrong.html

404 Campbell C (2010) Can GM crops feed the hungry? SciDev.net 21st January 2010. http://www.alertnet.org/thenews/newsdesk/scidev/126408590359.htm

405 Fortun M (2008) Promising genomics: Iceland and deCODE Genetics in a world of speculation. University of California Press.

406 Byers S (1999) Speech to the Biotechnology Industry Association Gala Dinner, London. 22nd January 1999. http://www.berr.gov.uk/ministers/archived/byers220199.html

407 Ziman J (2003) Non-instrumental roles of science. *Science and Engineering Ethics*, **9**, 17-27.

408 Sustainability (1997) Food integrity: Summary report on the stakeholder roundtable held in Brussels, Belgium on April 3 & 4, 1997. Sponsored by: Monsanto Company.

409 Marris C (2001) Public views on GMOs: deconstructing the myths. *EMBO Reports*, **2**(7), 545-548.

410 Jansen K, Roquas E (2005) Absentee expertise: science advice for biotechnology regulation in developing countries. In: Leach M, Scoones I, Wynne B (Eds) Science and citizens. Zed Books.

411 EU(2007) EU puts emphasis on innovation in the field of biotechnology. Press Release. 11th April 2007. http://europa.eu/rapid/pressReleasesAction.do?reference=IP/07/484

412 http://www.berr.gov.uk/bre/

413 Hampton P (2005) Reducing administrative burdens: effective inspection and enforcement. HM Treasury. March 2005. http://www.berr.gov.uk/files/file22988.pdf

414 Better Regulation Task Force (2005) Less is more: Reducing burdens, improving outcomes. March 2005. http://archive.cabinetoffice.gov.uk/brc/upload/assets/www.brc.gov.uk/lessismore.pdf

415 Cook G (2008) The nature of the argument. *The Ecologist*. November 2008. pp31-32.

416 Wynne B (2001) Creating public alienation: Expert cultures of risk and ethics on GMOs. *Science as Culture*, **10**(4), 445-481.

417 Mayer S, Stirling S (2002) Finding a precautionary approach to the evaluation of GM crops. *Journal of Agricultural and Environmental Ethics*, **15**(1), 57-71.

418 http://www.gmo-safety.eu/en/debate/657.docu.html

419 Oreszczyn S (2004) Precautionary expertise for GM crops. National report United Kingdom. March 2004. http://technology.open.ac.uk/cts/national/uk%20national%20report%20PEG.pdf

420 More information is available on: http://www.genewatch.org/sub-405264

421 Council of the European Union (2008) Council conclusions on genetically-modified organisms (GMOs). 2912th Environment Council Meeting. Brussels, 4th December 2008. http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressData/en/envir/104509.pdf

422 Rodgers C (2007) Coexistence or conflict? A European perspective on GMOs and the problem of liability. *Bulletin of Science, Technology and Society*, **27**(3), 233-250.

423 Dona A, Arvanitoyannis IS (2009) Health risks of genetically modified foods. *Critical Reviews in Food Science and Nutrition*, **49**, 164-175.

424 De Vendômois JS, Roullier F, Cellier D, Séralini G-E (2009) A comparison of the effects of three GM corn varienties on mammalian health. *International Journal of Biosciences*, **5**(7), 706-726.

425 Jiao Z, Si X-X, li G-K, Zhang Z-M, Xu X-P (2010) Unintended Compositional Changes in Transgenic Rice Seeds (Oryza sativa L.) Studied by Spectral and Chromatographic Analysis Coupled with Chemometrics Methods. *Journal of Agricultural and Food Chemistry*, **58**, 1746-1754.

426 Spök A (2007) Molecular farming on the rise GMO regulators still walking a tightrope *Trends in Biotechnology*, **25**(2), 74-82.

427 Anon (2004) Drugs in crops: The unpalatable truth. [Editorial]. *Nature Biotechnology*, **22**(2), 133.

428 Lund P (2008) The science: We have answers but not enough. In: GM foods: the wrong debate? *Food Ethics*, **3**(3), 2-4.

429 Waltz, E. (2009) Under wraps. *Nature Biotechnology*, **27**(10), 880-882.

430 Sharma AB (2007) Disclose biosafety data of GM crops: CIC. The Financial Express. 23rd November 2007. http://www.financialexpress.com/news/Disclose-biosafety-data-of-GM-crops-CIC/242626/

431 Patch C, Sequeiros J, Cornel MC (2009) Genetic horoscopes: Is it all in the genes? Points for regulatory control of direct-to-consumer genetic testing. *European Journal of Human Genetics*, 1-3. doi:10.1038/ejhg.2008.246

432 Gurwitz D, Bregman-Eschet Y (2009) Personal genomics services: whose genomes? *European Journal of Human Genetics*, 1-7. doi:10.1038/ejhg.2008.254

433 Flyvbjerg B (2003) Megaprojects and risk: An anatomy of ambition. Cambridge Press.

434 http://greenbook.treasury.gov.uk/

435 Sherden WA (1998) The big business of buying and selling predictions. Wiley.

436 Walker W (1999) Nuclear entrapment: THORP and the politics of commitment. IPPR, London.

437 http://www.hefce.ac.uk/news/hefce/2008/grant/letter.htm

438 http://www.berr.gov.uk/science/knowledge-transfer/heif/page12054.html

439 http://www.innovateuk.org/

440 http://www.foresight.gov.uk/index.asp

441 http://www.hm-treasury.gov.uk/media/2/5/spend04_sciencedoc_8-9_090704.pdf

442 http://www.food.gov.uk

443 Barling D, Henderson R (2000) Safety First? A map of public sector research into GM food and food crops in the UK. Centre for Food Policy, Thames Valley University. Discussion Paper 12. October 2000.

444 GM Freeze (2009) Blind Alley? June 2009. http://www.gmfreeze.org/uploads/blind_alley_final.pdf

445 http://www.fera.defra.gov.uk/

446 http://www.defra.gov.uk/evidence/science/index.htm

447 DEFRA (2003) Delivering the evidence: Defra's science and innovation strategy (2003-06). http://www.defra.gov.uk/science/documents/Delivering_The_Evidence.pdf

448 Curry D (2002) Farming and food: a sustainable future. Report of the Policy Commission on the Future of Farming and Food. January 2002.

http://archive.cabinetoffice.gov.uk/farming/pdf/PC%20Report2.pdf

449 DEFRA (2002) *Strategy for Sustainable Farming and Food: Facing the Future* 12 December 2002. http://www.defra.gov.uk/farm/policy/sustain/strategy.htm

450 http://www.defra.gov.uk/farm/policy/sustain/index.htm

451 http://www.defra.gov.uk/science/rpg/research_priorities.htm

452 DEFRA (2005) The First Report of the Sustainable Farming and Food Research Priorities Group. March 2005 http://www.defra.gov.uk/science/documents/RPG/Papers/FinalRPGreport.pdf

453 http://www.defra.gov.uk/science/documents/RPG/Papers/FinalRPGreport2.pdf

454 DEFRA (2006) Our approach to evidence and innovation. http://www.defra.gov.uk/science/how/documents/EvidenceAndInnovation.pdf

455 DEFRA (2006) Our approach to evidence and innovation. http://www.defra.gov.uk/evidence/science/how/documents/EvidenceAndInnovation.pdf

456 DEFRA (2010) Defra's evidence investment strategy: 2010-2013 and beyond. http://www.defra.gov.uk/evidence/science/how/documents/eis-100126.pdf

457 http://www.innovateuk.org/ourstrategy/innovationplatforms/sustainableagricultureandfood.ashx

458 http://www.innovateuk.org/ourstrategy/technology-areas/bioscience.ashx

459 http://www.innovateuk.org/aboutus/governingboard.ashx

460 http://www.efrc.com/manage/authincludes/article_uploads/WheatBreedingLINK%20Project%20Summary.pdf

461 http://www.efrc.com/manage/authincludes/article_uploads/project%20details%20for%20website%20-%20OATLINK.pdf

462 http://www.scotland.gov.uk/Topics/Research/About/EBAR/

463 http://www.scotland.gov.uk/Topics/Research/About/EBAR/future-research-strategy

464 http://www.scotland.gov.uk/About/purposestratobjs

465 Initial Scoping Review of the High Level SNIFFER report on the Strategic Research Review 2007 Strategic Themes for the next Scottish Government Rural, Environment and Marine Research Strategy: Final Report. 17th January 2008. http://www.scotland.gov.uk/Publications/2008/01/17154036/0

466 http://www.erff.org.uk/index.aspx

467 http://www.lwec.org.uk/

468 http://www.defra.gov.uk/farm/policy/levy-bodies/index.htm

469 http://www.ahdb.org.uk/

470 http://www.nihr.ac.uk/about/Pages/about_funding.aspx

471 http://www.abpi.org.uk/statistics/section.asp?sect=3

472 UK Clinical Research Collaboration (2006) UK Health Research Analysis. May 2006. http://www.ukcrc.org/PDF/UKCRC_Health_Research_Analysis_Report.pdf

473 http://www.nihr.ac.uk/Pages/default.aspx

474 Dusic N (2008) Would Haldane mind, in principle? Research Research. 21st May 2008.

475 IUSS Committee (2008) Science Budget Allocations. Fourth Report of Session 2007-08. House of Commons Innovation, Universities, Science and Skills Committee. HC 215-I. http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/215/215.pdf

476 Science and Technology Committee (2006) Third Report 2005/06: Research Council Support for Knowledge Transfer. HC 995-I and HC 995-II. http://www.publications.parliament.uk/pa/cm200506/cmselect/cmsctech/cmsctech.htm

477 RCUK(2006) Knowledge transfer in the eight Research Councils. Independent External Challenge Report to Research Councils UK. April 2006. http://www.rcuk.ac.uk/cmsweb/downloads/rcuk/documents/exchallenge.pdf

478 Denham J (2007) Speech for the launch of the Science Budget Allocations. Church House, London. 11th December 2007. http://www.dius.gov.uk/speeches/denham_science_budget_111207.html

479 D'Este P, Senker J, Costa J (2007) BioPolis Inventory and analysis of national public policies that stimulate research in biotechnology, its exploitation and commercialisation by industry in Europe in the period 20022005. National report of United Kingdom. SPRU, Brighton. March 2007. http://ec.europa.eu/research/biosociety/pdf/biopolis_unitedkingdom_en.pdf

480 DIUS (2007) The allocations of the science budget 2008/09 to 2010/11. http://www.dius.gov.uk/reports_and_publications/~/media/publications/U/URN07114

481 http://www.bbsrc.ac.uk/index.html

482 Corbyn Z (2008) New BBSRC chief 'Olympic gold medallist' of research. *Times Higher Educational Supplement*. 2nd October 2008. http://www.timeshighereducation.co.uk/story.asp?storycode=403769

483 http://www.gmwatch.org/profile1.asp?PrId=21

484 http://www.bbsrc.ac.uk/web/FILES/Conflicts/council_conflicts.pdf

485 BBSRC (2003) Bioscience for Society: A ten year vision "Towards Predictive Biology". http://www.bbsrc.ac.uk/publications/policy/bbsrc_vision.pdf

486 BBSRC (2010) The Age of Bioscience: Strategic Plan 2010-2015. http://www.bbsrc.ac.uk/publications/policy/strategy/strategic-plan-index.aspx

487 http://www.bbsrc.ac.uk/funding/apply/grants_guide.pdf

488 BBSRC (2007) Technology Strategy: Underpinning industrial needs. http://www.bbsrc.ac.uk/web/FILES/Publications/technology_strategy.pdf

489 http://www.mrc.ac.uk/Ourresearch/Portfolios/Overview/index.htm

490 Qinetiq deal 'cost UK taxpayers'. BBC Online. 23rd November 2007. http://news.bbc.co.uk/1/hi/business/7108444.stm

491 http://www.mrc.ac.uk/AboutUs/OurStructure/CEO/index.htm

492 MRC(2009) Health research opportunities meeting. Mar Hall, Renfrewshire, 1-3 December 2008. http://www.mrc.ac.uk/consumption/groups/public/documents/content/mrc005751.pdf

493 MRC (2009) Research changes lives. MRC Strategic Plan 2009-2014. http://www.mrc.ac.uk/About/Strategy/StrategicPlan2009-2014/index.htm

494 http://www.mrc.ac.uk/About/Strategy/StrategicPlan2009-2014/StrategicAim4/Useofpopulationbaseddata/index.htm

495 http://www.mrc.ac.uk/Sciencesociety/Publicinvolvement/Publicpanel/index.htm

496 http://www.mrc.ac.uk/Sciencesociety/Publicinvolvement/Consultations/index.htm

497 http://www.mrctechnology.org/home.htm

498 MRC & Ernst and Young (2007) Review of MRC roles, structures and operations. 1st June 2007. http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC003764

499 http://www.mrc.ac.uk/NewsViewsAndEvents/News/MRC004303

500 http://www.mrc.ac.uk/ApplyingforaGrant/CallsForProposals/Celltherapyresearch/index.htm

501 http://cordis.europa.eu/fetch?CALLER=PROGLINK_PARTNERS&ACTION=D&DOC=46&CAT=PROG&QUERY=011a4a05eda1:29ce:2ff9aea5&RCN=78

502 http://cordis.europa.eu/fetch?CALLER=PROGLINK_PARTNERS&ACTION=D&DOC=1&CAT=PROG&QUERY=011a4a075774:4d65:1eb0a89e&RCN=118

503 http://cordis.europa.eu/fetch?CALLER=PROGLINK_PARTNERS&ACTION=D&DOC=1&CAT=PROG&QUERY=011a4a0855f2:a04f:188ac081&RCN=156

504 http://www.biomatnet.org/secure/Fair/S1120.htm

505 http://cordis.europa.eu/fetch?CALLER=PROGLINK_PARTNERS&ACTION=D&DOC=47&CAT=PROG&QUERY=011a4a05eda1:29ce:2ff9aea5&RCN=192

506 http://cordis.europa.eu/fetch?CALLER=PROGLINK_PARTNERS&ACTION=D&DOC=49&CAT=PROG&QUERY=011a4a05eda1:29ce:2ff9aea5&RCN=191

507 Guy K, Amanatidou E, Psarra F (2005) Framework Programme 5 (FP5) impact assessment: a survey

conducted as part of the five-year assessment of European Union research activities (1999-2003). *Science and Public Policy*, **32**(5), 349-366.

508 Friends of the Earth Europe (2007) The EU's biotechnology strategy: mid-term review or mid-life crisis? March 2007. http://www.foeeurope.org/publications/2007/FoEE_biotech_MTR_midlifecrisis_March07.pdf

509 http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/07/130&format=HTML&aged=0&language=EN

510 EC (2007) Commission staff working document. Brussels, 10.4.2007 SEC(2007) 441. Http://ec.europa.eu/biotechnology/docs/commission_staff_working_document_sec_2007_441_en.pdf

511 http://cordis.europa.eu/search/index.cfm?fuseaction=proj.document&PJ_RCN=7981511

512 http://cordis.europa.eu/search/index.cfm?fuseaction=proj.document&PJ_LANG=EN&PJ_RCN=7900362&q=90D27D07A433B57D7872D58782148017&type=sim

513 http://cordis.europa.eu/search/index.cfm?fuseaction=proj.document&PJ_LANG=EN&PJ_RCN=8820547&q=1660367A70C60A98CF2E2C99EBBF7B47&type=sim

514 http://cordis.europa.eu/search/index.cfm?fuseaction=proj.document&PJ_LANG=EN&PJ_RCN=7517703&q=5F09D5EA88EBBE2E55CC2C8D14FB243B&type=sim

515 http://cordis.europa.eu/search/index.cfm?fuseaction=proj.document&PJ_LANG=EN&PJ_RCN=7492833&q=1D07A2601D86EA63E1EB7073C00FF3F6&type=sim

516 http://www.spas-project.eu/home

517 TAB working report No 104. Green genetic engineering transgenic plants of the 2nd and 3rd generation. http://www.tab.fzk.de/en/projekt/zusammenfassung/ab104.htm [summary]

518 Friends of the Earth Europe (2007) The relationship between the biotech industry and the European Commission. October 2007. http://mail.foeeurope.org/corporates/pdf/too-close-for-comfort.pdf

519 http://www.europabio.org/eu_index.htm

520 http://ec.europa.eu/research/eurab/index_en.html

521 ERAB (2004) European Advisory Board Report on European Technology Platforms. January 2004. http://ec.europa.eu/research/eurab/pdf/recommendations9.pdf

522 http://ec.europa.eu/research/eurab/members.html

523 http://ec.europa.eu/research/eurab/members_eurab2.html

524 http://ec.europa.eu/research/life-sciences/egls/index_en.html

525 http://ec.europa.eu/research/press/2004/pr1409en.cfm

526 http://ec.europa.eu/research/life-sciences/egls/pdf/conclusions_egls.pdf

527 Siune K, Schmidt EK, Aagaard K (2005) Implementation of European research policy. *Science and Public Policy*, **32**(5), 375-384.

528 Polt W, Streicher G (2005) Trying to capture additionality in Framework Programme 5. *Science and Public Policy*, **32**(5), 367-372.

529 Arnold E, Clark J, Muscio A (2005) What the evaluation record tells us about European Union Framework Programme performance. *Science and Public Policy*, **32**(5), 385-397.

530 EC(2005) Five year assessment of the European Union research Framework Programmes 1999-2003. http://www.euractiv.com/29/images/five_year_assessment_tcm29-135412.pdf

531 http://cordis.europa.eu/documents/documentlibrary/72284461EN6.pdf

532 ftp://ftp.cordis.europa.eu/pub/era/docs/com2004_353_en.pdf

533 http://cordis.europa.eu/fetch?ACTION=D&SESSION=&DOC=1&LAN=EN&RCN=6794&CALLER=FP7_LIB

534 http://cordis.europa.eu/fetch?ACTION=D&SESSION=&DOC=1&LAN=EN&RCN=6797&CALLER=FP7_LIB

535 http://cordis.europa.eu/fetch?ACTION=D&SESSION=&DOC=1&LAN=EN&RCN=6798&CALLER=FP7_LIB

536 http://cordis.europa.eu/fp7/flowchart_en.html

537 http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressData/en/misc/92236.pdf

538 EU issues first Framework call. [News in Brief]. *Nature Biotechnology*, **25**(1), 9.

539 http://cordis.europa.eu/fp7/understand_en.html

540 http://cordis.europa.eu/fp7/sis/about-sis_en.html

541 http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressData/en/misc/92236.pdf

542 http://ec.europa.eu/dgs/jrc/index.cfm?id=3800&lang=en

543 http://biotech.jrc.it

544 Gilbert N (2007) How the EU can fund your company. *Nature Biotechnology*, **25**(1), 21-24.

545 http://ec.europa.eu/enterprise/enterprise_policy/cip/index_en.htm

546 http://www.eurotransbio.net

547 http://www.eureka.be/about.do

548 http://cordis.europa.eu/era/concept.htm

549 http://erc.europa.eu

550 ftp://ftp.cordis.europa.eu/pub/technology-platforms/docs/etp3rdreport_en.pdf

551 http://cordis.europa.eu/technology-platforms/home_en.html

552 IDEA Consult (2008) Evaluation of the European Technology Platforms (ETPs). August 2008. ftp://ftp.cordis.europa.eu/pub/technology-platforms/docs/evaluation-etps.pdf

553 European Commission (2004)*Technology Platforms - from Definition to Implementation of a common Research Agenda.* Report compiled by a Commission Inter-Service Group on Technology Platforms. DG Research. ftp://ftp.cordis.europa.eu/pub/technology-platforms/docs/tp_report_defweb_en.pdf

554 http://cordis.europa.eu/technology-platforms/individual_en.html

555 http://www.epsoweb.org/catalog/tp

556 http://etp.ciaa.be/asp/home/welcome.asp

557 http://www.biofuelstp.eu

558 http://www.ifahsec.org/europe/EUPlatform/Platform.htm

559 http://www.forestplatform.org

560 http://www.eatpnet.eu/about.php

561 http://cordis.europa.eu/nanotechnology/nanomedicine.htm

562 http://ec.europa.eu/research/fp6/index_en.cfm?p=0_newsite&dest=1_innomed

563 http://www.textile-platform.org

564 http://www.suschem.org

565 Friends of the Earth Europe (2007) The EU's biotechnology strategy: mid-term review or mid-life crisis? http://www.foeeurope.org/publications/2007/FoEE_biotech_MTR_midlifecrisis_March07.pdf

566 Council of the European Union. Brussels European Council 20 and 21 March 2003: Presidency conclusions. Brussels, 5th May 2003. http://www.consilium.europa.eu/ueDocs/cms_Data/docs/pressData/en/ec/75136.pdf

567 http://www.epsoweb.org

568 http://www.epsoweb.org/Catalog/TP/Web_TP.htm

569 http://www.epsoweb.org/Catalog/TP/ssa_summary.PDF

570 EC(2004) Plants for the Future: 2025 a European Vision for plant genomics and biotechnology. EUR21359EN. http://www.epsoweb.org/Catalog/TP/Plants%20for%20the%20future-Dec04.pdf

571 http://www.epsoweb.org/Catalog/TP/EPSO%20pressrelease%20web_22Jun04.htm

572 http://www.europabio.org/articles/article_329_EN.doc

573 http://europa.eu/rapid/pressReleasesAction.do?reference=IP/04/801&format=HTML&aged=0&language=EN&guiLanguage=en

574 Plants for the Future (2005) The way there. Stakeholders proposal for a Strategic Research Agenda. Part I: Summary. http://www.epsoweb.org/Catalog/TP/docs/SRA-I.PDF

575 http://www.epsoweb.org/Catalog/TP/docs/SRA-II.PDF

576 http://www.epsoweb.org/Catalog/TP/TP%20launch_stakeholder_proposal.htm

577 http://www.epsoweb.org/Catalog/TP/docs/SRA-III.PDF

578 http://www.epsoweb.org/Catalog/TP/TP_plants%20for%20the%20future%20dec%20newspage.htm

579 http://www.epsoweb.org/Catalog/TP/docs/No512149_TP%20Plants&Health_Periodic%20ACTIVITY%20Report_14Nov05….pdf

580 European Technology Platform Plants for the Future. Strategic Research Agenda 2025. Summary. 25th June 2007. http://www.epsoweb.org/Catalog/TP/Launch_25June07/TP_SRA_Summary.pdf

581 http://www.epsoweb.org/Catalog/TP/SRA_PART_II.pdf

582 http://www.epsoweb.org/Catalog/TP/TP%20SRA.htm

583 http://etp.ciaa.be/documents/BAT%20Brochure%20ETP.pdf

584 CIAA(2007) European Technology Platform Food for Life: Strategic Research Agenda 2007-2020. 4th September 2007. http://etp.ciaa.be/documents/CIAA-ETP%20broch_LR.pdf

585 CIAA(2007) European Technology Platform Food for Life: Implementation Plan Working Document. 4th September 2007. http://etp.ciaa.be/documents/Implementation%20Plan_Working%20Document.pdf

586 http://ec.europa.eu/energy/res/legislation/doc/comm2001-547-en.pdf

587 http://ec.europa.eu/energy/res/legislation/doc/biofuels/en_final.pdf

588 http://ec.europa.eu/research/energy/pdf/gp/gp_events/biofuels/roj_en.pdf

589 http://ec.europa.eu/research/energy/gp/gp_events/etpbiofuels/article_3765_en.htm

590 http://www.biofuelstp.eu/downloads/2061rep.pdf

591 http://www.biofuelstp.eu/srasdd/080111_sra_sdd_web_res.pdf

592 http://www.epsoweb.org/Catalog/TP/EC_technology21265.pdf

593 European Commission (2003) Investing in research: an action plan for Europe. DG Research. EUR 20804 EN. COM (2003) 226 final. http://ec.europa.eu/invest-in-research/pdf/download_en/investing_en.pdf

594 http://ec.europa.eu/enterprise/leadmarket/leadmarket.htm

595 http://www.europe-innova.org/index.jsp?type=page&lg=en&classificationId=4975&classificationName=Home&cid=10022

596 EC(2007) A lead market initiative for Europe. Brussels, 21.12.2007 COM(2007) 860 final. http://ec.europa.eu/enterprise/leadmarket/doc/com_07_en.pdf

597 EC(2007) A lead market initiative for Europe. Annex I. Brussels, 21.12.2007 SEC(2007) 1729. http://ec.europa.eu/enterprise/leadmarket/doc/annex_1.pdf

598 http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/07/191

599 http://ec.europa.eu/information_society/newsroom/cf/itemlongdetail.cfm?item_id=3413

600 http://ec.europa.eu/research/health/imi/index_en.html

601 http://www.gmes.info

602 ftp://ftp.cordis.europa.eu/pub/esfri/docs/esfri-roadmap-report-26092006_en.pdf

603 http://www.eatris.eu/

604 http://www.biobanks.eu

605 Evans C (2002) Biotechnology: Discovering your future. Science year lecture. Natural History Museum. 16th April 2002. http://www.scienceyear.com/about_sy/events/pdfs/Chris%20Evans%20Transcript.pdf

606 http://www.dius.gov.uk/ministerialteam/index.html

607 http://www.dti.gov.uk/about/dti-ministerial-team/page8414.html

608 http://www.publications.parliament.uk/pa/ld/ldreg/reg22.htm

609 Woolf, M (2006) Cash for honours: What am I bid? £10,000? £1m? A loan, no questions asked? The Independent, 12th March 2006.

http://news.independent.co.uk/uk/politics/article350789.ece

610 http://politics.guardian.co.uk/cashforhonours/story/0,,2130966,00.html

611 Carr-Brown J (2002) Conflict of interest claims over Sainsbury biotech cash. Sunday Times. 24th November 2002. http://www.timesonline.co.uk/tol/news/uk/article834867.ece

612 Swinford S (2006) Sainsbury in row over GM research funding. The Sunday Times. 28th May 2006.

613 http://www.cabinetoffice.gov.uk/secretariats/committees/edsi.aspx

614 New Government Chief Scientific Adviser announced. Press Release. 1st October 2007.

http://www.number10.gov.uk/output/Page13362.asp

615 New Government Chief Scientific Adviser announced. Press Release. 5th October 2000. http://www.number10.gov.uk/output/Page2863.asp

616 Lean G (2007) War of the boffins: 'demob-happy' chief scientist under attack. The Independent. 14th January 2008. http://news.independent.co.uk/sci_tech/article3255701.ece

617 Poulter S (2007) Scientist who claimed GM crops could solve Third World hunger admits he got it wrong. Daily Mail. 18th December 2007. http://www.dailymail.co.uk/sciencetech/article-503339/Scientist-claimed-GM-crops-solve-Third-World-hunger-admits-got-wrong.html

618 Leake J (2008) I pushed Blair's nuclear button. The Sunday Times, 13th January 2008. http://www.timesonline.co.uk/tol/news/uk/science/article3176458.ece

619 http://www.berr.gov.uk/files/file33111.doc

620 http://www.berr.gov.uk/dius/science/science-tech-and-dti/dgsi/page8167.html

621 http://www3.imperial.ac.uk/newsandeventspggrp/imperialcollege/newssummary/news_22-7-2008-11-43-32

622 HP Sauce. Private Eye, 12-15 December 2003.

623 O'Nions RK (1995) UK Nirex Ltd Proof of Evidence of RK O'Nions: Scientific Case for the RCF. PE/NRX/17.

624 Haszeldine R.S. & Smythe D.K. (eds), *Radioactive waste disposal at Sellafield UK*, University of Glasgow, ISBN 085 261 524-8.

625 McDonald C (2007) Letter: Flaws in search for nuclear waste stite. The Guardian. 28th June 2007. http://www.guardian.co.uk/world/2007/jun/28/nuclear.uk

626 Editorial: Time to bury Nirex? New Scientist. 22nd March 1997. http://www.newscientist.com/article/mg15320740.200.html

627 Macalister T (2007) Sellafield 'not fit' for nuclear waste disposal. The Guardian. 2nd November 2007. http://www.guardian.co.uk/business/2007/nov/02/nuclearindustry.greenpolitics

628 Harvey F, Bream R (2007) Sellafield unsuitable for nuclear waste site. Financial Times. 2nd November 2007. http://www.ft.com/cms/s/0/cbc5e52a-88de-11dc-84c9-0000779fd2ac.html?nclick_check=1

629 McDonald C (2007) Letter: Flaws in search for nuclear waste stite. The Guardian. 28th June 2007. http://www.guardian.co.uk/world/2007/jun/28/nuclear.uk

630 Irving A (1999) Gosforth will fight dump. Whitehaven News. 8th April 1999.

631 House of Lords Science and Technology Committee (1999) Management of Nuclear Waste. 24 March 1999. 3rd Report of Session 1998-99 HL 41 ISBN 0 10 404199 4 http://www.publications.parliament.uk/pa/ld199899/ldselect/ldsctech/41/4109.htm#n51

632 Harvey F, Bream R (2007) Sellafield unsuitable for nuclear waste site. The Financial Times. 2nd November 2007.

633 http://www.defra.gov.uk/environment/radioactivity/waste/hilw/documents/cpg-crp-jointreport-may2007.pdf

634 Waste nuke storage probe. Whitehaven News. 11th January 2008. http://www.whitehaven-news.co.uk/2.1819/2.2837/1.9774

635 Nisse J (2007) Volunteer route to shorten nuclear waste site process. [Letter] The Financial Times. 25th October 2007.

636 Wilson J (2008) Search for somewhere to bury nuclear waste. Financial Times. 11th January 2008. http://search.ft.com/ftArticle?queryText=%22nuclear+waste%22&y=6&aje=false&x=7&id=080111000070&ct=0

637 http://www.erff.org.uk

638 http://www2.cst.gov.uk/cst/about/members.shtml

639 UK 'neglects nuclear waste'. 3rd May 2002. http://news.bbc.co.uk/1/hi/sci/tech/1964202.stm

640 The Royal Society (2006) The long term management of radioactive waste: the work of the Committee on Radioactive Waste (CoRWM). January 2006. http://royalsociety.org/displaypagedoc.asp?id=18773

641 ABC(2001) Melbourne's private university struggles to survive. http://www.abc.net.au/7.30/content/2001/s298664.htm

642 Swaine J (2009) Nuclear recycling plant costs £1.2 billion and still doesn't work. The Telegraph, 7th April 2009. http://www.telegraph.co.uk/earth/energy/nuclearpower/5117991/Nuclear-recycling-plant-costs-1.2-billion-and-still-doesnt-work.html

643 http://www.epsrc.ac.uk/Content/Documents/Biographies/SueIon.htm

644 http://www.bnes.com/templates/ld_templates/layout_133995.aspx?ObjectId=143602

645 http://www2.cst.gov.uk/cst/about/past.shtml

646 http://www2.cst.gov.uk/cst/business/meet140998.shtml

647 CST (1999) Review of S&T activity across Government. July 1999. http://www2.cst.gov.uk/cst/reports/files/science-government/sandtrep.pdf

648 http://www.innovateuk.org/aboutus/governingboard.ashx

649 http://www.foundation.org.uk/about/council/default.htm

650 http://royalsociety.org/

651 http://www.sciencecouncil.org/

652 The Science Council (2006) Election of new president. Press Release. 28th Novmebr 2006. http://www.sciencecouncil.co.uk/documents/NewPresidentPressReleaseFinal_002.pdf

653 Verdin M (2004) McKillop courts the curse of Labour. The Times, 3 December 2004. http://www.timesonline.co.uk/tol/life_and_style/health/article398542.ece

654 McKillop takes responsibility for RBS plight. The Guardian. 20 November 2008. http://www.guardian.co.uk/business/2008/nov/20/royal-bank-of-scotland-tom-mckillop

655 Barker A, Urry M, Larsen PT (2009) Brown accuses RBS of taking 'irresponsible risks'. Financial Times, 19 January 2009. http://www.ft.com/cms/s/0/7de5d2f8-e601-11dd-8e4f-0000779fd2ac.html

656 http://www.hm-treasury.gov.uk/newsroom_and_speeches/press/2006/press_53_06.cfm

657 UK to invest long-term in science. BBC News Online. 2nd December 2004. http://news.bbc.co.uk/1/hi/sci/tech/4061755.stm

658 http://www.researchresearch.com/news.cfm?pagename=newsStory&lang=EN&type=default&elementID=78211&noSearch=true

659 Dawber A (2009) Bioscience leaders attack ministers' inaction. The Independent, 8th May 2009. http://www.independent.co.uk/news/business/news/bioscience-leaders-attack-ministers-inaction-1681074.html

660 Farrar S (2000) UK considers national gene database. Times Higher Educational Supplement. 11th February 2000. http://www.timeshighereducation.co.uk/story.asp?storyCode=150080&sectioncode=26

661 More information is available on: http://www.genewatch.org/sub-563487

662 Glover D (2009) Undying promise: agricultural biotechnology's pro-poor narrative, ten years on. STEPS Centre Working Paper 15.

663 Bezold C, Miles I (2002) Social science research priorities related to genomics. *Foresight*, **4(**4), 36-42.

664 Justman M, Bezold C, Rowley WR (2002) Genomics and society: four scenarios for 2015. *Foresight*, **4**(4), 29-35.

665 Nightingale P, Martin PA (2004) The Myth of the biotech revolution. *Trends in Biotechnology*. **22** (11), 564 -569.

666 Woolf SH, Johnson RE (2005) The break-even point: when medical advances are less important than improving the fidelity with which they are delivered. *Annals of Family Medicine*, **3**(6), 545-552.

667 Séguin B, Hardy B-J, Singer PA, Daar AS (2008) Human genomic variation initaitives in emerging economies and developing countries. *Nature Reviews Genetics*, Supplement, October 2008. S3-S4.

668 Altieri M (2008) Sustainable agriculture: Small farms show big promise. In: GM foods: the wrong debate? *Food Ethics*, **3**(3), 1.

669 Levett R (2008) Choice: Less can be more. In: GM foods: the wrong debate? *Food Ethics*, **3**(3), 11.

670 Clarke AE, Mamo, L, Fishman JR, Shim JK, Fosket JR (2003) Biomedicalization: technoscientific transformations of health, illness, and US biomedicine. *American Sociological Review*, **68**, 161-194.

671 Groves T (2006) Pandemic obesity in Europe. *British Medical Journal*, **333**, 1081-2.

672 Beaglehold R, Bonita R, Horton R, Adams O, McKee M (2004). Public health in the new era: improving health through collective action. *The Lancet*, **363**, 2084-2086.

673 Wanless D (2004). Securing Good Health for the Whole Population: Final Report. February 2004. The Stationary Office, London.

674 Global Forum for Health Research (2004) Monitoring financial flows for health research. Geneva, Global Forum for Health Research. http://www.globalforumhealth.org/Site/002__What%20we%20do/005__Publications/004__Resource%20flows.php .

675 Public Citizen (2002) America's other drug problem: a briefing book on the Rx drug debate. Washington DC, Public Citizen. http://www.citizen.org/documents/dbbapril.pdf

676 Moynihan R, Heath I, Henry D (2002) Selling sickness: the pharmaceutical industry and disease mongering. *British Medical Journal*, **324**, 886-890.

677 Cook-Deegan R, Chan C, Johnson A (2000) World Survey of Funding for Genomics Research. Final Report to the Global Forum for Health Research and the World Health Organisation. September 2000. Available on: http://www.stanford.edu/class/siw198q/websites/genomics/finalrpt.pdf

678 Leroy JL, Habicht JP, Pelto G, Bertozzi SM (2007) Current priorities in health research funding and lack of impact on the number of child deaths per year. *American Journal of Public Health*, **97**(2), 219-223.

679 Leroy JL, Habicht J-P, Pelto G, Bertozzi SM (2007) [Letter]. *American Journal of Public Health*, **97**(10), 1733.

680 Kravitz RL (2005) Doing things better vs doing better things. *Annals of Family Medicine*, **3**(6), 483-485.

681 Woolf SH (2007) Potential health and economic consequences of misplaced priorities. *Journal of the American Medical Association*, **297**(5), 523-526.

682 Woolf SH, Johnson RE (2007) Inattention to the fidelity of health care delivery is costing lives. [Letter]. *American Journal of Public Health*, **97**(10), 1732-1733.

683 Sarraci R, Olsen J, Hofman A (2005) Health research policy in the European Union. *British Medical Journal*, **330**, 1459-1460.

684 Millward LM, Kelly MP, Nutbeam D (2003). Public health intervention research the evidence. London: Health Development Agency. Available on: www.had-online.org.uk/documents/pubhealth_intervention.pdf

685 Diabetes + Obesity = Diabesity. *RTD Info*. No. 51December 2006. http://ec.europa.eu/research/rtdinfo/51/article_5129_en.html

686 Diabetes Prevention Program Research Group (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England Journal of Medicine*, **346**(6), 393-403.

687 Jain A (2005) Treating obesity in individuals and populations. *The British Medical Journal*, **331**, 1387-1390.

688 Rose, G (1985), Sick Individuals and Sick Populations, *International Journal of Epidemiology*, **14** (1), 32-38.

689 Medical Technology and Diagnostics Industry (2008) 'Futures' submission to NHS Next Steps Review. March 2008. http://www.advisorybodies.doh.gov.uk/hitf/MMTSG%20180608%20HIC%20submission.pdf

690 Burrill GS (2008) Biotech/Healthcare 2009: Navigating the sea change. Burrill & Co. Global CONNECT

Annual Meeting. 11 December 2008. http://globalconnect.ucsd.edu/events/documents/StateoftheWorld-GlobalCONNECTAnnualMtgDec112008.pdf

691 Germaine JM (2009) Your genome: there's an app for that. Technology News World. 8th March 2009. http://www.technewsworld.com/story/67753.html?wlc=1250851529

692 PriceWaterhouseCoopers (2009) The new science of personalized medicine: translating the promise into practice. http://www.prnewswire.com/news-releases/232-billion-personalized-medicine-market-to-grow-11-percent-annually-says-pricewaterhousecoopers-78751072.html

693 Getting personal: the promise of cheap genome sequencing. The Economist. 16th April 2009. http://www.economist.com/specialreports/displaystory.cfm?story_id=13437974

694 Lohr S (2009) A push for the wired patient's bill of rights. New York Times Blogs. 22nd June 2009. http://bits.blogs.nytimes.com/2009/06/22/a-push-for-the-wired-patients-bill-of-rights/

695 Freemantle N, Hill S (2002). Medicalisation, limits to medicine, or never enough money to go round? *British Medical Journal*. 324, 864-5.

696 Anon(2005) US Obesity cost $96.7bn. *Red Herring*, 3 Jun 2005.

697 Abramson J (2004) Overdosed America: the broken promise of American medicine. New York; Harper Collins.

698 Lenzer J (2004). Scandals have eroded US public's confidence in drug industry. *British Medical Journal*, **329**, 247.

699 Trewby PN, Reddy AV, Trewby CS, Ashton VJ, Brennan G, Inglis J (2002). Are Preventive Drugs Preventive Enough? A Study of Patients' Expectation of Benefit from Preventive Drugs. *Clinical Medicine* 2(6), 527-533.

700 Lewis DK, Robinson J, Wilkinson E (2003). Factors Involved in Deciding to Start Preventive Treatment; Qualitative Study of Clinicians' and Lay People's Attitudes. *British Medical Journal*. **327**, 1-6.

701 ILSI (2002) Concepts of functional foods. ILSI Europe Concise Monograph Series. http://europe.ilsi.org/file/ILSIFuncFoods.pdf .

702 Food Ethics Council (2005) Genetic personal: shifting responsibilities for dietary health. December 2005. London, Food Ethics Council.

703 Séguin B, Hardy B-J, Singer PA, Daar AS (2008) Genomics, public health and developing countries: the case of the Mexican National Institute of Genomic Medicine (INMEGEN). *Nature Reviews Genetics*, Supplement, October 2008. S5-S9.

704 Hardy B-J, Séguin B, Singer PA, Mukerji M, Brahmachari K, Daar AS (2008) From diversity to delivery: the case of the Indian Genome Variation initiative. *Nature Reviews Genetics*, Supplement, October 2008. S9-S14

705 Séguin B, Hardy B-J, Singer PA, Daar AS (2008) Universal health care, genomic medicine and Thailand: investing in today and tomorrow. *Nature Reviews Genetics*, Supplement, October 2008. S14-S19.

706 Hardy B-J, Séguin B, Ramesar R, Singer PA, Daar AS (2008) South Africa: from species cradle to genomic applications. *Nature Reviews Genetics*, Supplement, October 2008. S19-S23.

707 Hardy B-J, Séguin B, Goodsaid F, Jimenez-Sanchez G, Singer PA, Daar AS (2008) The next steps for genomic medicine: challenges and opportunities for the developing world. *Nature Reviews Genetics*, Supplement, October 2008. S19-S23.

708 Petersen A (2006) The genetic conception of health: is it as radical as claimed? *Health*, **10**(4), 481-500.

709 Lichtenstein P, Holm NV, Verkasalo PK, Iliadou A, Kaprio J, Koskenvuo M, Pukkala E, Skytthe A, Hemminki K (2000) Environmental and heritable factors in the causation of cancer analyses of cohorts of twins from Sweden, Denmark, and Finland. *New England Journal of Medicine*, **343**(2), 78-85.

710 de Hollander AEM, Melse JM, Lebret E, Kramers PGN (1999) An aggregate public health indictor to represent the impact of multiple environmental exposures. *Epidemiology*, **10**(5), 606-617.

711 Monbiot G (2003) Guard dogs of perception: the corporate takeover of science. *Science and Engineering Ethics*, **9**, 49-57.

712 Frank et al. Large life-course cohorts for characterizing genetic and environmental contributions: the need for more thoughtful designs. Epidemiology, 17, 595-598. November 2006.

713 WHO(2008) Closing the gap in a generation. Commission on Social Determinants of Health. http://whqlibdoc.who.int/publications/2008/9789241563703_eng.pdf

714 http://www.who.int/mediacentre/news/releases/2008/pr29/en/index.html

715 Marmot M (2010) Fair Society, Healthy Lives. Strategic review of health inequalities in England post-2010. February 2010. http://www.ucl.ac.uk/gheg/marmotreview

716 GeneWatch UK (2002) Human genetic technologies: implications for preventive health care. World Health Organisation Human Genetics Programme. WHO/HGN/Rep/02.1

717 Hedgecoe A (2004) The politics of personalized medicine. Cambridge University Press.

718 Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM (2004) Adverse drug reactions as a cause of admission to hospital: prospective analysis of 18,820 patients. *British Medical Journal*, **329**, 15-19.

719 Audit Commission (2001) A Spoonful of Sugar: Medicines Management in NHS Hospitals. http://www.audit-commission.gov.uk/health/nationalstudies/other/Pages/aspoonfulofsugar_copy.aspx

720 Henderson M (2009) Genetic mapping of babies by 2019 will transform preventive medicine. The Times. 9th February 2009.

721 ttp://www.sciencehorizons.org.uk/resources/1652_SH_Scenes_Mind%20&%20Body_AW.pdf

722 Dialogue by Design (2007) Science Horizons: Deliberative Panel Report. September 2007. http://www.sciencehorizons.org.uk/resources/sciencehorizons_deliberative_panel.pdf

723 Crop Science Review Panel (2004) Review of BBSRC-funded research relevant to crop science. A report for BBSRC Council. http://www.bbsrc.ac.uk/about/pub/reports/crop_sci_review12_05_04.pdf

724 Botha, GM, Viljoen, CD (2008) Can GM sorghum impact Africa? *Trends in Biotechnology*, 26 (2), 64-69.

725 Gardner G, Halweil B (2000) Underfed and overfed: the global epidemic of malnutrition. WorldWatch Paper 250. Washington DC, World Watch Institute. Available on: http://www.worldwatch.org/pubs/paper/150

726 http://www.who.int/dietphysicalactivity/media/en/gsfs_obesity.pdf

727 Edgerton MD (2009) Increasing crop productivity to meet global needs for food and fuel. Plant Physiology, **149**, 7-13.

728 http://www.fapri.iastate.edu/outlook/2008/

729 Biggies from agribusiness join new biofuels lobbying group. 25th July 2008. http://www.livemint.com/2008/07/25130050/Biggies-from-agribusiness-join.html

730 GM crop: top ten facts and figures. 8th October 2009. http://checkbiotech.org/node/27660

731 Malthus TR (1798) An essay on the principle of population. Oxford World Classics (1993). Oxford University Press.

732 Inglis B (1971) Poverty and the industrial revolution. Panther Books, London.

733 The CornerHouse (2000) The Malthus factor: Poverty, politics and population in capitalist development. Briefing 20, The CornerHouse, July 2000. http://www.thecornerhouse.org.uk/pdf/briefing/20malth.pdf

734 Ensor G (1818) An inquiry concerning the population of nations containing a refutation of Mr. Malthus' essay on population. Reprinted in 1967 by Augustus M. Kelly, New York.

735 Steele J (2001) Food for thought. *The Guardian*. 31st March 2001.

736 Sen A (1994) Population: delusion and reality. September 22nd 1994. http://www.uwmc.uwc.edu/geography/malthus/sen_NYR.htm

737 Pearce F (2009) Consumption dwarfs population as main environmental threat. The Guardian. 15th April 2009. http://www.guardian.co.uk/environment/2009/apr/15/consumption-versus-population-environmental-impact

738 Walker P (2008) Food Security. John Hopkins University, Bloomberg School of Public Health. http://ocw.jhsph.edu/courses/nutritionalhealthfoodproductionandenvironment/PDFs/FoodEnv-sec1d_LawrenceOCW.pdf

739 Brown L (2009) The geopolitics of food scarcity. Der Spiegel International. 11th February 2009. http://www.spiegel.de/international/world/0,1518,606937,00.html

740 Chastre C, Duffield A, Kindness H, LeJeune S, Taylor, A (2007) The minimum cost of a healthy diet. Save the Children UK. June 2007. http://www.savethechildren.org.uk/en/docs/The_Minimum_Cost_of_a_Healthy_Diet_Final.pdf

741 Lobstein T (2004) Suppose we all ate a healthy diet…? *Eurohealth*, **10**(1), 8-12. http://www.sustainweb.org/pdf/afn_m6_p2.pdf

742 Gittelsohn J, Haberle H, Vastine AE, Dyckman W, Palafox NA (2003) Macro- and Microlevel processes affect food choice and nutritional status in the Republic of the Marshall Islands. *Journal of Nutrition*, **133**, 310S-313S.

743 Aguirre P (2004) Socioanthropological aspects of obesity in poverty. *Obesity and Poverty*, **1**(1), 11-22.

744 Drewnowski A, Specter SE (2004) Poverty and obesity: the role of energy density and energy costs. *American Journal of Clinical Nutrition*, **79**,6-16.

745 Vaughan A (2009) Elimination of food waste could lift 1bn out of hunger, say campaigners. The Guardian. 8th September 2009. http://www.guardian.co.uk/environment/2009/sep/08/food-waste

746 Tilman D, Cassman KG, Matson PA, Naylor RR, Polasky S (2002) Agricultural sustainability and intensive production practices. *Nature*, **418**, 671-677.

747 McMichael AJ, Bambrick HJ(2005) Meat consumption trends and health: casting a wider risk assessment net. *Public Health Nutrition*, **8**(4), 341-343.

748 Lang T, Heasman M (2004) Food wars: the global battle for mouths, minds and markets. London, Earthscan.

749 NABC (1998) Vision for agricultural research and development in the 21st century. http://nabc.cals.cornell.edu/pubs/vision.cfm

750 Eaglesham A (2001) Changing the nature of nature: corporate, legal and ethical fundamentals. Description of the presentation by Ralph Nader. in NABC(2001) The bio-based economy of the 21st century: agriculture expanding into health, energy, chemical and materials. NABC Report 12. http://nabc.cals.cornell.edu/pubs/nabc_12.pdf

751 Levitan L (2001) How many ways can we skin this cat called Earth? Risks and constraints to the biobased economy. In: NABC Report 12 (Op Cit).

752 FAO(2008) Soaring food prices: facts, perspectives, impacts and actions required. High-level conference on world food security: the challenges of climate change and bioenergy. Rome, 3 - 5 June 2008. http://www.fao.org/fileadmin/user_upload/foodclimate/HLCdocs/HLC08-inf-1-E.pdf

753 Thompson, J., Millstone, E., Scoones, I., Ely, A., Marshall, F., Shah, E. and Stagl, S. (2007) Agri-food System Dynamics: pathways to sustainability in an era of uncertainty. STEPS Working Paper 4, Brighton: STEPS Centre. http://www.steps-centre.org/PDFs/Final_steps_agriculture.pdf

754 http://www.id21.org/society/insights61art1.html

755 UN(2009) Seed policies and the right to food: enhancing agrobiodiversity and encouranging innovation. Report of the Special Rapporteur on the right to food. 23rd July 2009.

756 Suhai S [Editor] (2004) Relevance of GM technology to Indian agriculture and food security. GeneCampaign, New Delhi.

757 Orton L (2003) GM crops going against the grain. ActionAid, May 2003. http://sarpn.org.za/documents/d0000364/P345_GM_crops.pdf

758 Gurian-Sherman D (2009) Failure to yield. Union of Concerned Scientists. April 2009. http://www.ucsusa.org/food_and_agriculture/science_and_impacts/science/failure-to-yield.html

759 Rosset PM (2005) Transgenic crops to address Third World hunger? A critical analysis. *Bulletin of Science, Technology & Society*, **25**, 306-313.

760 Scoones, I (2008) Mobilizing Against GM Crops in India, South Africa and Brazil. *Journal of Agrarian Change*, **8** (2-3), 315-344.

761 Eicher CK, Maredia K, Sithole-Niang I (2006) Crop biotechnology and the African farmer. *Food Policy*, **31**(6), 504-527.

762 Davies, KM (2007) Genetic modification of plant metabolism for human health benefits, *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, **622**(1-2), 122-137.

763 Nestle, M (2002) Food politics. University of California Press, Berkeley.

764 Lang T, Heasman M (2004) Food wars: the global battle for mouths, minds and markets. London, Earthscan.

765 Meikle E (2005) When food makes medicine kill, not cure. *The Guardian*, 11 Apr 2005.

766 Gulati OP, Ottaway PB (2006) Legislation relating to nutraceuticals in the European Union with a particular focus on botanical-sourced products. *Toxicology*, **221**, 75-87.

767 Coppens P, Fernandes da Silva M, Pettman S (2006) European regulations on nutraceuticals, dietary supplements and functional foods: A framework based on safety. *Toxicology*, **221**, 59-74.

768 Jacobs Jr DR, Murtaugh MA (2000) It's more than an apple a day: an appropriately processed plat-centred dietary pattern may be good for your health. *American Journal of Nutrition*, **72**, 899-900.

769 Pollan M (2008) Unhappy meals. *New York Times*. 28 January 2007. http://www.nytimes.com/2007/01/28/magazine/28nutritionism.t.html

770 Watkins SM, Hammock BD, Newman JW, German JB (2001) Individual metabolism should guide agriculture toward foods for improved health and nutrition. *American Journal of Clinical Nutrition*, **74**, 283-286.

771 www.goldenrice.org

772 Brown P (2001) GM rice promoters 'have gone too far'. The Guardian, 12th Feb 2001.

773 Krawinkel MB (2007) What we know and don't know about Golden Rice. *Nature Biotechnology*, **25**(6), 623-624.

774 http://www.who.int/nutrition/topics/vad/en/index.html

775 Food Ethics Council (2003) GM crops for global justice? http://www.foodethicscouncil.org/files/gmnutrition.pdf

776 Omenn GS, Goodman GE, Thornquist MD et al (1996) Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *New England Journal of Medicine*, **334**, 1150-1155.

777 The Alpha-Tocopherol BCCPSG (1994) The effect of vitamin E, beta carotene on the incidence of lung cancer and other cancers in male smokers. *New England Journal of Medicine*, **330**, 1029-1035.

778 Omenn GS (2007) Chemoprevention of lung cancers: lessons from CARET, for the beta-carotene and retinol efficacy trial, and prospects for the future. *European Journal of Cancer Prevention*, **16**, 184-191.

779 Goodman GE, Thornquist MD, Balmes J, Cullen MR, Meyskens FL, Omenn GS, Valanis B, Williams JH (2004) The Beta-Carotene and Retinol Efficacy Trial: Incidence of lung cancer and cardiovascular disease mortality during 6-year follow-up after stopping â-carotene and retinol supplements. Journal of *the National Cancer Institute*, **96**(23), 1743-1750.

780 Duffield-Lillico AJ, Begg CB (2004) Reflections on the landmark studies of â-carotene supplementation. *Journal of the National Cancer Institute*, **96**(23), 1729-1731.

781 Expert Group on Vitamins and Minerals (2003) Safe Upper Levels for vitamins and minerals. May 2003. www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf .

782 National Institutes of Health (2006) State-of-the-Science conference statement: multivitamin/mineral supplements and chronic disease prevention. Annals of Internal Medicine, 145:000-000. http://consensus.nih.gov/2006/2006MultivitaminMineralSOS028Statementhtml.htm

783 Watkins SM, Hammock BD, Newman JW, German JB (2001) Individual metabolism should guide agriculture toward foods for improved health and nutrition. *American Journal of Clinical Nutrition*, **74**, 283-286.

784 Kryder RD, Kowalski SP, Krattiger AF (2000) The intellectual and technical property components of pro-Vitamin A rice (GoldenRice™): A preliminary freedom-to-operate review. http://lsr.nellco.org/cgi/viewcontent.cgi?article=1007&context=piercelaw_facseries

785 Paine JA, Shipton CA, Chaggar S, Howells RM, Kennedy MJ, Vernon G, Wright SY, Hinchliffe E, Adams JL, Silverstone AL, Drake R (2005) A new version of Golden Rice with increased pro-vitamin A content. *Nature Biotechnology*, 23, 482-487.

786 Stein AJ, Meenakshi JV, Qaim M, Nestel P, Sachdev HPS, Butta ZA (2005) Analyzing the health benefits of biofortified crops by means of the Disability-Adjusted Life Years approach: a handbook focusing on iron, zinc and vitamin A. Harvest Plus Technical Monograph Series, 4. http://www.harvestplus.org/pdfs/tech04.pdf

787 GeneWatch UK response to EFSA consultation on updated guidance document of the Scientific Panel on Genetically Modified Organisms (GMO) for the risk assessment of genetically modified plants and derived food and feed. September 2008.

788 Jasanoff S (2005) 'Let them eat cake': GM foods and the democratic imagination. In: Leach M, Scoones I, Wynne B (Eds) Science and citizens. Zed Books.

789 Richards P (2005) Plant biotechnology and the rights of the poor: a technograpic approach. In Leach M, Scoones I, Wynne B (Eds) Science and citizens. Zed Books.

790 Watkinson AR, Freckleton RP, Robinson RA, Sutherland WJ (2000) Predictions of biodiversity response to genetically modified herbicide tolerant crops. *Science*, **289**, 1554-1557.

791 Ponti L (2005) Transgenic crops and sustainable agriculture in the European context. *Bulletin of Science, Technology & Society*, **25**, 289-305.

792 Pengue WA (2005) Transgenic crops in Argentina: The ecological and social debt. *Bulletin of Science, Technology & Society*, **25**, 314-322.

793 Garcia MA, Altieri MA (2005) Transgenic crops: Implications for biodiversity and sustainable agriculture. *Bulletin of Science, Technology & Society*, **25**, 335-353.

794 Altieri MA (2005) The myth of co-existence: Why transgenic crops are not compatible with agroecologically based systems of production. *Bulletin of Science, Technology & Society*, **25**, 361-371.

795 Henry C (2006) Cumulative long-term effects of genetically modified (GM) crops on human/animal health and the environment: risk assessment methodologies. Reference: NO 07-0402/2005/414455/MAR/B4. Central Science Laboratory (CSL). http://ec.europa.eu/environment/biotechnology/pdf/report310306.pdf

796 Henry, C. (2006) Cumulative long-term effects of genetically modified (GM) crops on human/animal health and the environment: risk assessment methodologies. Central Science Laboratory. Reference: No 07-0402/2005/414455/MAR/B4

797 Sandermann H (2006) Plant biotechnology: ecological case studies on herbicide resistance. *Trends in Plant Science*, **11**(7), 324-328.

798 Qiu J (2008) Is China ready for GM rice? *Nature*, **455**, 850-852.

799 Ashikari M, Matsuoka, M (2006) Identification, isolation and pyramiding of quantitative trait loci for rice breeding. *Trends in Plant Science*, 11(7), 344-350.

800 Keeley J (2005) Interrogating China's biotechnology revolution. In: Leach M, Scoones I, Wynne B (Eds) Science and citizens. Zed Books.

801 Ortega E, Cavalett O, Bonifácio R, Watanabe M (2005) Brazilian soybean production: Emergy analysis with an expanded scope. *Bulletin of Science, Technology & Society*, **25**, 323-334.

802 Bohanec M, Messéan A, Scatasta S, Angevin F, Griffiths B, Krogh PH, Žnidaršiè M, Džeroski S (2008) A qualitative multi-attribute model for economic and ecological assessment of genetically modified crops. *Ecological Modelling*, **215** (1-3), 247-261.

803 Liebman M, Gibson LR, Sundberg DN, Heggenstaller AH, Westerman PR, Chase CA, Hartzler RG, Menalled FD, Davis AS, Dixon PM (2008) Agronomic and Economic Performance Characteristics of Conventional and Low-External-Input Cropping Systems in the Central Corn Belt. *Agronomy Journal*, **100**, 600-610.

804 Cavigelli MA, Teasdale JR, Conklin AE (2008) Long-Term Agronomic Performance of Organic and Conventional Field Crops in the Mid-Atlantic Region. *Agronomy Journal*, **100**, 785-794. DOI: 10.2134/agronj2006.0373

805 Mitchell CC, Delaney DP, Balkcom KS (2008) A Historical Summary of Alabama's Old Rotation (circa 1896): The World's Oldest, Continuous Cotton Experiment**.** *Agronomy Journal*, **100** (5): 1493 DOI: 10.2134/agronj2007.0395

806 Miller PR, Buschena DE, Jones CA, Holmes JA(2008) Transition from intensive tillage to no-tillage and organic diversified annual cropping systems. *Agronomy Journal*, **100**, 591-599.

807 Proper Management Can Make Lower Corn Yields Profitable. *ScienceDaily*, July 10, 2007. http://www.sciencedaily.com/releases/2007/07/070709102323.htm

808 Halliday J (2009) Organic shift would drive healthier diets: report. Dairyreporter.com. 24th June 2009. http://www.dairyreporter.com/Publications/Food-Beverage-Nutrition/FoodNavigator.com/Financial-Industry/Organic-shift-would-drive-healthier-diets-report/?c=TUMKruuz4xhb%2F6JfUqBtDg%3D%3D&utm_source=newsletter_daily&utm_medium=email&utm_campaign=Newsletter%2BDaily

809 http://www.apd.reading.ac.uk/AgriStrat/projects/org_exec.html

810 Tanji KK, Kielen NC(2002) Agricultural drainage water management in arid and semi-arid areas. FAO Irrigation and Drainage Paper 61. ftp://ftp.fao.org/agl/aglw/docs/idp61e.pdf

811 The Comprehensive Assessment of Water Management in Agriculture. 2007. Earthscan. http://www.iwmi.cgiar.org/assessment/

812 Ten African Experiences. Secretariat of the United Nations Convention to Combat Desertification (UNCCD), Bonn, Germany. 2006. http://www.unccd.int/regional/africa/docs/tenAfricanExpr-eng.pdf

813 Stern N (2006) Stern Review on the Economics of Climate Change. HM Treasury 7 Cabinet Office, 2006. http://www.hm-treasury.gov.uk/independent_reviews/stern_review_economics_climate_change/sternreview_index.cfm

814 The future of small farms. Proceedings of a research workshop. Wye, UK. June 26-29 2005. *Jointly organized by* International Food Policy Research Institute (IFPRI) / 2020 Vision Initiative Overseas Development Institute (ODI), Imperial College, London. http://www.ifpri.org/events/seminars/2005/smallfarms/sfproc/sfproc.pdf

815 Kinhi A (2003) Plot Size and Maize Productivity in Zambia: The Inverse Relationship Re-examined. The Center for Agricultural Economic Research, The Hebrew University of Jerusalem. Discussion Paper No. 10.03. http://departments.agri.huji.ac.il/economics/kimhi-zambia2.pdf

816 Tessema W (2004) Population Pressure and Farm Size-Productivity Relationship in subsistence constrained agriculture. http://www.umb.no/ior/bulletinen/DP19-04.pdf

817 Fan S, Chan-Kang C (2003) Is small beautiful? Farm Size, Productivity and Poverty in Asian Agriculture. Invited plenary paper to be presented at the 2003 International Association of Agricultural Economists, Durban. http://www.iaae-agecon.org/conf/durban_papers/papers%5CFan.pdf

818 Fening JO, Gyapong TA, Ababio F, Gaisie E (2006) Intercropping maize with planted fallows on smallholder farms in Ghana. *Tropical Science*, **45**(4), 155-158.

819 Chamango AMZ (2001) Improving grain yield of smallholder cropping systems: a farmer participatory research (FPR) approach with legumes for soil fertility improvement in central Malawi. Seventh Eastern and Southern Africa Regional Maize Conference, 11th-12th February, 2001. pp.413-417.

820 Bertomeu M (undated) Small-scale farm forestry: an adoptable option for smallholder farmers in the Philippines? http://www.worldagroforestry.org/downloads/publications/PDFs/bc05136.doc

821 Jeranyama P, Waddington SR, Hesterman OB, Harwood RR (2007) Nitrogen effects on maize yield following groundnut in rotation on smallholder farms in sub-humid Zimbabwe. *African Journal of Biotechnology*, **6** (13), 1503-1508.

822 http://www.publications.parliament.uk/pa/cm200708/cmhansrd/cm080609/wmstext/80609m0001.htm#column_6WS

823 IAASTD (2008) Executive summary of the synthesis report of the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD). http://www.agassessment.org/docs/SR_Exec_Sum_280508_English.pdf

824 IAASTD (2008) International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD) global summary for decision makers. http://www.agassessment.org/docs/Global_SDM_060608_English.pdf

825 UN (2008) Organic agriculture and food security in Africa. UNEP-UNCTAD Capacity-building Task Force on Trade, Environment and Development. http://www.unep-unctad.org/cbtf/publications/UNCTAD_DITC_TED_2007_15.pdf

826 Toleda A, Burlingame B (2006) Biodiversity and nutrition: a common path toward global food security and sustainable development. *Journal of Food Composition and Analysis*, **19**, 477-483.

827 The National Academies (1996) Lost crops of Africa: Volume I, Grains. http://www7.nationalacademies.org/dsc/Lost_Crops_of_Africa.html

828 The National Academies (2006) Lost crops of Africa: Volume II, Vegetables. http://www7.nationalacademies.org/dsc/Lost_Crops_of_Africa.html

829 The National Academies (2008) Lost crops of Africa: Volume III, Fruits. http://www7.nationalacademies.org/dsc/Lost_Crops_of_Africa.html

830 Hobhouse H (1999) Seeds of change: Six plants that transformed mankind. Papermac, London.

831 Pakenham T (1991) The scramble for Africa. Abacus, London.

832 http://www.sustainablecities.org.uk/

833 Nanok T, Taylor P, Tollens E, Vandenbosch T(2008) Policies for enhancing food security through relevant basic education. In: Hout W(Ed), EU Development Policy and Poverty Reduction: Enhancing Effectiveness, Ashgate, London.

834 Charman AJE (2008) Empowering Women Through Livelihoods Oriented Agricultural Service Provision: A consideration of evidence from South Africa, Research Paper 2008/01, UNU-WIDER, January 2008. http://www.wider.unu.edu/publications/working-papers/research-papers/2008/en_GB/rp2008-01/

835 Adam D (2007) Down on the pharm. The Guardian. 30th April, 2007.

836 Global financial crisis making biotech business model unsustainable according to Ernst & Young. Ernst and Young Press Release. 5th May 2009. http://www.ey.com/GL/en/Newsroom/News-releases/Media---Press-Release---Global-financial-crisis-making-biotech-business-model-unsustainable-according-to-Ernst---Young

837 Dellenbach R (2008) VC funding for biotech companies withering. *Genetic Engineering and Biotechnology News*. 3rd September 2008. http://greenbio.checkbiotech.org/news/2008-09-04/VC_funding_for_biotech_companies_withering/

838 Productivity improvements needed to improve pharmaceutical profits. http://pharmalicensing.com/public/articles/view/1026736460_3d32c14cab037

839 Kopp K (2007) Big pharma pipeline in need of priming. *Triangle Business Journal*. 14th September 2007.

840 Wishart A (2009) The unbearable cost of living. *The Sunday Times*. 7th June 2009. http://www.timesonline.co.uk/tol/news/uk/health/article6430926.ece

841 NICE warns industry on cost-effectiveness. In-Pharm. 9th February 2010. http://www.inpharm.com/news/nice-warns-industry-cost-effectiveness

842 Kollewe J (2008) Big Pharma besieged from all sides. The Guardian, 30th August, 2008. http://www.guardian.co.uk/business/2008/aug/30/pharmaceuticals.medicalresearch?gusrc=rss&feed=networkfront

843 G20 economic stimulus packages offer little direct aid to branded pharmaceutical players. iStockAnalyst. 9th April 2009. http://www.istockanalyst.com/article/viewiStockNews/articleid/3189182

844 Col, N (2003), The use of gene tests to detect hereditary predisposition to chronic disease: Is cost-effectiveness analysis relevant? Medical Decision Making, 23, 441-448.

845 Rogowski W (2007) Current impact of gene technology on healthcare. A map of economic assessments. *Health Policy*, **80**(2), 340-357.

846 Rogowski W, Grosse SD, Khoury M (2009) Challenges of translating genetic tests into clinical and public health practice. *Nature Reviews Genetics*, **10**, 489-494.

847 Henderson M (2009) Cashing in on your genes. *The Times*. 7th January 2010. http://www.timesonline.co.uk/tol/news/science/eureka/article6975520.ece?token=null&offset=0&page=1

848 Cruddas J (2004) Neo-classical Labour. http://www.joncruddas.org.uk/index.php?getPage=newsTemp&story=9

849 Cruddas J (2006) A Trade Union Freedom Bill and the economy. http://www.joncruddas.org.uk/index.php?getPage=newsTemp&story=10

850 BBSRC (2009) Economic Impact Baseline, 2009 Update. http://www.bbsrc.ac.uk/web/FILES/Publications/economic_impact_baseline_2009_update.pdf

851 IPTS(2007) The Biotechnology for Europe Study (BIO4EU): Consequences, opportunities and challenges of modern biotechnology for Europe. http://bio4eu.jrc.es/index.html

852 http://sdw.ecb.europa.eu/quickview.do?SERIES_KEY=119.ESA.A.V1.N.0000.B1G000.1000.YC_E.V.U.A

853 Genome Valley: the economic potential and strategic importance of biotechnology in the UK. http://www.berr.gov.uk/files/file28709.pdf

854 Doubleday R (2008) The knowledge economy: good intentions drive more innovation. In: GM foods: the wrong debate? *Food Ethics*, **3**(3), 21.

855 Young T (2008) Drop in organic sales no indicator of green consumerism. Accountancy Age. 4 Sept 2008. http://www.accountancyage.com/business-green/news/2225353/drop-organic-sales-canary-green

856 Organic pace gains momentum in France. 23rd June 2009. http://www.dairyreporter.com/Industry-markets/Organic-pace-gains-momentum-in-

France/?c=TUMKruuz4xiGFCHuW1Q%2B7w%3D%3D&utm_source=newsletter_daily&utm_medium=email&utm_campaign=Newsletter%2BDaily

857 Consumers in France reject genetically modified crops ahead of French parliament vote. 5th February 2008. http://www.webinfrance.com/consumers-in-france-reject-genetically-modified-crops-ahead-of-french-parliament-vote-205.html

858 According to biotech industry sources there were 114 million hectares of GM crops and trees grown in the world in 2007(source: www.isaaa.org). The total area of agricultural land in the world is 1.4 billion hectares of arable land, plus 3.4 billion hectares of pasture, and there are around 140 million hectares of commercial forestry (sources: http://faostat.fao.org/Portals/_Faostat/documents/pdf/world.pdf and ftp://ftp.fao.org/docrep/fao/008/A0400E/A0400E00.pdf).

859 King JL & Schimmelpfennig D (2005) Mergers, acquisitions, and stocks of agricultural biotechnology intellectual property. *AgBioForum*, **8**, 83-88.

860 Brennan M, Pray C, Naseem A & Oehmke JF (2005) An innovation market approach to analyzing impacts of mergers and acquisitions in the plant biotechnology industry. AgBioForum 8: 89-99.

861 Some GM questions answered. The Ecologist. 1st July 2003. http://www.theecologist.org/News/news_analysis/268552/some_gm_questions_answered.html

862 Vollmer S (2009) Gene-altered crop studies grow. The News and Observer (Raleigh, N.C.) 1st January 2009. http://seattlepi.nwsource.com/national/394482_plantgenes02.html

863 Mitchell P (2007) GM giants pair up to do battle. *Nature Biotechnology*, **25**(7), 695-696.

864 Interview with Dr Hambrecht. Checkbiotech. 26th August 2009. http://checkbiotech.org/node/27179

865 BASF (2010) BASF and Embrapa's Cultivance soybeans receive approval for commercial cultivation in Brazil. 5th February 2010. http://www.basf.com/group/pressrelease/P-10-148

866 Tait J, Chataway J, Wield D (2002) The life science industry sector: evolution of agro-biotechnology in Europe. *Science and Public Policy*, **29**(4), 253-258.

867 Petersen C (2008) Monsanto hurting Iowa and US farmers. Des Moines Register. 17 October 2008. http://www.organicconsumers.org/articles/article_15219.cfm

868 Monsanto's profit jumps, raises 2008 forecast. Reuters. 3rd January 2008. http://uk.reuters.com/article/ousiv/idUKWNAS553620080103

869 McWilliams J(2008) Monsanto raises its earnings outlook again. St Louis Post. 2nd October 2008. http://www.stltoday.com/stltoday/business/stories.nsf/story/E40CA12BF1C028BD862574D6005B7147?OpenDocument

870 Monsanto raises its fiscal 2008 guidance. Associated Press. 2nd October 2008. http://www.iht.com/articles/ap/2008/10/02/business/NA-US-Monsanto-Guidance.php

871 Gilham C (2009) Monsanto beats view, to restructure Roundup unit. Reuters. 24th June 2009. http://www.publicbroadcasting.net/wgvu/news.newsmain/article/0/0/1521735/Business/Monsanto.beats.view..to.restructure.Roundup.unit

872 Ligi A (2009) BASF says its dividend is increasingly difficult to maintain. Bloomberg. 23rd June 2009. http://www.bloomberg.com/apps/news?pid=20601100&sid=aXvjZXNRDLlQ

873 European Commission Grants Approval for Bayer's LibertyLink Brand Soybeans. http://www.soyatech.com/news_story.php?id=10182

874 Bayer Crop Science completes acquisition of biotech company Athenix Corp. Checkbiotech. 3rd November 2009. http://greenbio.checkbiotech.org/news/bayer_cropscience_completes_acquisition_biotech_company_athenix_corp

875 Bayer Crop Science to consolidate European plant biotechnology research in Ghent. 6th April 2009. http://checkbiotech.org/node/25471

876 British Retail Consortium (2002) New food products and processes (genetically modified foods). October 2002. http://www.brc.org.uk/Downloads/GM%20Statement.pdf

877 JRC (2008) Biofuels in the European context: Facts and uncertainties. JRC44464. http://ec.europa.eu/dgs/jrc/downloads/jrc_biofuels_report.pdf

878 http://www.defra.gov.uk/environment/gm/crops/index.htm

879 Fernandez-Cornejo J & McBride WD (2002) Adoption of Bioengineered Crops. United States Department of Agriculture Economic Research Service Agricultural Economic Report Number 810.

880 Gibbons DW et al (2006) Weed seed resources for birds in fields with contrasting conventional and genetically modified herbicide-tolerant crops. Proc R Soc B 273: 1921-1928.

881 Owen, MDK, & Zelaya, IA. (2005) Herbicide-resistant crops and weed resistance to herbicides. Pest Management Science 61:301311.

882 Benbrook CM (2003) Impacts of Genetically Engineered Crops on Pesticide Use in the United States: The First Eight Years. BioTech InfoNet Technical Paper Number 6. http://www.biotech-info.net/Technical_Paper_6.pdf

883 Tabashnik BE, Gassman AJ, Crowder DW, Carriére Y (2008) Insect resistance to Bt crops: evidence versus theory. *Nature Biotechnology*, **26**, 199 202.

884 Wang S., Just DR & Pinstrup-Andersen P (2006) Tarnishing Silver bullets: Bt technology adoption, bounded rationality and the outbreak of secondary pest infestations in China. Paper presented at the American Agricultural Economics Association Meeting, Long Beach CA, July 22-26, 2006. http://www.grain.org/research_files/SWang_tarnished.pdf

885 Cattaneo MG, Yafuso C, Schmidt C *et al* (2006) Farm-scale evaluation of the impacts of transgenic cotton on biodiversity, pesticide use, and yield PNAS 103: 7571-7576.

886 Gebbers R, Adamchak VI (1010). Precision agriculture and food security. *Science*, **327**, 828-831.

887 Smale M, Zambrano P, Falck-Zepeda J, Guère G (2006) Parables: Applied Economics Literature About the Impact of Genetically Engineered Crop Varieties in Developing Economies. EPT Discussion Paper 158.

888 Gordon B (2007) Manganese Nutrition of Glyphosate-Resistant and Conventional Soybeans (North America). Better Crops, 91(4), 12. http://www.ipni.net/ppiweb/bcrops.nsf/$webindex/70ABDB50A75463F085257394001B157F/$file/07-4p12.pdf

889 Gomez-Barbero M, Rodriguez-Cerezo E (2006) Economic impact of dominant GM crops worldwide: a review. Institute for Prospective Technological Studies, European Commission Joint Research Centre. EUR 22547 EN. http://81.0.228.70/attachments/Econ_Impact_GM_world.pdf

890 Gomez-Barbero M, Berbel J, Rodriguez-Cerezo E(2008) Bt corn in Spain the performance of the EU's first GM crop. *Nature Biotechnology*, 26(4), 384-386.

891 Pemsl D, Waibel H, Gutierrez AP (2006) The economics of biotechnology under ecosystem distruption. Contributed paper prepared for presentation at the

International Association of Agricultural Economists Conference Gold Coast, Australia, August 12-18, 2006. http://ageconsearch.umn.edu/bitstream/25335/1/cp060906.pdf

892 Conventional soybeans offer high yields at lower cost. News from University of Missouri Extension. 8th September 2008. http://agebb.missouri.edu/news/ext/showall.asp?story_num=4547&iln=49

893 Soleri D, Cleveland DA, Glasgow G, Sweeney SH, Cuevas FA, Fuentes MR, Ríos HL (2008) Testing assumptions underlying economic research on transgenic food crops for Third World farmers: Evidence from Cuba, Guatemala and Mexico. *Ecological Economics*, **67**, 667-682.

894 Johnson DD, Lin W, Vocke G (2005) Economic and welfare impacts of commercializing an herbicide tolerant, biotech wheat. *Food Policy*, **30**, 162-184.

895 Food firms launch Brazil GMO-free grain group. Reuters. 9 September 2008. http://www.reuters.com/article/rbssHealthcareNews/idUSN0927664920080909

896 Bock A-K ,Lheureux, Libeau-Dulos M, Nilsagård H & Rodriguez-Cerezo E (2002) Scenarios for co-existence of genetically modified, conventional and organic crops in European agriculture. IPTS - JRC Report EUR 20394EN ftp://ftp.jrc.es/pub/EURdoc/eur20394en.pdf.

897 http://www.coextra.eu/

898 Greenpeace (2007) Rice industry in crisis: Major rice markets close doors to genetically engineered rice after contamination of the global food supply chain. January 2007.

899 Bayer to pay $1.5m in 2nd lawsuit over GM rice. Reuters. 5th February 2010. http://uk.reuters.com/article/idUKLDE61421W20100205

900 Smyth S, Kachatourians GG, Phillips PWB(2002) Liabilities and economics of transgenic crops. *Nature Biotechnology*, **20**, 537-541.

901 Triffid seed threatens flax industry. CBC News. 20th January 2010. http://www.cbc.ca/canada/manitoba/story/2010/01/20/mb-flax-triffid-manitoba.html

902 http://www.gmcontaminationregister.org/

903 Demont M, Wesseler J, Tollens E(2003) Biodiversity versus transgenic sugar beet: the one euro question. Paper prepared for presentation at the 25th International Conference of Agricultural Economists, August 16-22, 2003, Durban, South Africa. http://www.iaae-agecon.org/conf/durban_papers/papers/022.pdf

904 Rodgers CP (2007) Coexistence or Conflict? A European Perspective on GMOs and the Problem of Liability. *Bulletin of Science, Technology & Society*, **27** (3), 233-250.

905 Belcher K, Nolan J, Phillips PWB (2005) Genetically modified crops and agricultural landscapes: spatial patterns of contamination. *Ecological Economics*, 53(3), 387-401.

906 Munro A (2008) The spatial impact of genetically modified crops *Ecological Economics*, **67**(4), 658-666.

907 Universitat Autonoma de Barcelona (2008) An Impossible Coexistence: Transgenic And Organic Agriculture." *ScienceDaily* 2 July 2008. http://www.sciencedaily.com-/releases/2008/06/080630102731.htm

908 Nestle, M (2002) Food politics. University of California Press, Berkeley.

909 Strategy Unit (2008) Food: an analysis of the issues. January 2008 (updated August 2008). http://www.cabinetoffice.gov.uk/~/media/assets/www.cabinetoffice.gov.uk/strategy/food/food_analysis%20pdf.ashx

910 Foresight (2007) Tackling obesities: Future Choices. Project report. Government Office for Science. http://www.foresight.gov.uk/Obesity/17.pdf

911 Dibb S, Mayer S (2000) Biotech the next generation: good for whose health? The Food Commission and GeneWatch UK. Summary available on: http://www.genewatch.org/CropsAndFood/Reports/FoodSumm.htm .

912 Mayer S (2003) Non-food GM crops: New dawn or false hope? Part 1: Drug production. GeneWatch UK, August 2003. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Part_1___Producing_Drugs_in_GM_Crops_A4.pdf

913 Mayer S (2004) Non-food GM crops: New dawn or false hope? Part 2: Grasses, flowers, trees, fibre crops and industrial uses. GeneWatch UK, March 2004. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Part_2___Grasses__Flowers__Trees__Fibre_Crops_and_Industrial_Uses.pdf

914 Sparrow PAC, Irwin JA, Dale PJ, Twyman RM, Ma JKC (2007) Pharma-Planta: Road testing the developing regulatory guidelines for plant-made pharmaceuticals. *Transgenic Research*, **16**, 147-161.

915 USA Rice Federation (2007) Re: Docket No. APHIS-2007-0006 - Ventria Bioscience; Availability of an Environmental Assessment for Field Tests of Rice Genetically Engineered To Express Lactoferrin, Lysozyme, or Serum Albumin. 29th March 2008. http://www.usarice.com/industry/communication/Final_Ventria_Kansas_comments.pdf

916 DTZ(2008) Economic impact of the John Innes Centre. March 2008. http://www.jic.ac.uk/corporate/about/publications/impact/economic_impact.pdf

917 Thirtle C, Bottomley P, Palladino P, Schimmelpfennig D, Townsend R (1998) The rise and fall of public sector plant breeding in the United Kingdom: a causal chain model of basic and applied research and diffusion. *Agricultural Economics*, **19**, 127-143.

918 Rees J (2002) Complex disease and the new clinical sciences. *Science*, **296**, 698-701.

919 Getting the message across. *Nature*, **453**, 839.

920 Sinclair TR, Purcell LP (2005) Is a physiological perspective relevant in a 'genocentric' age? *Journal of Experimental Botany*, **56**(421), 2777-2782.

921 Contopoulos-Ioannidis DG, Nitzani E, Ioannidis JP (2003) Translation of highly promising basic science research into clinical applications. *American Journal of Medicine*, **114**, 503-505.

922 To thwart disease, appply now. [Editorial]. *Nature*, **453** (7179), 823.

923 Travis K (2007) Special feature: translational research careers. Science, August 17 2007.

http://sciencecareers.sciencemag.org/career_development/previous_issues/articles/2007_08_17/caredit_a0700116

924 Ledford H (2008) The full cycle. *Nature*, **453**, 843-845.

925 Maher B (2008) Egg shortage hits race to clone human stem cells. *Nature*, **453**, 828.

926 Sexton S (1999) If cloning is the answer, what was the question? *The Corner House*. October 1999. http://www.thecornerhouse.org.uk/pdf/briefing/16clone.pdf

927 Martin P, Morrison M (2006) Realising the potential of genomic medicine. IGBiS, Nottingham. July 2006. Printed in Great Britain by the Royal Pharmaceutical Society of Great Britain. ISBN: 0-9550029-3-1. http://www.bioscienceresource.org/docs/GeneticMedicine.pdf

928 Duyk G (2003) Attrition and translation. *Science*, **302**, 602-5.

929 Millikan RC (2006) Commentary: The Human Genome: philosopher's stone or magic wand? *International Journal of Epidemiology*, **35**, 578-580.

930 Gohlke JM, Portier CJ (2007) The forest for the trees: a systems approach to human health research. *Environmental Health Perspectives*, **115**(9), 1261-1263.

931 Wilkie A (2006) Polygenic inheritance and genetic susceptibility screening. Encyclopedia of Life Sciences. DOI: 10.1002/9780470015902.a0005638. http://mrw.interscience.wiley.com/emrw/9780470015902/els/article/a0005638/current/abstract?hd=All,9780470015902.a0005638
Article Online Posting Date: September 15, 2006

932 Carmichael M (2010) The worlds most successful failure. Newsweek, 12th February 2010. http://www.newsweek.com/id/233494

933 Gene tests fail to predict women's heart risks. Reuters, 17th February 2010. http://abcnews.go.com/Technology/wireStory?id=9857168

934 Department of Health (2003) Our inheritance, our future: realising the potential of genetics in the NHS, June 2003, Cm 5791-II (London, The Stationary Office).

935 Strohman RC (1997) The coming Kuhnian revolution in biology. *Nature Biotechnology*, **15**:194-200

936 Holtzman NA, Marteau TM (2000) Will genetics revolutionize medicine? *New Engl J Med*, **343**, 141-144.

937 Vineis P, Schulte P, McMichael AJ (2001) Misconceptions about the use of genetic tests in populations. *Lancet*, **357**: 709-712.

938 Baird P (2001) The Human Genome Project, genetics and health. *Community Genet*ics, **4**, 77-80.

939 Cooper RS, Psaty BM (2003) Genetics and medicine: distraction, incremental progress, or the dawn of a new age? *Ann Intern Med*, **138**, 576-580.

940 Zeggini E, Weedon MN, Lindgren CM, Frayling TM, Elliott KS, Lango H, Timpson NJ, Perry JRB, Rayner NW, Freathy RM, Barrett JC, Shields B, et al. (2007) Replication of genome-wide association signals in UK samples reveals risk loci for type 2 diabetes. *Science*, **316**, 1136-1341.

941 Janssens ACJW, Gwinn M, Subramonia-Iyer S, Khoury M (2006) Does genetic testing really improve the prediction of type 2 diabetes? *PLoS Medicine*, **3**(2), e114.

942 Janssens ACJW, Gwinn M, Valdez R, Narayan K, Khoury M (2006) Predictive testing for type 2 diabetes. *British Medical Journal*, **333**, 509-510.

943 Meigs JB, Shrader P, Sullivan LM, McAteer JB, Fox CS, Dupuis J, Manning AK, Florez JC, Wilson PWF, D'Agostino RB, Cupples LA (2008) Genotype score in addition to common risk factors for prediction of Type 2 Diabetes. *New England Journal of Medicine*, **359**, 2208-2219.

944 Talmud PJ, Hingorani AD, Cooper JA, Marmot MG, Brunner EJ, Kumari M, Kivimaki M, Humphries SE (2010) Utility of genetic and non-genetic risk factors in prediction of type 2 diabetes: Whitehall II prospective cohort study. *British Medical Journal*, **340**:b4838

945 Breast Cancer Association Consortium. Commonly studied single-nucleotide polymorphisms and breast cancer: results from the Breast Cancer Association Consortium. J Natl Cancer Inst. 2006 Oct 4;98(19):1382-96. Erratum in: J Natl Cancer Inst. 2007 May 7;99(5):411.

946 Ioannidis JP (2006) Common genetic variants for breast cancer: 32 largely refuted candidates and larger prospects. *J Natl Cancer Inst*., **98**(19):1350-3.

947 Pharoah PD, Tyrer J, Dunning AM, Easton DF, Ponder BA; SEARCH Investigators. Association between common variation in 120 candidate genes and breast cancer risk. PLoS Genet. 2007 Mar 16;3(3):e42.

948 Gail MH (2008) Discriminatory accuracy from Single-Nucleotide Polymorphisms in models to predict breast cancer risk. Journal of the National Cancer Institute, **100**, 1037-1041.

949 Liu W, Zhao W, Chase GA (2004) Genome scan meta-analysis for hypertension. Am J Hypertens., **17**, 1100-6.

950 Newton-Cheh C, Johnson T, Gateva V, Tobin MD, Bochud M, et al. (2009) Genome-wide association study identifies eight loci associated with blood pressure. *Nature Genetics*, **41**(6), 666-676.

951 Ntzani EE, Rizos EC, Ioannidis JP (2007) Genetic effects versus bias for candidate polymorphisms in myocardial infarction: case study and overview of large-scale evidence. Am J Epidemiol., **165**(9), 973-84.

952 Myocardial Infarction Genetics Consortium (2009) Genome-wide association of early-onset myocardial infarction with single nucleotide polymorphisms and copy number variants. *Nature Genetics*, **41**(3), 334-341.

953 Kathitesan S, Melander O, Anevski D, et al. (2008) Polymorphisms associated with cholesterol and risk of cardiovascular events. *The New England Journal of Medicine*, **358**, 1240-1249.

954 Frayling TM, Timpson NJ, Weedon MN, Zeggini E, Freathy RM, Lindgren CM, Perry JR, Elliott KS, Lango H, Rayner NW, Shields B, Harries LW, Barrett JC, Ellard S, Groves CJ, Knight B, Patch AM, Ness AR, Ebrahim S, Lawlor DA, Ring SM, Ben-Shlomo Y, Jarvelin MR, Sovio U, Bennett AJ, Melzer D, Ferrucci L, Loos RJ, Barroso I, Wareham NJ, Karpe F, Owen KR, Cardon LR, Walker M, Hitman GA, Palmer CN, Doney AS, Morris AD, Smith GD, Hattersley AT, McCarthy MI (2007). A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science, 316(5826), 889-94.

955 Sabatti C, Service SK, Hartikainen A-L, Pouta A, Ripatti S, Brodsky J et al. (2009) Genome-wide association analysis of metabolic traits in a birth cohort from a founder population. Nature Genetics, 41(1), 35-701.

956 Liu W, Zhao W, Chase GA (2004) Genome scan meta-analysis for hypertension. American Journal of Hypertension, 17, 1100-6.

957 Levy D, Ehret GB, Rice K, Verwoert GC, Launer LJ, Dehghan A, et el. (2009) Genome-wide association study of blood pressure and hypertension. *Nature Genetics*, **41**(6), 677-687.

958 Maniolo TA (2009) Cohort studies and the genetics of complex disease. *Nature Genetics*, **41**(1), 5-6.

959 Jakobsdottir J, Gorin MB, Conley YP, Ferrell RE, Weeks, DE (2009) Interpretation of genetic association studies: markers with replicated highly significant odds ratios may be poor classifiers. PLoS Genetics, 5(2), e1000337.

960 Goldstein DB (2009) Common genetic variation and human traits. New England Journal of Medicine, 360, 17.

961 Munafò MR (2009) The clinical utility of genetic tests. *Addiction*, 104, 127-128.

962 Janssens ACJW, van Duijn CM (2008) Genome-based prediction of common diseases: advances and prospects. Human Molecular Genetics, 17(R2), R166-R173

963 Johnson L, van Jaarsveld CHM, Emmett PM, Rogers IS, Ness AR, Hattersley AT, Timpson NJ, Davey Smith G, Jebb SA (2009) Dietary Energy Density Affects Fat Mass in Early Adolescence and Is Not Modified by *FTO* Variants. PLoS One. 4(3): e4594. doi:10.1371/journal.pone.0004594

964 Heard-Costa NL, Zillikens MC, Monda KL, Johansson Å, Harris TB, et al. 2009 *NRXN3* Is a Novel Locus for Waist Circumference: A Genome-Wide Association Study from the CHARGE Consortium. PLoS Genet 5(6): e1000539. doi:10.1371/journal.pgen.1000539.

965 Baker SG, Kaprio J (2006) Common susceptibility genes for cancer: search for the end of the rainbow. *British Medical Journal*, **332**, 1150-1152.

966 Mayo O (2007) The rise and fall of the Common Disease-Common Variant (CD-CV) hypothesis: How the sickle cell disease paradigm led us all astray (or did it?). *Twin Research and Human Genetics*, **10**(6), 793-804.

967 Janssens ACJW, Gwinn M, Bradley LA, Oostra BA, van Duijn CM, Khoury MJ (2008) A Critical Appraisal of the Scientific Basis of Commercial Genomic Profiles Used to Assess Health Risks and Personalize Health Interventions. The American Journal of Human Genetics **82**, 593599. http://www.ajhg.org/AJHG/fulltext/S0002-9297(08)00145-6.

968 Lewontin RC (1991) Biology as Ideology. Anansi Press Ltd, Canada.

969 Keller EF (2000) The century of the gene. Harvard University Press.

970 Moss L (2003) What genes can't do. MIT Press.

971 Sarkar S (1998) Genetics and reductionism. Cambridge University Press.

972 Wade N (2009) Genes show limited value in predicting diseases. New York Times. 15th April 2009. http://www.nytimes.com/2009/04/16/health/research/16gene.html?_r=2&ref=global-home

973 Wallace HM (2006) A model of gene-gene and gene-environment interactions and its implications for targeting environmental interventions by genotype. *Theoretical Biology and Medical Modelling*, **3** (35), doi:10.1186/1742-4682-3-35. http://www.tbiomed.com/content/3/1/35

974 Wallace HM (2009) Genetic screening for susceptibility to disease. Encyclopedia of Life Sciences. In press.

975 Wilson AJ, Pemberton JM, Pilkington JG, Coltman DW, Mifsud DV, Clutton-Brock TH, Kruuk LEB(2006) Environmental coupling of selection and heritability limits evolution. *PloS Biology*, **4**(7), e26.

976 Slatkin M (2008) Exchangable models of complex inherited diseases. *Genetics*, **179**, 2253-2261.

977 Wei Z, Wang K, Qu H-Q, Zhang H, Bradfield J, Kim C, Frackleton E, Hou C, Joseph T. Glessner JT, Chiavacci R, Stanley C, Monos D, Grant SFA, Polychronakos C, Hakonarson H (2010) From Disease Association to Risk Assessment: An Optimistic View from Genome-Wide Association Studies on Type 1 Diabetes. PLoS Genetics, 5(10): e1000678. doi:10.1371/journal.pgen.1000678

978 Gardiner SJ, Begg EJ(2006) Pharmacogenetics, drug-metabolizing enzymes, and clinical practice. *Pharmacological Reviews*, 58(3), 521-590.

979 Matchar DB, Thakar ME, Grossman I, McCrory DC, Orlando LA, Steffens DC, Goldstein DB, Cline KE, Gray RN (2006) Testing for Cytochrome P450 polymorphisms in adults with non-psychotic depression treated with selective serotonin reuptake inhibitors (SSRIs). AHRQ Publication No. 07-E002. November 2006.

980 Sanderson S, Emery J, Higgins J. CYP2C9 gene variants, drug dose, and bleeding risk in warfarin-treated patients: a HuGEnet systematic review and meta-analysis. Genet Med. 2005 Feb;7(2):97-104.

981 Wiwanitkit V. Pharmacogenomic effect of cytochrome P450 2C9 polymorphisms in different populations. Clin Appl Thromb Hemost. 2006 Apr;12(2):219-22.

982 Ozdemir V, Kalow W, Tothfalusi L, Bertilsson L, Endrenyi L, Graham JE (2005) Multigenic control of drug response and regulatory decision-making in pharmacogenomics: the need for an upper-bound estimate of genetic contributions. *Clinical Pharmacogenomics*, **3**, 53-71.

983 Kangelaris KN, Bent S, Nussbaum RL, Garcia DA, Tice JA (2009) Genetic testing before anticoagulation? A systematic review of pharmacogenetic dosing of warfarin. *Journal of Genetics and Internal Medicine*, **24**(5): 656664.

984 Burton H, Alberg C, Stewart S (2009) Heart to heart: Inherited cardiovascular conditions services: A needs assessment and service review. June 2009. The PHG Foundation. www.phgfoundation.org

985 Schalkwyk LC, Meaburn EL, Smith R, Dempster EL, Jeffries AR, Davies MN, Plomin R, Mill J (2010) Allelic skewing of DNA methylation is widespread across the genome. *The American Journal of Human Genetics*, **86**(2), 196-212.

986 Ashraf M, Akram NA (2009) Improving salinity tolerance of plants through conventional breeding and genetic engineering: an analytical comparison. *Biotechnology Advances*, **27**, 744-752.

987 Porter J, Wollenweber B (2010) The Rubisco enzyme and agricultural productivity. [Letter] *Nature*, **463**(18), 876.

988 Zulassung - Emsland Stärke GmbH sieht Bedenken wegen Genkartoffel Amflora. Ad Hoc News. 3rd March 2010. http://www.ad-hoc-news.de/zulassung-emsland-staerke-gmbh-sieht-bedenken-wegen--/de/Politik/21097831

989 Chafin J (2010) Genetically modified potato wins EU approval. Financial Times. 2nd March 2010. http://www.ft.com/cms/s/0/e00b505a-2630-11df-aff3-00144feabdc0.html

990 Graffe GD, Zilberman D, Bennett AB (2009) The contraction of agbiotech quality innovation. [Correspondence} *Nature Biotechnology*, **27**(8), 702-704.

991 Stein AJ, Rodríguez-Cerezo E (2009) The global pipeline of new GM crops: Implications of asynchronous approvals for international trade. JRC Scientific and Technical Reports. European Commission JRC; Institute for Prospective Technological Studies. EUR 23486 EN 2009.

992 India divided over plans for GM aubergine. BBC News Online. 9th February 2010. http://news.bbc.co.uk/1/hi/world/south_asia/8503825.stm

993 Narain S (2010) Consumers should have choice on Bt brinjal. Times of India. 14th February 2010. http://timesofindia.indiatimes.com/home/sunday-toi/all-that-matters/Consumers-should-have-choice-on-Bt-brinjal/articleshow/5570673.cms

994 Bt brinjal debate goes to people. Times of India. 16th October 2009. http://timesofindia.indiatimes.com/india/Bt-brinjal-debate-goes-to-people/articleshow/5128675.cms

995 Challenges posed by Bt Brinjal. Times of India. 6th February 2010. http://timesofindia.indiatimes.com/india/Challenges-posed-by-Bt-Brinjal/articleshow/5541948.cms

996 Godfray HCJ, Beddington JR, Crute IR, Haddad L, Lawrence D, Muir JF, Pretty J, Robinson S, Thomas SM, Toulmin C (2010) Food security: the challenge of feeding 9 billion people. *Science*. www.sciencexpress.org / 28 January 2010 / Page 1 / 10.1126/science.1185383

997 http://www.foresight.gov.uk/OurWork/ActiveProjects/FoodandFarmingFutures/FoodandfarmingProjectHome.asp

998 FAO (2007) Marker-assisted selection: current status and future perspectives in crops, livestock, forestry and fish. FAO, Rome, 2007. ftp://ftp.fao.org/docrep/fao/010/a1120e/a1120e.pdf

999 Flowers TJ(2004) Improving crop salt tolerance. *Journal of Experimental Botany*, **55**(396), 307-319.

1000 Tuberosa R, Salvi S (2006) Genomics-based approaches to improve drought tolerance of crops . *Trends in Plant Science*, **11**(8), 405-412.

1001 Cattivelli L, Rizza F, Badeck F-W, Mazzucotelli E, Mastrangelo AMM, Francia E, Marè C, Tondelli A, Stanca AM (2008) Drought tolerance improvement in crop plants: An integrated view from breeding to genomics. *Field Crops Research*, **105**(1-2), 1-14.

1002 Potočnik J (2008) Biorefineries – new generation. Info day on the biorefinary joint call. 16th September 2008. http://ec.europa.eu/commission_barroso/potocnik/news/docs/20080916_speech_biorefineries.pdf

1003 http://cordis.europa.eu/fp7/dc/index.cfm?fuseaction=UserSite.FP7DetailsCallPage&call_id=150

1004 Connor S (2005) Scientists guilty of hyping benefits of gene research. The Independent, 5th September 2005.

1005 http://www.dius.gov.uk/science/science_and_society/public_engagement/public_attitudes

1006 Reynolds, L and Szerszynski, B, Kousis, M and Volakakis, Y. PAGININI Project. Workpackage 6: GM Food. http://www.univie.ac.at/LSG/paganini/finals_pdf/WP6_FinalReport.pdf

1007 DTI (2003) GM Nation? The findings of the public debate. http://www.aebc.gov.uk/reports/gm_nation_report_final.pdf

1008 Grove-White R, Macnaughton P, Mayer S, Wynne B (1997) Uncertain world: Genetically Modified Organisms, Food and Public Attitudes in Britain. Lancaster University. March 1997.

1009 Marris C (2000) Swings and roundabouts: French public policy on agricultural GMOs 1996-1999. Centre d'Economie et d'Ethique pour l'Environment et le Development. Cahier No. 00-02 February 2000.

1010 PABE (2001) Public Perceptions of Agricultural Biotechnologies in Europe. Final Report of the PABE research project, funded by the Commission of European Communities. Contract No.: FAIR CT98-3844 (DG12-SSMI). http://csec.lancs.ac.uk/pabe/docs/pabe_finalreport.pdf

1011 Weldon S, Levitt M (2004) Public databases and privat(ized) property. In Arnason,G., Nordal, S. and Arnason, V. (Eds.) Blood and Data: ethical, legal and social aspects of human genetic databases. University of Iceland; Reykjavik.

1012 Levitt M, Weldon S (2005) Public perceptions of the governance of DNA databases. *Critical Public Health*, **15**(4), 311-321.

1013 Watson S (2010) Newborns' DNA routinely harvested for Government biobanks. Infowars.net. 8th February 2010. http://www.prisonplanet.com/newborns-dna-routinely-harvested-for-government-biobanks.html

1014 EC BEPA(2005) The attitudes of citizens of the European Union towards the renewed strategy of Lisbon: Qualitative study. September 2005. http://ec.europa.eu/dgs/policy_advisers/publications/docs/rapport_strategie_de_lisbonne_en.pdf

1015 http://www.sciencehorizons.org.uk

1016 Dialogue by Design (2007) Science Horizons, Strands 1-3: Summary Report. September 2007. http://www.sciencehorizons.org.uk/resources/sciencehorizons_summary_report.pdf

1017 Dialogue by Design (2007) Science Horizons: Deliberative Panel Report. September 2007. http://www.sciencehorizons.org.uk/resources/sciencehorizons_deliberative_panel.pdf

1018 Vanderburg W (2006) Can the university escape from the labyrinth of technology? Part 4: Extending the strategy to medicine, the social sciences, and the university. *Bulletin of Science, Technology & Society*, **26**(3), 204-216.

1019 Lehoux P, Williams-Jones B, Miller F, Urbach D, Tailliez S (2008) What leads to better health care innovation? Arguments for an integrated policy-orientated research agenda. Journal of *Health Services Research and Policy*, **13**(4), 251-254.

1020 Smith K (2005) Changing economic landscape: liberalisation and knowledge infrastructures. *Science and Public Policy*, **32**(5), 339-347.

1021 Sainsbury D (2007) Corrected transcript of oral evidence to be published as HC 113-i. House Of Commons Minutes Of Evidence taken before the Innovation, Universities And Skills Committee. http://www.parliament.the-stationery-office.co.uk/pa/cm200708/cmselect/cmdius/c113-i/c11302.htm

1022 European Science Foundation (2009) Roadmapping science in society: Impact, evaluation and accountability. A meeting for ESF member organisations. Conceptual background. http://www.esf.org/index.php?eID=tx_nawsecuredl&u=0&file=fileadmin/be_user/research_areas/social_sciences/documents/SCSS/Roadmapping%20Science%20in%20Society_Conceptual%20background.pdf&t=1245841199&hash=9eb298cee723b279ec26682ab80f6b20

1023 Sarewitz D (2010) Better all the time. *Nature*, **463**, 607.

1024 Stirling A (1998) On the economics and analysis of diversity. SPRU Electronic Working Papers Series. Paper No. 28. http://www.sussex.ac.uk/Units/spru/publications/imprint/sewps/sewp28/sewp28.pdf

1025 McKelvey M, Bohlin E (2005) Conclusion: Conditions for innovation in biotechnology and telecommunications. Innovation: Management, Policy & Practice, 7(1), 97

1026 http://www.innovation-enterprise.com/archives/vol/7/issue/1/article/1371/conditions-for-innovation-in-biotechnology-and

1027 http://www.foresight.gov.uk/OurWork/ActiveProjects/Obesity/Obesity.asp

1028 King DA, Thomas SA (2007) Big lessons for a healthy future. *Nature*, **449**, 791-792.

1029 Vanderburg WH (2006) Can the university escape from labyrinth of technology? Part 2: Intellectual map-making and the tension between breadth and depth. *Bulletin of Science, Technology and Society*, **26**(3), 178-188.

1030 Vanderburg WH (2006) Can the university escape from labyrinth of technology? Part 3: A strategy from transforming the professions. *Bulletin of Science, Technology and Society*, **26**(3), 189-203.

1031 Vanderburg WH (2006) Can the university escape from labyrinth of technology? Part 1: Rethinking the intellectual and professional division of labor and its knowledge infrastructure. *Bulletin of Science, Technology and Society*, **26**(3), 171-177.

1032 Tomes N (2007) Patient empowerment and the dilemmas of late-modern medicalisation. *The Lancet*, **369**, 698-369.

1033 Fischer F (2005) Are scientists irrational? Risk assessment in practical reason. In: Leach M, Schooones I, Wynne B (2005) Science and citizens. Zed Books.

1034 Biosciences: Challenges and Opportunities for Government. Seminar discussion paper. The Wellcome Trust and the Strategy Unit, Cabinet Office. February 2003.

1035 Mayer S (2003) Science out of step with the public: the need for public accountability of science in the UK. *Science and public policy*, 30(3), 177-181.

1036 Felt U, Wynne B (2007) Science and Governance: Taking European Knowledge Society Seriously. Report of a Working Group of the European Commission Directorate General for Research (EC DG RTD). http://www.bmbf.de/pub/EuropeanKnowledge(6).pdf .

1037 Tallon D, Chard J, Dieppe P (2000) Relation between agendas of the research community and the research consumer. *The Lancet*, **355**, 2037-2040.

1038 MacMillan T (2004) Engaging in innovation: towards an integrated science policy. IPPR. 22nd July 2004. http://www.foodethicscouncil.org/taxonomy/term/33/1?page=1&PHPSESSID=391d36c93fa857d17b8367552f8efd53

1039 MacMillan T, Seshia S (2004) Farming and food research and the public good. July 2004. http://www.foodethicscouncil.org/files/ccelsresearch.pdf

1040 Food Ethics Council (2004) Agri-food research: Participation and the public good. http://www.foodethicscouncil.org/files/agrifoodworkshop.pdf

1041 Weldon, S. (2004) 'Public consent' or 'scientific citizenship'? in Tutton, R & Corrigan, O (Eds), Genetic databases: socio-ethical issues in the collection and use of DNA. Routledge, London.

1042 ITDG (2004) Democratising technology: Reclaiming science for sustainable development. November 2004.

1043 Wilsdon J, Willis R (2004) See-through science: Why public engagement needs to move upstream. August 2004. DEMOS, London.

1044 Wilsdon J, Wynne B, Stilgoe J (2005) The public value of science: Or how to ensure that science really matters. DEMOS, London.

1045 Felt U (rapporteur), Wynne B (chair) (2007) Science and governance: taking European knowledge society seriously. Report of the Expert Group on Science and Governance to the Science, Economy and Society Directorate, Directorate-General for Research, European Commission. http://www.bmbf.de/pub/EuropeanKnowledge(6).pdf

1045 Rogers-Hayden T, Pidgeon N (2007) Moving engagement “upstream”? Nanotechnologies and the Royal Society and Royal Academy of Engineering's inquiry. *Public Understanding of Science*, 16, 345-364.

1046 Stirling A (2005) Opening up or closing down? Analysis , participation and power in the social appraisal of technology, in M. Leach, I. Scoones, B. Wynne, Science, Citizenship and Globalisation, Zed, London.

1047 Murlidhar V (2005) Demystifying occupational and environmental health: experiences from India. In: Leach M, Schoones I, Wynne B (2005) Science and Citizens. Zed Books.

1048 Mauthner NS, Doucet A (2008) 'Knowledge once divided can be hard to put together again': An epistemological critique of collaborative and team-based research practices. *Sociology*, **42**(5), 971-985.

1049 Karner S (2009) Wild-shoot branching of KBE: Alternative Agro-Food Networks (AAFNs). The knowledge based economy: a critical perspective. Workshop, 5.-6. February 2009, Graz, Austria. http://www.ifz.tugraz.at/index.php/article/articleview/1680/1/18/

1050 Visvanathan S (2005) Knowledge, justice and democracy. In: Leach, M, Scoones, I, Wynne (Eds) Science and Citizens. Zed Books.

1051 Public attitudes to science 2008. RCUK. March 2008. http://www.rcuk.ac.uk/sis/pas.htm

1052 Doubleday R, Jasanoff S, Kearnes M, Macnaughten P, Owens S, Stirling A, Wynne B et al. (2008) Open letter to Lord Drayson. Response to the consultation on: A Vision for Science and Society. 16 October 2008.

1053 GeneWatch UK(2008) Response to the DIUS consultation 'A vision for science and society'. October 2008. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/GW_DIUS08.doc

1054 Scots scientists top of the class. Scottish Government Press Release. 4 February 2008. http://www.scotland.gov.uk/News/Releases/2008/02/04085534

1055 Research world leader - First Minister. Scottish Government. Press Release. 29th January 2010. http://www.scotland.gov.uk/News/Releases/2010/01/29115308

1056 Participatory Science and Scientific Participation: The role of Civil Society Organisations in decision-making about novel developments in biotechnologies. November 2008. http://www.participationinscience.eu/psx2/final/PSX2_final%20report.pdf

1057 Mirowski P, Van Horn R (2005) The Contract Research Organisation and the commercialisation of scientific research. *Social Studies of Science*, **35**(4), 503-548.

1058 MacMillan T (2008) Editorial. In: GM foods: the wrong debate? *Food Ethics*, **3**(3), 1.