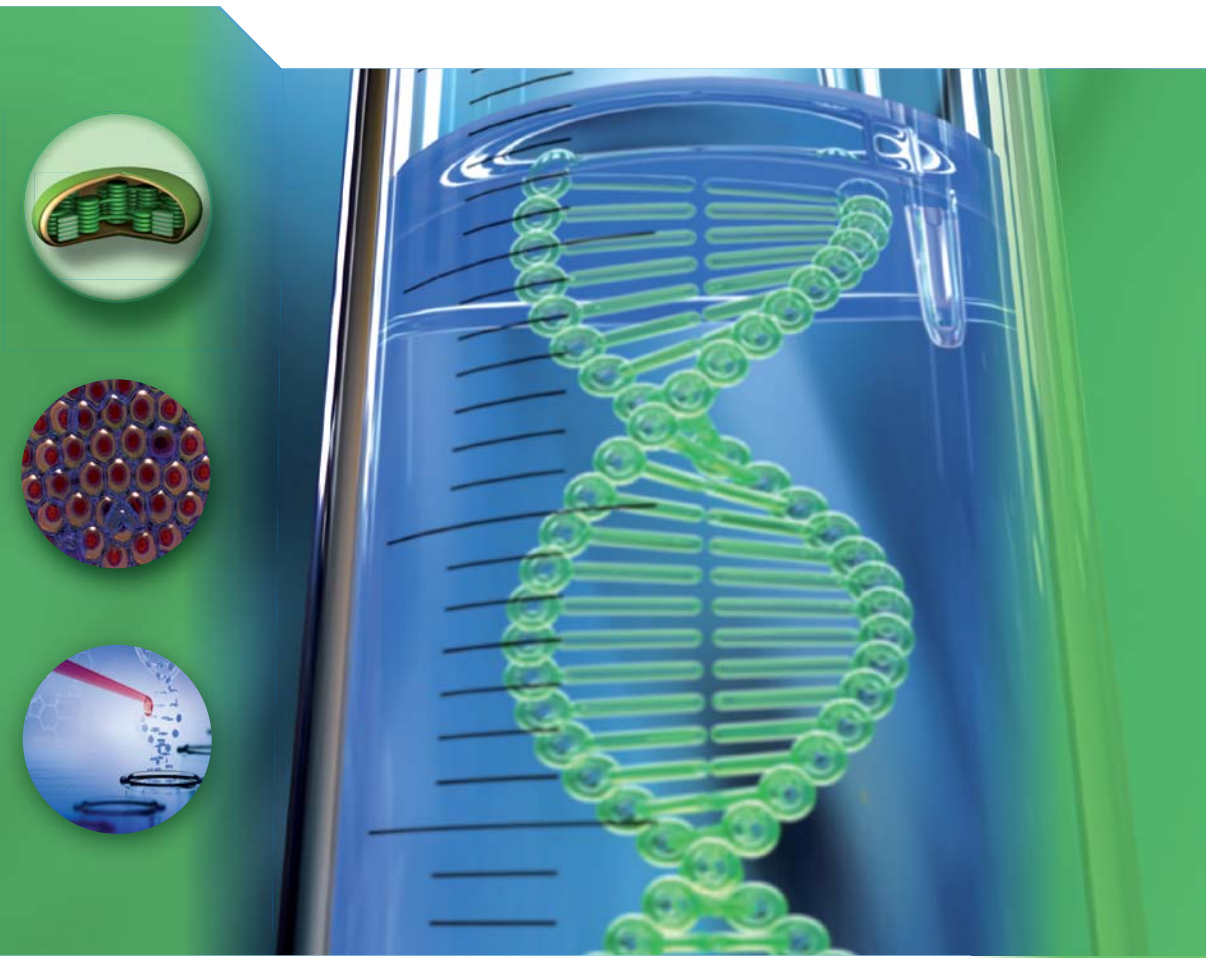
Future Prospects for Industrial Biotechnology



OECD

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Foreword

Industrial biotechnology is a key technology for future economic development. It is the application of biotechnology to the eco-efficient production and processing of chemicals, materials and bio-energy. It utilises the extraordinary capabilities of micro-organisms and enzymes, and their diversity, efficiency and specificity, to make products in sectors such as chemicals, food and feed, pulp and paper, textiles, automotive, electronics and, crucially, energy. Many economies recognise this potential; this was made clear during the 2004 meeting of Science and Technology Ministers of the OECD countries plus China and South Africa.

The outlook for industrial biotechnology is promising owing to the timely convergence of drivers of industrial biotechnology with the unprecedented progress in the biological sciences. The barriers are many, and they have to be tackled through national, regional and internationally harmonised policy.

This report considers the outlook for industrial biotechnology in OECD member countries and some of their key partners. It considers key technological developments and bottlenecks, analyses policy developments at the national and international level, and identifies a number of potential areas of high growth in which policy action may be warranted (*e.g.* bioplastics). Finally, it looks at opportunities to leverage financing for new developments in biotechnology and briefly reviews recent innovations in business strategy.

The report draws on workshops hosted by the Austrian Ministry for Economics, Family and Youth in Vienna on 13-14 January 2010 and by the Russian Federation on 28-29 October 2010 in St. Petersburg, as well as on recent developments in the literature and in industry. Expert oversight of the project was provided by the OECD Task Force on Industrial Biotechnology under the direction of the OECD Working Party on Biotechnology.

The report was drafted by Jim Philp and Iain Gillespie and draws on earlier work by other members of OECD's Biotechnology Unit, including Alexandre Bartsev and Robert Wells, who deserve special thanks.

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Executive summary

Industrial biotechnology is a key technology for future economic development. It is the application of biotechnology to the eco-efficient production and processing of chemicals, materials and bio-energy. It utilises the extraordinary capabilities of micro-organisms and enzymes, their diversity, efficiency and specificity, to make products in sectors such as chemicals, food and feed, pulp and paper, textiles, automotive, electronics and, crucially, energy. Biological processes are generally more environmentally benign than industrial chemical processes as they take place at low temperature and pressure, have lower energy input requirements and lower greenhouse gas (GHG) emissions. Also, the raw materials for production are renewable, agricultural feedstocks.

Many drivers of industrial biotechnology are clearly linked to the global challenges of climate change, energy security and the financial crisis, yet there are still many barriers to its growth and optimal uptake across industry sectors. Technical barriers are not as daunting as they once were, as biology research is maturing rapidly. Progress in DNA sequencing, strides in proteomics, and the emergence of the field of synthetic biology are leading to unprecedented progress in the biological sciences. When allied to fermentation and biochemical engineering, these form a potent set of enabling technologies to drive the commercialisation of industrial biotechnology.

Among the persistent barriers are the very high investment costs required in all areas. Research and development (R&D) is high-risk and costly, pilot and demonstrator plants are needed in order to lower production risks, full-scale production is not well characterised, and getting the agricultural raw materials to the production sites has huge infrastructure implications. Above all there is the need to secure large quantities of biomass and control its costs. Moreover, public awareness varies greatly in different parts of the world, industrial biotechnology could inherit concerns regarding genetic modification in agricultural biotechnology, and there is the issue of land use for non-food crops when the world's population is growing rapidly.

Current global revenues for goods produced using industrial biotechnology are estimated at between EUR 50 billion and EUR 60 billion annually, according to data released by industry trade publications. There are many predictions of future market values. For example, one estimate is that by 2030 the global market for industrial biotechnology could reach roughly EUR 300 billion. Much of the activity now is in biofuels, but there is also an established market for bio-based chemicals. While bioplastics currently have a small market share, new applications are being discovered in a wide range of industries and are being adopted by some of the largest multinational organisations. Much of the success enjoyed by biofuels can be attributed to policy measures, which are varied and can be seen throughout the value chain. Bio-based chemicals and bioplastics do not enjoy such policy commitment at present, but some positive trends are emerging.

The outlook is promising: the convergence of industrial biotechnology drivers with the unprecedented progress in the biological sciences is timely. The barriers are many; they must be tackled by national, regional and internationally harmonised policy.

Chapter 1

Introduction – Scope and drivers for industrial biotechnology

Industrial biotechnology has achieved spectacular new growth and interest in recent years, mainly as a result of global interest in biofuels. This chapter reviews the drivers for this growth spurt. In the United States the interest has mainly derived from the desire for energy independence, and biofuels production has benefited from a wide range of policy support mechanisms, as well as massive public spending. In Europe there has been more interest in maintaining a competitive chemicals industry. Over 70 countries now have bioenergy targets. The drivers vary from stimulation of the rural environment, to concerns over climate change, to fossil fuel price volatility. It is also clear that Asia will have a major role in the future development of industrial biotechnology.

Industrial biotechnology is not a new discipline of the applied biosciences. The idea of using proteases in industry – specifically in detergents – goes back to the use of pancreatic extracts in 1913. Only with the availability of enzymes from bacteria in the 1960s, however, did their use become efficient in the technical as well as in the economic sense. Table 1.1 shows a 2002 view of the development of the use of enzymes in the chemicals industry. By that stage a major hurdle had been overcome – confidence in this relatively new technology was starting to ride high. And in May 2007, Walter Solomon, Vice President and Chief Growth Officer, Ashland Inc., was able to state:

> *"We believe the chemical market has reached a tipping point where bio-based and petroleum-based options are both desired by the market and practical to produce. To be in a position where Ashland can offer bio-based specialty chemical products in the future, we need to help foster the creation of bio-based basic chemicals now."*

Table 1.1. A 2002 view of the impact of enzymes on various sectors

	Impact (estimated)		
Industry	**Today**	**Near future**	**Far future**
Organics			
Food and feed additives	+++	+++	++
Fine chemicals	+	++	+++
Drugs	++	++	++
Plastics materials, synthetics	+	++	++
Soaps, cleaners, personal care products	+	++	++
Inorganics	-	+	+
Miscellaneous (adhesives, pulp, textile, oil processing, wastewater treatment)	+	+	++
Agricultural chemicals (*e.g.* herbicides)	+	+	++

Source: Adapted from Schmid A, Hollmann F, Park JB & Bühler B (2002). The use of enzymes in the chemical industry in Europe. *Current Opinion in Biotechnology* 13, 359-366.

Industrial biotechnology can be seen to have come of age with the huge developments made in the global production of liquid biofuels. Between 2005 and 2010, fuel ethanol production worldwide more than doubled (FO Licht, 2010a), and biodiesel production more than quadrupled (FO Licht, 2010b). The integrated biorefinery able to produce one or several low-volume, high-value bio-based chemicals with a low-value, high-volume liquid transport fuel is set to transform the economics of bio-based chemicals production.

This report covers three distinct sectors: biofuels, bio-based chemicals and bioplastics. It deliberately avoids active pharmaceutical ingredients and agricultural biotechnology products because both these areas have their own highly specialised and established policy regimes and because they are generally regarded separately. They have their own market and economic dynamics and could easily confuse the discussion of the relatively newer industrial biotechnology.

Global drivers

A complex web of factors lies behind the drive for the development of industrial biotechnology from the research bench to full-scale production at the global level. The world's environmental challenges coupled with the global financial crisis have driven a search for economic recovery through more environmentally and socially sustainable growth. This "green growth" challenge is faced by developing and developed countries alike (OECD, 2010).

Environmental and social considerations

The consequences of climate change have necessitated the search for technologies that are less environmentally damaging and have lower greenhouse gas (GHG) emissions. A recent analysis estimates that, world-wide, 1 million mobile phones, 10 million plastic cups, 1 billion plastic bottles, and 10 billion plastic bags are disposed of every day (Ravenstijn, 2010).

Added to the converging economic and environmental dilemmas is the increase in global population and per capita income. It is estimated that the global population will reach approximately 8.3 billion in 2030, with 97% of the growth occurring in developing countries (OECD, 2009). The consequences of such a population rise are obvious: impact on land use and water resources, increased waste and wastewater production, impact on food prices through growing demand.

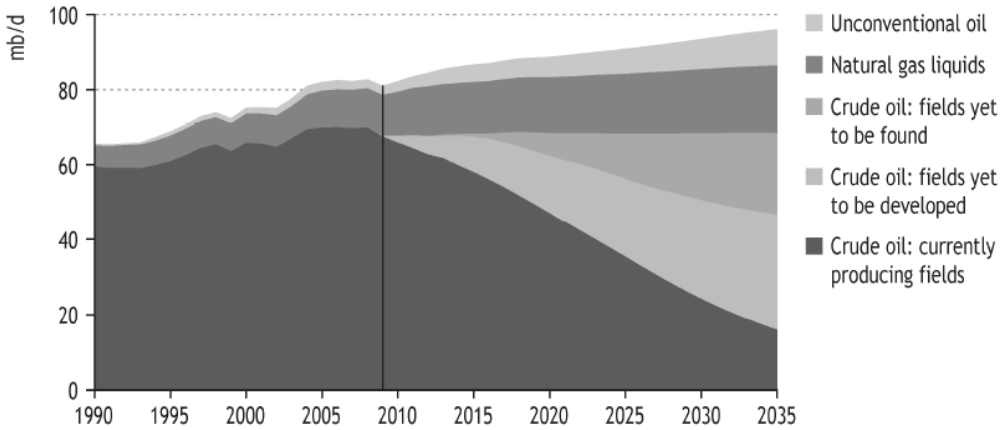
Energy security and independence

In early March 2011 the price of Brent crude hovered around USD 115 per barrel (*The Economist*, 5 March 2011). From the end of 2010 the price of oil had risen by over USD 20 per barrel. The International Monetary Fund (IMF) has calculated that a 10% increase in the price of crude oil shaves 0.2-0.3% off global GDP in one year. A large spike in the price of oil can do great damage. High prices and oil shocks have contributed significantly to historical recessions (Jones *et al.*, 2004). The same dynamic that drove oil prices skyward in 2008 is steadily re-emerging. Supply has not increased

significantly, and demand has increased dramatically (world demand grew by a huge 2.7 million barrels per day in 2010) (Figure 1.1). This price volatility, coupled with the geography of crude oil distribution, has led to the search for energy security and independence. As Paul Bryan, Program Manager, US Department of Energy Biomass Program, noted:

> *"When oil prices are high, it is usually easier to support programs for alternative fuels, but because R&D, and particularly the creation of new infrastructure, requires persistent and consistent effort, the challenge is to maintain the momentum on these initiatives through the periods of lower prices, in order to be better prepared the next time oil prices swing upward."* (cited in Shaw *et al.,* 2011)

Figure 1.1. World oil production by type in the New Policies Scenario



Source: IEA (2010), *World Energy Outlook 2010*.

Global oil production reaches 96 mb/d in 2035 on the back of rising output of natural gas liquids & unconventional oil, as crude oil production plateaus. In the New Policies Scenario, the average IEA crude oil price rises from just over USD 60 in 2009 to USD 113 per barrel (in year-2009 dollars) in 2035. It is likely that much of the crude oil to be found will be more expensive, and increasingly so, as companies explore more remote and dangerous environments.

Ongoing globalisation

Globalisation is acting as a general driver. The challenge from the Asian chemical industry is causing the European Union and the United States to look at industrial biotechnology as a means of sustaining competitiveness. Another aspect of globalisation is that feedstocks and their costs vary across

the globe. For example, feedstocks for biofuel production include sugar cane in Brazil, maize in the United States, wheat in Europe, palm oil in Indonesia. Sub-Sahara Africa has huge feedstock cultivation potential, with less oil-dependent growth.

All this is occurring during a period of unprecedented progress in the key underpinning enabling technologies of the modern biological sciences, such as metagenomics, quantitative proteomics, metabolic engineering and synthetic biology. Combined with novel fermentation and downstream process technology (Villadsen, 2007), these are the engines of progress that will make industrial biotechnology products and processes more efficient and more cost-competitive. The multi-disciplinarity of industrial biotechnology is demonstrated when the essential role of chemical engineering is also considered (*e.g.* process engineering, separation science and traditional thermo-chemical conversion processes).

There are now many examples of industry employing industrial biotechnology products and creating more demand for these and new products. For example, the maturation of bioplastics from the laboratory bench to large-scale production is finding new industry customers, now including the automotive and consumer electronics industries.

Regional drivers

The US top-down approach

There are regional differences in the drivers for the development of industrial biotechnology. The widening ban on the use of the contaminating and potentially carcinogenic MTBE as a gasoline oxygenate necessitates an alternative, and ethanol is gaining share (LoGerfo, 2005). Apart from the use of ethanol as a fuel, its use as a fuel additive is itself a billion-dollar market. But the much larger issue and driving force in the United States is the growing concern over energy security and independence which led the United States to make vast investments in bioethanol development. The US industrial biotechnology drive has been led centrally, initiated by government and/or the administration, with massive public research funding (Lorenz and Zinke, 2005).

A further dimension of the US driving force for industrial biotechnology is regeneration of the rural environment, as huge numbers of agricultural jobs have been lost owing to increased efficiency (USDA, 2010). Over the last 60 years, the share of the US population directly involved in agricultural production has dropped from 15% to less than 2%. However, the average farmer today produces food for 155 people, while his counterpart 60 years ago produced food for only 25.

The EU chemical industry and a bottom-up approach

In the EU the drivers are different. The development of industrial biotechnology in the EU has derived from the desire of the chemical industry to remain competitive. Data for the ten years from 1999 to 2009 indicate that the EU has been the clear leader in terms of world chemical sales, but that it has gradually lost ground to Asia, principally owing to the rise of China. Still, EU exports of chemicals in 2009 accounted for 46% of global chemical exports (Hadhri, 2010). Nonetheless, the threat to its position from Asia is indubitable and is due to high production costs. The role of SusChem, the European Technology Platform for Sustainable Chemistry (*www.suschem.org*), is to enhance the European chemical industry, and industrial biotechnology is one of its key strategic areas. Overall, the EU approach to industrial biotechnology has been bottom-up, motivated by the chemical industry.

In general terms, the United States has focused on biomass-based energy supply and bulk chemicals, whereas the EU has focused more on the manufacture of novel, high-margin products. The EU has also been relatively more concerned with environmental impacts, *e.g.* compliance with the Kyoto protocol. The European Commission (2010) has set out the key demands for sustainable supplies of raw materials, fuels and food, and asserts that in future these must be met through biological means. In the United Kingdom, for example, the potential of industrial biotechnology to meet its sustainability targets was part of the reason why the UK Department of Business, Innovation and Skills (BIS) created the Industrial Biotechnology Innovation and Growth Team. The UK Biotechnology and Biological Sciences Research Council (BBSRC) has produced a five-year strategic plan that identifies industrial biotechnology as one of three high-level strategic priority areas for which investment and leadership will have a significant impact (*Industrial Biotechnology*, 2011 Industry Report).

Germany has for decades been involved in industrial biotechnology and is home to some 40% of Europe's SMEs active in the field (Bug, 2010). A perceived critical factor for success is strategic partnerships, and Germany leads the way in Europe, with a EUR 60 million initiative to support industrial biotechnology clusters (the Federal Ministry for Education and Research's BioIndustry 2021 initiative). A clear driver for Germany is the wish to maintain its chemical industry's market position.

Biomass utilisation in Japan

Japan is developing a national strategy for biotechnology, which it sees as a transformative technology of strategic importance (Lynskey, 2006). In March 2006, the Japanese government renewed the Biomass Nippon Strategy of 2002, approved by the Cabinet to promote biomass utilisation and implement new measures (Kiyoshi, 2006). The 2006 renewal emphasised greater use of transport biofuels and acceleration of the creation of biomass towns, local municipalities with infrastructure for utilising biomass.

In June 2009, after a review of the achievements of the Biomass Nippon Strategy, a basic law on promotion of the utilisation of biomass was enacted so that the government could take more comprehensive, concrete measures to promote biomass use. The basic law established a committee, which released in December 2010 a basic plan to promote biomass utilisation that was consistent with the New Growth Strategy and the Basic Energy Plan approved by the Cabinet in June 2010.

For oil, Japan relies entirely on imports to satisfy its demand. Owing to limited agricultural resources and the food versus fuel debate, Japan is to focus strongly on biofuels derived from cellulosic or other materials which do not compete with food supply (USDA Foreign Agricultural Service, 2009). In 2007, the Executive Committee on the Biomass Nippon Strategy released a report, "Boosting the Production of Biofuels in Japan". The report set a 2030 goal of producing biofuels equivalent to 10% of domestic fuel consumption from cellulosic materials such as rice straw, wood and resource crops such as sugar cane and sugar beet.

The rise of Asia

The Asian chemical industry as a whole has overtaken the EU in terms of sales, and there are good prospects for the use of biofuels as transport fuel in developing countries. Most of these countries face severe energy insecurity and have large agricultural sectors able to support production of biofuels from energy crops (Liaquat *et al.,* 2010). Population and GDP growth and environmental and social pressures in developing countries could be significant drivers for competitiveness in industrial biotechnology. The literature reveals the depth and breadth of industrial biotechnology research and innovation in Asian countries such as China (Zhang *et al*., 2011); India (Gupta *et al*., 2008); Japan (Anazawa, 2010; Sanda *et al*., 2011); Malaysia (Hassan and Yaacob, 2009); Chinese Taipei (Lin *et al*., 2010); Thailand (Hniman *et al*., 2011); Vietnam (Thanh *et al*., 2008).

China will be a world force

China has clearly signalled its intention to be a world force in industrial biotechnology, with a focus on biofuels. Drivers include a long history of expertise in fermentation, a desire for energy security and rapidly increasing energy consumption, volatility of fossil fuel prices, environmental concerns, and providing farmers with an additional income stream to support rural areas (Nesbitt, 2009).

Long-term support for industrial biotechnology is reflected in China's 11th Five-Year Plan (Wang *et al*., 2009), which expects to spend billions of dollars on biofuels and renewable energy. China is the world's third largest producer of ethanol. Existing bio-based production includes vitamin C and citric acid, and the Chinese chemical industry is making increasing use of industrial biotechnology, particularly in biopolymers. China is mapping out a five-year development plan (2011-15) to help further concentrate its bio-industry and raise its international profile. The 12th Five-Year Plan is to have a continuing focus on promotion of innovation and industrialisation of the biotechnology industry (Research and Markets, 2010).

Countries are clearly making progress in how they apply industrial biotechnology in their economies. The OECD follows this progress, and key messages from a follow-up workshop held in St Petersburg in October 2010 (Building an Efficient Bioeconomy through Industrial Biotechnology) are presented in Annex B.

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Chapter 2

Emerging synthetic enabling technologies

Industrial biotechnology cannot grow simply by developing technology for commercial-scale industrial production. Now is a time of unprecedented progress in the life sciences and industrial biotechnology benefits from advances in a range of core technologies in molecular biology, especially high throughput genomics. This approach is being used to investigate microbial life in extreme environments such as deep oceans. Other technologies that can be used to modify and improve genes and enzymes are metabolic engineering and directed evolution. All of these technologies seem to come together in the new discipline of synthetic biology, which, although already a billion dollar business, is in its infancy. Synthetic biology offers the prospect of creating synthetic life forms and enzymes that either make new materials more effectively, or can create completely new products in a single organism that were previously not possible.

Advances in biosciences technology are helping to increase the scope and breadth of industrial biotechnology in the economy. The vast majority of biocatalytic processes employed in industrial production, of which there are over 300, use enzymes of microbial origin. The inability to characterise the biodiversity of bacteria is one of the factors that has held back the development of bacteriology. The so-called "great plate count anomaly" refers to the difference in orders of magnitude between the numbers of cells from natural environments that can be cultured in the laboratory and the numbers countable by microscopic examination (Connon and Giovannoni, 2002).

It is widely accepted that only a fraction of the world's bacteria has been described. The massive potential of industrial biotechnology is enclosed within this diversity, but the plethora of as yet undiscovered bacteria and their enzymes cannot by themselves lead to the major breakthroughs required. Naturally occurring enzymes often cannot cope optimally with the industrial requirements of high activity, specificity and stability under potentially stressful process conditions, such as high pH (Zhao *et al*., 2002). Genetic modification is routinely required to make bioprocesses viable at the industrial scale.

The techniques of molecular biology that are helping to unlock the potential of industrial biotechnology can be broadly classed as discovery and modification, or optimisation, techniques. The combination is exceptionally potent, especially if untapped extreme environments can be harnessed. Extreme environments are important sources of new biological resources as they contain life forms that have not been described in other places. For example the isolation of bacteria at high temperature and pressure may be a rich source of enzymes that work better under industrial process conditions (see below).

Discovery technologies

The great plate count anomaly cannot be overcome simply by improvements in culture techniques, but has come to rely more on "–omics" technologies. Donachie *et al*. (2007) argued that strategies combining both high throughput culture and molecular biology are required before the full extent of microbial diversity can be understood.

Genomics and metagenomics

According to Lorenz and Eck (2005), "Metagenomics, together with *in vitro* evolution and high-throughput screening technologies, provides industry with an unprecedented chance to bring biomolecules into industrial application." In particular, metagenomics is unravelling the unknowns of

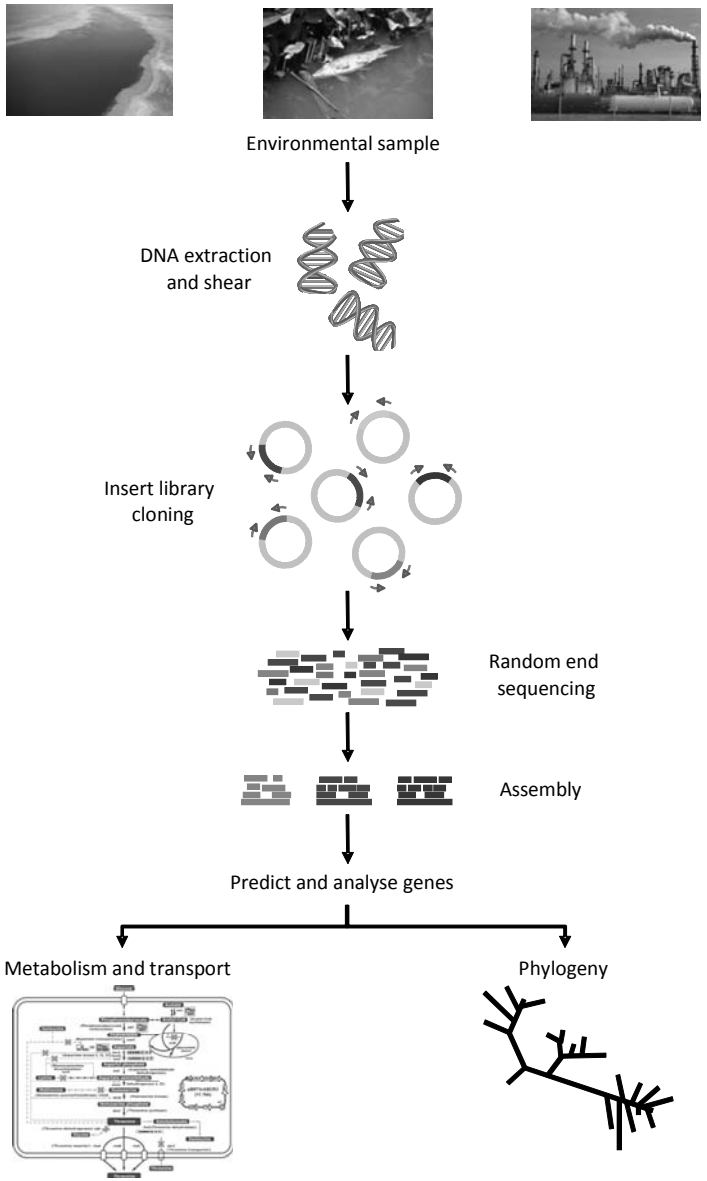
bacterial diversity. It enables the study of uncultured microbes by sequencing the entire community in an environmental sample (Figure 2.1) rather than an individual organism. This has many applications beyond the long-sought understanding of which microbes are present in a community. The treasure chests of bacterial diversity – soil (*e.g.* Daniel, 2004), the deeper subsurface (Vasconcellos *et al.*, 2010) and the marine environment (*e.g.* Worden *et al.*, 2006) – have begun to be investigated in this manner. Second-generation sequencing has greatly enabled the capability of metagenomics, but all of the various technologies have their limitations. Third-generation sequencing, which is capable of long-sequence reading without amplification, is now at an advanced stage of development (Wooley *et al.*, 2010).

The effort to bring the cost of high-quality human genome sequencing down to USD 1 000 or less began in 2004. At the time of the Human Genome Project, a high-quality draft of a human genome cost around USD 10 million. It seems inevitable that USD 1 000 genome sequencing technology will be available in the near future.

Despite the breakthroughs of metagenomic analysis drawn from clone libraries, the technique is somewhat cumbersome and has flaws that limit its ability to uncover all the microbial diversity in a sample. It requires PCR [polymerase chain reaction] amplification, which is known to introduce bias (*e.g.* Sipos *et al.*, 2007). Additionally, many deficits exist in the expression of genes in *E. coli* and other expression vector libraries (Ferrer *et al.*, 2007), and metagenomic communities dominated by archaea, for example, may be seriously underestimated in terms of diversity. Hong *et al.* (2009) estimated that typical rRNA environmental gene surveys miss a significant amount – around 50% – of microbial diversity.

The introduction of new sequencing technologies such as pyrosequencing removes some of the bias (Mardis, 2008). Pyrosequencing has resulted in several successful metagenomic studies (*e.g.* Petrosino *et al.*, 2009). Single molecule sequencing is a novel approach that simplifies the DNA sample preparation process and avoids many biases and errors. At the single-molecule level, metagenomics will be able to give more accurate assessments with poorer samples (Blow, 2008). For the metagenomics community this next-next-generation promises higher throughput, lower costs and better quantitation of genes. If it becomes the standard in metagenomic studies, the bottleneck will be in bioinformatic analysis, not sequence acquisition.

Figure 2.1. A typical clone library metagenomic analysis



Note: The DNA from an entire sample is isolated and stored in fragments in "libraries".

Source: Modified from: *http://legacy.camera.calit2.net/images/figure_map.jpg*

Precision proteomics and high throughput protein analysis

Proteomics lags far behind genomics technically because of the complexity of protein molecules compared to the relatively simple DNA polymer. This has left protein biochemistry in the low throughput, pre-genomic era (Maerkl, 2011). The challenge of expressing thousands of full-length proteins and immobilising them in a native state on a chip (in a manner similar to DNA arrays) is daunting. As a result protein arrays have played a limited role. The best hope for converting proteomics into a high throughput practice comes from recent advances in mass spectrometry. Precision proteomics (Mann and Kelleher, 2008), a combination of high mass accuracy and high mass resolving power, is becoming a reality as a result of such advances. The new precision proteomics can now identify and quantify almost all peptides, but the technology and know-how are currently limited to a very few specialist laboratories. The challenge in the next few years is to roll out the level of performance to other laboratories.

Indeed protein biochemistry in general has lagged behind DNA-based technologies. The lack of simple and scalable methods such as digestion, ligation and amplification has meant that a great deal of time and effort is required to characterise proteins and elucidate their functions. A range of promising technologies to overcome these difficulties has started to emerge (Maerkl, 2011), but to date only one of these can be considered high throughput (Maerkl and Quake, 2007).

Modification/optimisation technologies

Microbial diversity does not necessarily rely on nature alone, as it is possible to generate further diversity through genetic intervention. This is particularly important for production-scale industrial biotechnology, as natural microbes or enzymes may not be suited to the necessary conditions, such as high substrate concentrations. The solution is to achieve such conditions by creating the required characteristics and expressing them stably in a production strain.

Metabolic engineering

Metabolic engineering is the practice of optimising genetic and regulatory processes within cells through rational alteration to increase the production of a certain substance. Conventionally, the first step in the rational alteration process is to identify the rate-limiting step in a given metabolic process (Vemuri and Aristidou, 2005). Overcoming bottlenecks has involved either over-expressing the gene(s) responsible for affecting the rate-limiting step(s) or inactivating the inefficient pathway(s) that help to form by-products (and thus channel resources away from delivering the

intended end product). This approach has enjoyed some success, but the focus of metabolic engineering is shifting towards engineering the regulatory control mechanisms, as these counteract the genetic mutation by employing alternative pathways to achieve continued robust performance. This is an altogether more difficult approach which is still being developed.

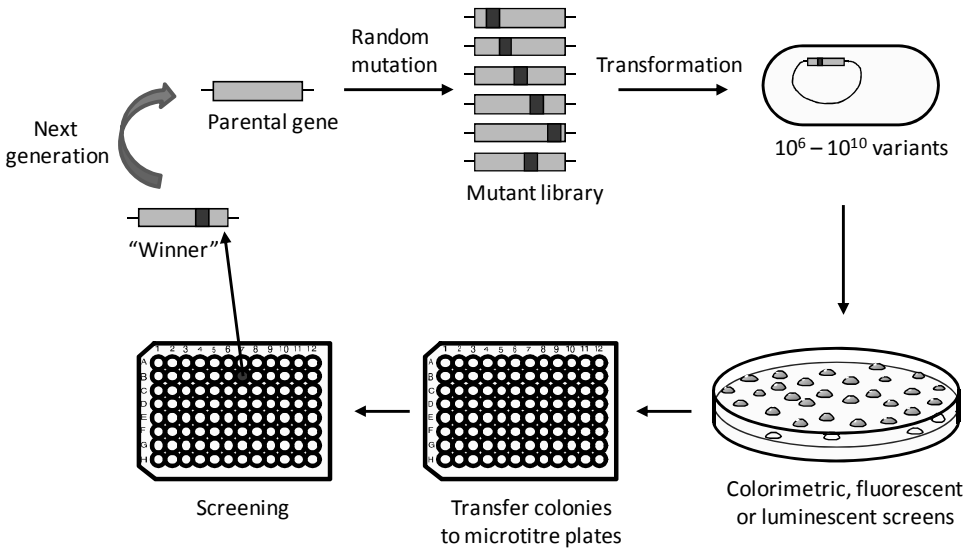
Mannheimia succiniciproducens, MBEL55E, is a naturally occurring bacterium that over-produces succinic acid, a very promising bio-based platform chemical. However, concomitant production of metabolic by-products, such as acetic, formic and lactic acids, is a problem because it reduces the succinic acid yield and makes the purification process difficult and costly. Metabolic engineering by Lee *et al*. (2006) led to near-complete elimination of the common fermentation by-products, with a highly significant increase in succinic acid yield.

Directed evolution

Directed evolution (Figure 2.2) involves the generation and selection of molecular diversity in the gene encoding the protein of interest. The generation is carried out using various random mutagenesis and/or gene recombination methods, and selection of functionally improved variants is then achieved by a high throughput screening step (Zhao *et al*., 2002). The desired variants are then amplified many-fold; this allows the sequencing of the DNA and then it is possible to understand what mutations have occurred. This constitutes one "round" of evolution and results in the "parents" for the next round of evolution. A considerable advantage of the directed evolution approach over, say, metabolic engineering, is that the researcher need not understand the mechanism of the desired activity in order to improve it. The application of robotic technology to directed evolution has allowed its commercialisation, *e.g.* Verenium has commercialised its DirectEvolution technology, which combines discovery with laboratory evolution to develop robust, novel, high-performance enzymes (*www.verenium.com/Ver_Packet/Verenium_Corporate_Fact_Sheet.pdf*).

Within just a decade, directed evolution has emerged as a standard methodology in protein engineering and can therefore be used in combination with rational protein design to meet the demand for industrially applicable biocatalysts that exhibit the desired selectivity and also withstand process conditions *i.e.* high substrate concentrations, solvents, temperatures, long-term stability (Böttcher and Bornscheuer, 2010).

Figure 2.2. The directed evolution process



Synthetic biology brings all the elements together

Synthetic biology takes molecular biology beyond the realm of understanding how biological processes work into designing new processes. Put simply, it is the step from reading the genetic code to writing it (Newman *et al*., 2010). Many see synthetic biology as an engineering discipline. For example, the Registry of Standard Biological Parts, created at MIT, is "a continuously growing collection of genetic parts that can be mixed and matched to build synthetic biology devices and systems" (*http://partsregistry.org/Main_Page*). The registry contains a catalogue of biological parts and devices that shares some terminology with electronics, and there is much reference in the literature to "genetic circuitry". Quite clearly, biology is entering a new era with a focus on products. The implications for industrial biotechnology are clear: the construction of new life forms, especially microbes, if stable in large-scale fermentation processes, is a way to avoid problems such as unwanted by-products and process instability. It could even simplify the downstream processing steps in a bioprocess which frequently make the overall process uneconomical, so that, with the changes, the process makes economic sense.

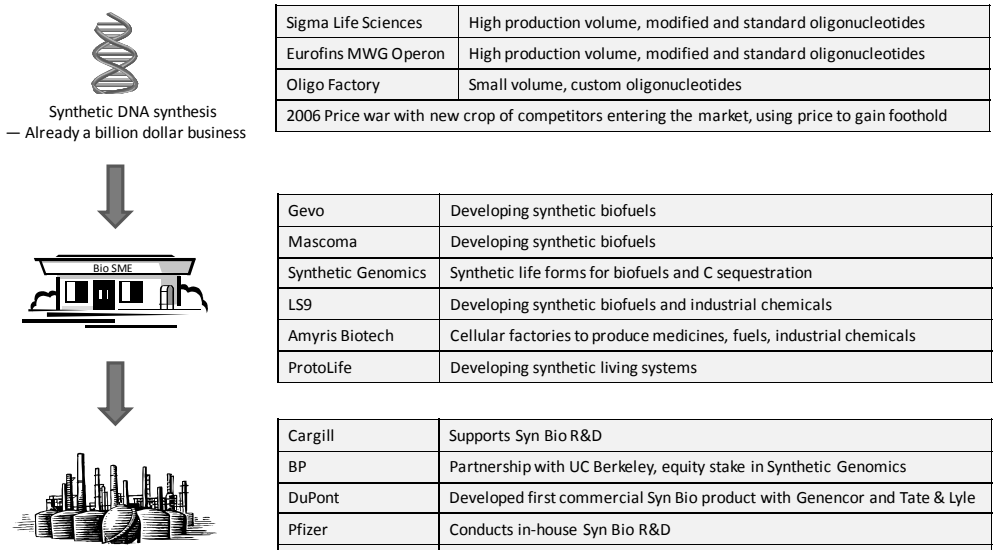
The first self-replicating synthetic bacterium has been constructed (Gibson *et al*., 2010). If the methods described can be generalised, the design, synthesis, assembly and transplantation of synthetic chromosomes will no longer be a barrier to the progress of synthetic biology. Roll-out of

the techniques to other laboratories will lead to a lowering of the cost of DNA synthesis, as has happened with DNA sequencing. Lower synthesis costs combined with automation will enable broad applications for synthetic genomics.

A very good example of the capability of synthetic biology in industrial biotechnology is the design of micro-organisms optimised for the production of bio-hydrogen, which is under development at the J. Craig Venter Institute:

> *"The goal of our research is to develop a microbe that will form the basis for a viable, cost-effective, photobiological process to produce renewable hydrogen fuel. By combining the properties of two micro-organisms — cyanobacteria and photosynthetic bacteria — we hope to develop a novel, hybrid microbe with two highly desirable traits not found together in nature: the ability to produce hydrogen in the presence of oxygen, using water as the feedstock."*
>
> *(www.jcvi.org/cms/research/projects/hydrogen-from-water-in-a-novel-recombinant-cyanobacterial-system/overview/)*

Figure 2.3. The emerging synthetic biology business



Sigma Life Sciences	High production volume, modified and standard oligonucleotides
Eurofins MWG Operon	High production volume, modified and standard oligonucleotides
Oligo Factory	Small volume, custom oligonucleotides
2006 Price war with new crop of competitors entering the market, using price to gain foothold	

Gevo	Developing synthetic biofuels
Mascoma	Developing synthetic biofuels
Synthetic Genomics	Synthetic life forms for biofuels and C sequestration
LS9	Developing synthetic biofuels and industrial chemicals
Amyris Biotech	Cellular factories to produce medicines, fuels, industrial chemicals
ProtoLife	Developing synthetic living systems

Cargill	Supports Syn Bio R&D
BP	Partnership with UC Berkeley, equity stake in Synthetic Genomics
DuPont	Developed first commercial Syn Bio product with Genencor and Tate & Lyle
Pfizer	Conducts in-house Syn Bio R&D
Virgin Group	Investor in Syn Bio

Source: Adapted and modified from Syndustry – The Big Shots of the SynBio World, *www.etcgroup.org/en/node/4799*.

Synthetic biology is in its infancy, but with the convergence of high throughput technologies in molecular biology, its technological development is guaranteed to be rapid. The United States is very much in the lead in this area, and other interested nations and regions will need to invest to catch up. There will follow the need for a dedicated policy space to encompass many issues, such as biosecurity, ethics and public acceptance, industry governance, and the potential for misuse (OECD, 2010).

Figure 2.3 depicts the value chain from the generation of synthetic DNA to full-scale industrial use of synthetic life forms for the production of chemicals, medicines, fuels and polymers as well as for carbon sequestration. The production of synthetic DNA, right at the start of this chain, is already an annual billion dollar business.

The role of extreme environments

Micro-organisms from extreme environments, such as deep, hot oceanic waters, contain extreme enzymes (extremozymes) that are active and/or stable under extreme conditions. As such, they are of great practical significance for industrial applications (Podar and Reysenbach, 2006) as such applications are often non-ambient in terms, for example, of temperature and pressure. But the use of extremophiles is constrained by the inability to culture them on laboratory media. As already described, metagenomics allows this almost untapped resource to be investigated without the need for cell culture, and is enabling high throughput discovery of new enzymes (Table 2.1) for industrial bioconversions (Ferrer *et al*., 2007). Genome and metagenome sequencing of extremophiles that have industrial applications in 2007 accounted for 4% of all sequencing projects.

Table 2.1. Some extremozymes discovered by metagenomic studies

Enzyme	Properties		Source
	pHopt	Topt (°C)	
Cellulase	5.5-9.0	40	Soil metagenome
9 Endoglucanases	3.0-11.0	40-60	Cow rumen metagenome
Xylanase	6.0	15-20	Environmental DNA library
Esterase	10.5	55	Deep-sea sediment metagenome
12 Esterases	7.0-11.0	60	Cow rumen metagenome
5 Esterases	8.0-9.0	48-67	Deep-sea metagenome
Polyphenol oxidase	3.5-9.5	60	Cow rumen metagenome
3 S oxygenase reductases	--	75-80	Gold-bearing metagenome

Source: Adapted from Ferrer M, Golyshin O, Beloqui A and Golyshin PN (2007). Mining enzymes from extreme environments. *Current Opinion in Microbiology* 10, 207-214.

In addition to the scientific significance of mining of extremozymes through metagenomics to overcome technical barriers in industrial biotechnology, there are some commercial considerations:

- Discovery of a single enzyme backbone with an entirely new sequence would be useful to avoid infringing intellectual property rights of competitors and would boost competition.

Most industrial metagenomic discoveries reported have been made by small and medium-sized enterprises (SMEs) or academic groups working with larger companies (Lorenz and Eck, 2005). This has helped drive a networked, productive and efficient open-innovation approach to industrial biotechnology R&D, and the translation of that science into production.

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Chapter 3

Trends in industry and products

This chapter examines recent trends in biofuels, bio-based chemicals and bioplastics. There is also some discussion of the future critical role of the integrated biorefinery. Biofuels have, unsurprisingly, dominated industrial biotechnology of late, and is reflected in recent country policies to promote biofuels production. The platform chemicals concept is explored and the platform chemicals that are likely to be important initially in the integrated biorefinery are identified. Bio-based chemicals also cover bulk, fine and specialty chemicals. Recent advances in biodegradable plastics and bio-based plastics have seen the market potential grow quickly as applications far beyond traditional packaging applications have started to emerge. In particular, the emergence of bio-based thermoplastics is set to affect the plastics world significantly, with very steep growth predicted over the next few years. Biofuels have enjoyed a wide range of supportive policy measures, but bio-based chemicals and bioplastics have not.

This chapter looks at recent developments in the liquid biofuels industry and some of the international policy issues involved. A significant development in 2010 was the US volume mandates which also specified the required reductions of greenhouse gas (GHG) emissions for the different categories of these fuels to 2022. In addition, bioplastics production has increased sufficiently to treat them separately from other bio-based chemicals. In future there may be a blurring of the boundaries between bio-based chemicals and biopolymers, as indicated by the production of bio-based ethylene to produce polyethylene.

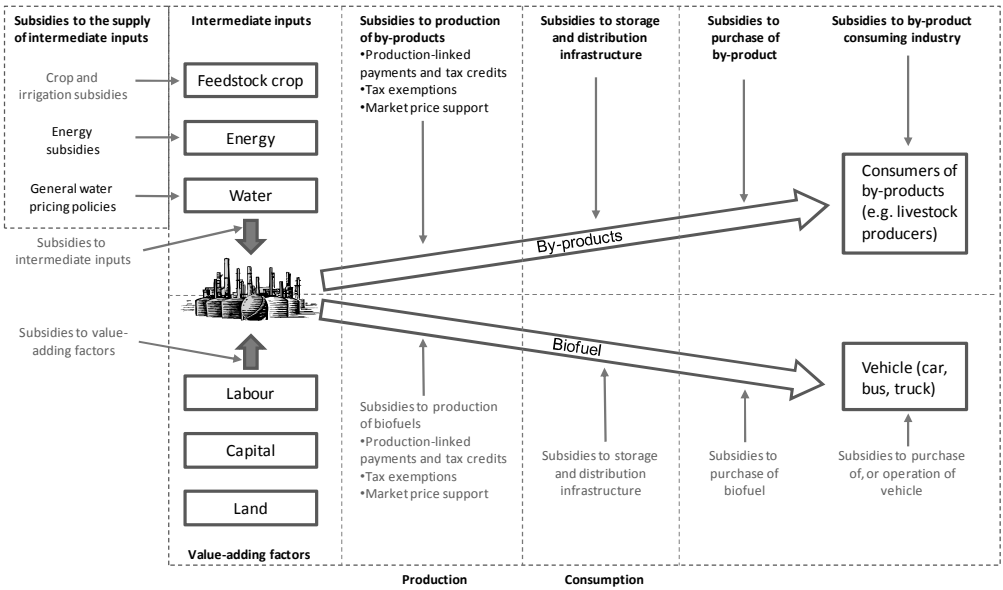
Biofuels

To some extent, biofuels have taken over the industrial biotechnology agenda in recent years. The year 2005 has been regarded as the tipping point for biofuels, when the demand created by drivers such as energy security put biofuels, and arguably industrial biotechnology more generally, high on the policy agenda. As noted by *Industrial Biotechnology – News* (2009), "Assuming an average biorefinery size of 40 million gallons per year, the USDA estimates that meeting the RFS2 advanced biofuels goals will mean the building of 527 biorefineries, at a cost of USD 168 billion". Between 2005 and 2008 the construction of corn ethanol plants in the United States exploded. One of the desired effects was a revitalisation of rural America; to some extent this seems to have happened (Wyse, 2008).

It was not long before controversies arose, such as the debates on sustainability (Goldemberg *et al.,* 2008) and food *vs.* fuel (Zhang *et al.,* 2010; Mueller *et al.,* 2011). Land use is an absolutely central issue in both of these debates (Heinen and Johnson, 2008). Policy and investment interest started to shift to biofuels other than corn-derived ethanol. Soaring oil prices help to maintain interest in biofuels at a high level, and indeed there is evidence that the food price spikes of 2007-08 had more to do with oil prices than with biofuels (Harvey and Pilgrim, 2011).

US policy measures, if successful, will drive the large-scale development of biofuels. In particular the Energy Independence and Security Act (EISA) (2007) and the Farm Bill (2008), which between them set volume mandates, created tax incentives, and provided funding for demonstration plants, will pave the way for very large investments in research and infrastructure and create further rural regeneration while working towards the aim of energy security. In fact, governments can and have intervened at many different points in the value chain for biofuels. Figure 3.1, for example, demonstrates the different points at which subsidies (direct and indirect) can be applied.

Figure 3.1. Different points in the biofuel supply chain to which subsidies can be applied



Source: Steenblik R (2007). Biofuels – at what cost? Government support for ethanol and biodiesel in selected OECD countries. The Global Subsidies Initiative (GSI) of the International Institute for Sustainable Development (IISD).

Biofuel categories

As noted, "biofuels policy" has gone well beyond corn-based ethanol and now applies to a broad range of biofuels. A useful categorisation of existing and future biofuels is as follows (US EPA, 2010):

- *Renewable fuel* refers to bioethanol and biobutanol derived from cornstarch (in terms of the volume mandate, the vast majority is bioethanol from cornstarch, more generally known as first-generation bioethanol).
- *Biomass-based diesel* refers to both biodiesel and renewable diesel from soy oil or waste oils, fats, and greases, as well as biodiesel and renewable diesel produced from algal oils.
- *Advanced biofuels* accommodates ethanol from sugarcane. It complies with the applicable 50% greenhouse gas (GHG) reduction threshold for advanced biofuels.

- *Cellulosic biofuels* refers to cellulosic ethanol and cellulosic diesel. For the EISA volume mandate, this effectively refers to cellulosic ethanol. It is also known as second-generation ethanol.

Potential disruptive technology on the horizon

Much of the effort on the supply side for biofuels currently focuses on overcoming remaining barriers, with "disruptive technologies" receiving much attention. In a study of disruptive technologies in transport fuels conducted by Accenture (Stark *et al*., 2009), "disruptive" was defined as:

- Scalable: potential impact of greater than 20% on hydrocarbon fuel demand by 2030.
- GHG: savings greater than 30% relative to the hydrocarbon it replaces.
- Cost: competitive at an oil price of USD 45 to USD 90 per barrel, at commercial date.
- Time to market: commercialisation in less than five years.

Production of algal biofuels in particular has the potential to be disruptive due to the potentially very high yields (Table 3.1).

Table 3.1. Yields of oil from various crops, compared with the potential of algae

Crop	Oil yield (gallons/acre)
Corn	18
Cotton	35
Soybean	48
Mustard seed	61
Sunflower	102
Rapeseed	127
Jatropha	202
Oil palm	635
Algae	10 000

Source: Pienkos PT (2009). Algal biofuels: ponds and promises. Presented at the 13th Annual Symposium on Industrial and Fermentation, 1 May 2009, NREL/PR-510-45822.

However, of all the technologies Accenture reviewed, algal technology was deemed the most difficult and the one that would take the longest to achieve commercial scale. Nonetheless, some companies claim that the first commercial plants will be available soon. Darzins (2008) indicated that, as of 2008, seven US government laboratories, 30 US universities, and around 60 biofuels companies were conducting research in this area. Intense efforts are also being made in other parts of the world, including Australia, Europe, the Middle East and New Zealand (Pienkos and Darzins, 2009).

Algae are attracting the attention of the oil majors. ExxonMobil has committed to invest USD 600 million in algae research in co-operation with Synthetic Genomics; Chevron has investment in Solazyme; Valero in Solix; Shell in Cellana (now wholly owned by HR BioPetroleum); and BP in Martek. This would indicate that the major oil companies are in algae for the long term.

Joule Unlimited Inc. of the United States is working on a direct algal process that combines an engineered cyanobacterial organism supplemented with a product pathway and secretion system to produce and secrete continuously an alkane diesel product. The process is closed and uses industrial waste CO_2 at concentrations 50-100 times higher than atmospheric (Robertson *et al.*, 2011). If successful this technology has the potential to change the dynamics of biofuel production as it does not require the extraction of fuels from large amounts of biomass.

Outlook for biofuels

The outlook is encouraging. It is being driven mainly by regulatory support (Denis and Oberman, 2010). The global market will likely grow from 25 billion gallons of biofuels a year in 2010, to 65 billion by 2020. Of the anticipated 65 billion gallons, 10-15 billion are expected to be second-generation biofuels.

According to Denis and Oberman, regulation is crucial for ensuring this growth, with 31% of survey respondents naming government mandates as the major driver. Improved energy security was identified as a key driver by 20%, development of affordable fuels by 19%, the need for sustainable fuels by 19% and other drivers by 11%.

However, the biofuels industry faces several major challenges:

- Availability of broader biomass feedstocks at affordable prices: in 2008, the cost of feedstock was quoted as the most significant impediment to the growth of industrial biotechnology (USITC, 2008).

- Next-generation biofuels (lignocellulosic ethanol, biodiesel, bio-butanol) must quickly reach steady-state economics, which requires the industry to think of the whole value chain. The United States has incentives at many points in the chain.
- There must be agreement on a blend wall solution (Carey, 2008), for example, by increasing the ethanol-in-gasoline blend beyond 10%.
- Robust yet practical sustainability standards must be established. In this regard, the industry faces either too few regulations or too many. For an overview on progress to date, O'Connell *et al.* (2009) make specific statements about relevance of biofuel standards to biomaterials.
- Investor confidence must be restored. Lack of capital ranks as the second largest impediment to commercialisation of liquid biofuels or bio-based chemicals.

The importance of government mandates

The US Renewable Fuels Standard (RFS2) (Federal Register, 2010) lays out the strategy and targets for the United States to 2022. It therefore covers current and near-term biofuels development, but also has a provision for the inclusion of new technologies.

The mandated RFS2 goal is to use at least 36 billion gallons of bio-based transport fuels by 2022 (USDA, 2010), of which 15 billion gallons can come from conventional biofuel sources such as corn ethanol, *i.e*. the renewable fuel category. Of the remaining 21 billion gallons of advanced biofuels needed to achieve the total 36 billion gallon goal, 16 billion gallons must come from advanced cellulosic biofuels (fuels made from cellulosic feedstocks that reduce greenhouse gas emissions by at least 60% relative to gasoline), and biomass-based diesel must contribute no less than 1 billion gallons. An additional 4 billion gallons are to come from advanced biofuels. In all, the mandate will displace about 14% of the motor gasoline demand in 2022.

The US EPA projects that by 2022 15 billion gallons of conventional biofuels could come from the current or planned production capacity of cornstarch ethanol. The US biofuels industry is on track to produce 1 billion gallons of biodiesel by 2022. The greatest challenge is to meet the volume mandate for cellulosic fuels. The intention is to develop strategic partnerships with the private sector to expedite the development and deployment of research, development and demonstration projects, facilitate the siting of biorefineries, and identify potential barriers to meeting transport and distri-

bution needs for an advanced biofuels industry. Without doubt, this is the most difficult volume mandate to meet by 2022.

Assuming an average biorefinery size of 40 million gallons a year, the USDA estimates that meeting the RFS2 advanced biofuels goals will mean building 527 biorefineries, at a cost of USD 168 billion. The infrastructural implications seem daunting, but the USDA expects the market to react to this need (USDA, 2010).

An interesting policy aspect of EISA 2007 and the volume mandates is the inclusion of targets on the lifecycle analysis (LCA) of these different types of biofuels. Standardisation and LCA are policy areas that are ripe for more detailed study. For each renewable fuel pathway, GHG emissions were evaluated over the full lifecycle, including production and transport of the feedstock; land use change; production, distribution and blending of the renewable fuel; and end use of the renewable fuel. The GHG emissions were then compared to the lifecycle emissions of 2005 petroleum baseline fuels (base year established as 2005 by EISA) displaced by the renewable fuel, such as gasoline or diesel. The thresholds are specified in Table 3.2. This is significant because it is the first time that lifecycle emissions reduction has become a legal requirement.

Table 3.2. Greenhouse gas thresholds as specified in EISA

Percentage of reduction from 2005 baseline

Fuel	GHG threshold as specified in EISA
Renewable fuel	20%
Advanced biofuel	50%
Biomass-based diesel	50%
Cellulosic biofuel	60%

Source: US EPA (2009). EPA proposes new regulations for the national renewable fuel standard program for 2010 and beyond. EPA-420-F-09-023, May.

To achieve the 36 billion gallons of renewable biofuels by 2022, the USDA concluded that:

- A rapid build-up in production capabilities is needed to meet the targets for cellulosic biofuels.
- The monetary investment for biorefineries is substantial. Second-generation biofuels may imply a very high capital cost, perhaps over five times that of similar capacity starch ethanol plants (Wright and Brown, 2007).

- It is important to consider both sides of the market – the production/ supply side and demand/consumption side – and how they respond to the RFS2 mandate.
- Current infrastructure needs, in the form of blender pumps and rail and trucking infrastructure, even the construction of dedicated pipelines, are in varying stages of being addressed by the market.
- The US farm sector is capable of producing a diverse complement of feedstocks to make the biofuels industry a truly national effort.
- A process for identifying bottlenecks and barriers related to locating biorefineries, involving the federal government, Congress, states, the industry and interested stakeholders, can help facilitate a biorefinery system that is national in scope.

Table 3.3 shows the support given to the construction of major biofuels facilities by the US Department of Energy (DoE), as published at the end of 2009. The USDA has also been instrumental in funding many necessary aspects of biofuels and other bio-based materials development in the United States *e.g.* basic and applied research, incentives to promote the production of biomass, loan guarantees and grants to support development of processing facilities for bioproducts, importantly including biofuels.

Table 3.3. US Department of Energy grants for biorefineries announced at end of 2009

Grantee	DoE grant (USD millions)	Non-federal (USD millions)	Location (state)	Description
Pilot scale				
Algenol Biofuels	25	33.915	TX	Ethanol from CO_2 and seawater, 100 000 gallons fuel-grade ethanol per year.
American Process	17.944	10.148	MI	890 000 gallons ethanol and 690 000 gallons potassium acetate per year.
Amrys Biotechnologies	25	10.489	CA	Diesel substitute from sorghum fermentation, co-products lubricants, polymers and other petrochem substitutes.
Archer Daniel Midland	24.834	10.946	IL	Acid treatment of biomass to make liquid fuels. Will also make ethyl acrylate.
Clearfuels Tech	23	13.433	CO	Diesel and jet fuel from woody biomass.
Elevance Renewable Sciences	2.5	0.625	IA	Preliminary engineering design for a future facility producing jet fuel, renewable diesel and high value chemicals

Grantee	DoE grant (USD millions)	Non-federal (USD millions)	Location (state)	Description
Gas Technology Institute	2.5	0.625	Il	Preliminary engineering design for green gasoline and diesel from woody biomass, agricultural residues and algae.
Haldor Topsoe	25	9.701	Il	Convert wood to green gasoline through gasification, 21 tons feedstock per day.
ICM	25	6.268	MO	Modify ethanol plant to produce cellulosic ethanol from switchgrass and sorghum.
Logos Technologies	20.445	5.113	CA	Convert switchgrass and woody biomass to ethanol by biochemical process.
Renewable Energy Institute	19.980	5.116	OH	Green diesel from agricultural and forest residues, 25 tons of feedstock per day.
Solazyme	21.765	3.857	PA	Validate economics of commercial-scale production of advanced biofuels, algal oil that can be converted to oil-based fuels.
UOP LLC	25	6.685	HI	Green gasoline, diesel, jet fuel from agricultural residue, woody biomass, algae.
ZeaChem	25	48.4	OR	Hybrid poplar trees for fuel-grade ethanol.
Demonstration scale				
BioEnergy International LLC	50	89.589	LA	Succinic acid from sorghum.
Enerkem Corp	50	90.470	MS	Woody biomass and municipal solid waste (MSW) biomass for ethanol and green chemicals
INES New Planet Energy LLC	50	50	FL	Ethanol and electricity from wood and vegetable residues, 8 million gallons ethanol and 2 megawatts electricity per year.
Sapphire Energy	50	85.064	NM	Algae in ponds to convert to green fuels.
Increased funding to existing biorefinery projects				
Bluefire LLC	81.134	223.227	MS	Ethanol from woody biomass, mill residues and sorted MSW.

Source: Adapted from Industrial Biotechnology (2009). December 2009, 5(4): 193-205, *http://dx.doi.org/10.1089/ind.2009.5.193*

Tariffs and other trade barriers

Most countries producing ethanol apply a most-favoured nation (MFN) tariff that adds at least 25%, or USD 0.13 per litre, to the cost of imported ethanol. Some tariffs, such as the EU's for denatured alcohol, can add 50% to the import cost. Mandating increasing levels of biofuels in national transport fuel mixes, while maintaining such barriers to cheaper imports, may inhibit the growth and development of developing countries, many of which have a comparative advantage in production of biofuels compared with most OECD members (Steenblik, 2007).

Subsidies

Although subsidies are generally thought of as cash payments to a particular company or an individual, this simple definition misses many of the other means that governments use to assist the biofuels industry (Doornbosch and Steenblik, 2007). A wide range of policies, including special reductions, privileged tax advantages and relatively low insurance requirements are used to provide benefits to specific groups (OECD, 2007).

The Global Subsidies Initiative has developed a framework to examine support levels at different points in the supply chain for biofuels, from the production of feedstocks to final consumers. At the beginning of the supply chain are subsidies to intermediate inputs. In several countries, the largest of these are subsidies to producers of feedstock crops used to make biofuels. Further down the chain are subsidies directly linked to output; these include the protection from foreign competition provided by import tariffs on ethanol and biodiesel; exemptions from fuel excise taxes; and grants or tax credits based on the volume produced, sold or blended. For a more comprehensive discussion of the wide range of subsidy-based policy instruments, see Doornbosch and Steenblik (2007).

National bio-energy policies and activities

In addition to the US policies that have led to the rapid and marked expansion of the biofuels industry in that country, many others have biofuel policies in place or in formulation. REN21, the Renewable Energy Policy Network for the 21st Century, reported that 73 countries (many of them developing countries) had bioenergy targets as of early 2009 (REN21, 2009). Some of the following draws heavily on a recent paper on the subject (Wonglimpiyarat, 2010).

Australia

As Australia eyes a USD 25 billion trade deficit in petroleum products by 2015, the federal government is providing AUD 20 million from the Australian Centre for Renewable Energy (ACRE) to establish an Australian Biofuels Research Institute. This builds on other support for alternative fuels including the AUD 15 million Second Generation Biofuels Research and Development Program (GEN2) through ACRE. These programmes are part of the government's AUD 5 billion Clean Energy Initiative which supports the development of clean energy and energy efficiency technologies. The government has also provided AUD 11 million for the development of biomass conversion capabilities in five facilities, as part of the National Collaborative Research Infrastructure Strategy.

Brazil

In the 1970s oil shock, the Brazilian government introduced fuel ethanol to reduce oil consumption. In 1975 it launched the national alcohol programme PróÁlcool. Soaring oil prices put Brazil at the forefront of the biofuel movement. Brazil subsidised biofuel during market development until economies of scale allowed fair competition with oil products. Fuel ethanol production was 22.5 million kl (kilolitres) in 2007. By 2004, ethanol in Brazil had become economically competitive with gasoline based on international prices for oil (equivalent to USD 40 per barrel) (Goldemberg, 2008). At these costs, the production of ethanol from sugarcane is much cheaper that from crops such as corn, wheat and sugar beet. The Brazilian federal policy on biodiesel is aimed at alleviating rural poverty (stimulating rural activities to increase employment in rural areas). It is an interesting historical note that energy security was the main driver at the time of the launch of the PróÁlcool programme. At the time climate change had only just started to emerge as a global concern. However, GHG emissions savings has become an additional driver for bioethanol production in Brazil.

Canada

Like the United States, Canada has introduced mandates and subsidy programmes in support of infrastructure for biofuel facilities and ethanol and biodiesel production (*e.g.* the ecoAgriculture Biofuels Capital Initiative and the ecoENERGY for Biofuels programme). Canada has set a national mandate of 5% of renewables, and Ottawa has pledged financial support of CAD 100 million in its Climate Change Plan.

China

As an agricultural country with a population of 1.3 billion, China cannot sacrifice food security for energy. Government policy supports food self-sufficiency for the sake of national security. The Chinese government has therefore clamped down on the use of corn and other edible grains to produce biofuel. However, biofuel production is seen as an essential and strategic component of a secure economy and diversified energy policy. China cultivates jatropha for biodiesel production of 1.76 billion gallons a year and has encouraged the production of biofuel, such as ethanol and methane, from renewable resources in order to reduce dependence on imported oil. In 2005, the National Key R&D Programme included development of cellulosic ethanol and has now set a target of 15% of biofuel in total transport fuels by 2020.

China is establishing industrial parks for chemical R&D. Tianjin Economic-Technological Development Area (TEDA), one of three national demonstration eco-industrial parks (EIPs), has created a complex network based on industrial symbiosis. One of its four pillar industries is biotechnology and pharmaceuticals (Shi *et al*., 2010). High-technology projects for liquid biofuels and bio-based products are funded by the National High-Technology R&D programme. Feedstock prices are regulated, reportedly held below international levels, and sometimes frozen. Support for biofuels includes tax benefits, preferential loans, and assistance for demo-scale plants from non-food feedstocks. Support for bio-based chemicals includes various incentives for profitable and efficient producers, and preferential tax treatment for selected firms in emerging biochemical industries.

China leads efforts to re-commercialise the acetone, butanol, ethanol (ABE) fermentation process for the production of bio-butanol. Over USD 200 million has recently been invested in China to install annual capacity of 0.21 million tonnes of solvent with plans to expand to 1 million tonnes. Six major plants produce about 30 000 tonnes of butanol a year from cornstarch (Green, 2011).

European Union

Europe has many political, environmental and scientific initiatives that involve industrial biotechnology, but they are somewhat uncoordinated. In January 2007, an energy and climate change package proposed to cut greenhouse gas emissions by at least 20% by 2020 (largely through energy measures).

In the early years of EU bioenergy policy, biofuels were supported mainly through Directive 2003/30 (Official Journal of the European Union, 2003). The main objective was to trigger domestic production and consumption in member countries through fiscal stimulus and incentives (Ninni, 2010).

A major EU landmark was the publication of the Renewable Energy Directive (Official Journal of the European Union, 2009), which established a common framework for the promotion of energy from renewable sources. It set mandatory national targets for the overall share of energy from renewable sources in gross final consumption of energy and for the share of energy from renewable sources in transport. It also established sustainability criteria for biofuels and bioliquids. In light of recent research on the risks of biofuels, the European Commission proposed to favour the use of biofuels produced from wastes, residues, non-food cellulosic material, and ligno-cellulosic material over the use of first-generation biofuels (Bringezu *et al*., 2009).

Germany

In 2004 the German government made available a biofuel tax exemption in a bid to reduce CO_2 emissions. It also introduced subsidy programmes which have helped the German biodiesel industry to become a world force. Germany has been the world leader in biodiesel production and use, with about two-fifths of global production and almost half of global consumption in 2006 (Bringezu *et al*., 2009). Biodiesel production capacity in 2007 was 5 million tons. Biodiesel has helped Germany make the transition to the next generation of biofuels; the government aimed to meet the EU's target for biofuel use of 5.75% in 2010.

India

India stands sixth in the world in energy demand and accounts for 3.5% of the world's commercial energy consumption. The transport sector mainly relies on diesel. India has turned to bio-based energy to reduce dependence on imported oils. It has about two-thirds of the world's jatropha plantations and thus leads the way in planting and cultivating jatropha on industrial scale for biodiesel production (600 million gallons a year). It aims to replace 20% of India's diesel consumption with biodiesel by blending petro-diesel with a planned 13 million metric tons of jatropha-based biodiesel by 2013.

Japan

Japan is the world's third-largest oil consumer after the United States and China. Following the oil crises of the 1970s, the Japanese government embarked on national projects to develop alternative energy resources and raise the productivity of bioethanol production. Currently, the government allows oil companies to blend about 3% of ethanol into gasoline. In future, oil companies plan to introduce ethyl tertiary butyl ether (ETBE) mixed gasoline to meet potential demand of approximate 1.8 million kl per year. Japan planned to replace about 500 000 kl (3.14 million barrels) per year of transport fuels with bioethanol by 2010.

Japan is engaged in a mixture of public and private investment and development projects in other countries. In order to help reduce GHG emissions Japan will provide technical assistance to Southeast Asia, in particular to Thailand and Vietnam. Several Japanese trading companies have started to invest in Malaysia and Indonesia to produce biodiesel from palm oil and bioethanol from sugar cane and jatropha. Some Japanese trading companies have shown interest in Brazilian ethanol investments (USDA Foreign Agricultural Service, 2009).

Malaysia

Energy security and rural and economic development drove Malaysian R&D on biodiesel derived from palm oil as early as 1982. It is the world's second largest producer of palm oil. The federal government's National Biofuel Policy was launched in 2005 with a strong focus on biodiesel. The policy aims to reduce the country's fuel import bill, to promote the demand for palm oil, the primary commodity for biofuel production, and to shore up the price of palm oil, especially during periods of low export demand. In Southeast Asia, Malaysia dominates the biodiesel market in terms of production capacity. It planned to mandate the use of biodiesel blend (2% blend) in fossil fuel used for transport in 2008 but postponed biodiesel mandates owing to poor economic conditions.

Thailand

Thailand typifies the developing world's dilemma of sustaining growth while being highly dependent on imports of crude oil (which currently account for more than 10% of GDP) (Siriwardhana *et al.*, 2009). The Thai government has supported power generation using all types of renewable fuel. The development of biodiesel for use in the transport sector is one of the top priorities of the current National Energy Policy and Strategy's efforts to strengthen energy self-reliance. The country plans to have ethanol contribute 10% and biodiesel up to 3% of total fuel consumption in the

transport sector by 2011. A study by Silalertruksa and Gheewala (2010) concluded that to enhance the long-term security of feedstock supply for sustainable bioethanol production in Thailand, policy makers should urgently promote increasing use of sugarcane juice, improved yields of existing feedstocks and production of bioethanol from agricultural residues.

Thailand is also encouraging the use of natural gas, ethanol-blended gasoline and biodiesel for industrial use. It has successfully encouraged the use of 10–20% ethanol blends through adoption of fiscal incentives. The Thai government has introduced E10 and E20 gasohol and subsidised the gasohol price with tax exemption from oil-related taxes.

An added dimension of the globalisation of biofuels is the growing need for internationally recognised standards. A tripartite task force involving Brazil, the European Union and the United States has begun working on establishing an internationally compatible standard for ethanol, in the interest of encouraging international trade (Tripartite Task Force Brazil, European Union and United States of America, 2007). In a White Paper published at the end of 2007, the committee outlined areas in which the fuel standards of the three regions could find common ground. These include the water content of ethanol, pH levels of the ethanol to be traded, and levels of phosphorus and other non-alcohol materials. The committee found that the only substantial difference among the standards was the EU water content requirement. Although the difference may seem small, the EU requirement means that US and Brazilian exporters that wish to send ethanol to Europe must add an additional step to ensure that the fuel they produce meets European standards. This incurs extra time and production costs and hinders the growth of international markets.

Research and development in biofuels

Like industrial biotechnology more generally, R&D and innovation are centrally important to the competitiveness and productivity of biofuels companies. In the United States, probably the most visible area of biofuels research is the development and adoption of cellulosic ethanol, a shift from the use of food crops to non-food crops as feedstock. A number of significant pilot and demonstration plants producing cellulosic ethanol have started operation.

R&D can have very large impacts on the industry. For example, Petrobras of Brazil and Novozymes have entered into an agreement to develop a production process for biofuel from sugarcane bagasse, a fibrous material remaining after sugar cane extraction (*Industrial Biotechnology*, 2010a). The agreement covers the development of enzymes and processes to produce lignocellulosic ethanol by an enzyme process. Bagasse-to-ethanol technology

has the potential to increase Brazil's ethanol production by up to 40% without increasing crop areas. This will allow regional cellulosic ethanol production, getting around the problem of long-distance ethanol transport.

US R&D activities were robust in 2008, but the 2008 USITC survey identified major impediments (Table 3.4). Significantly, over one-quarter of respondents reported that these were severe enough to dissuade them from pursuing any industrial biotechnology R&D activity.

Table 3.4. Impediments to R&D in industrial biotechnology

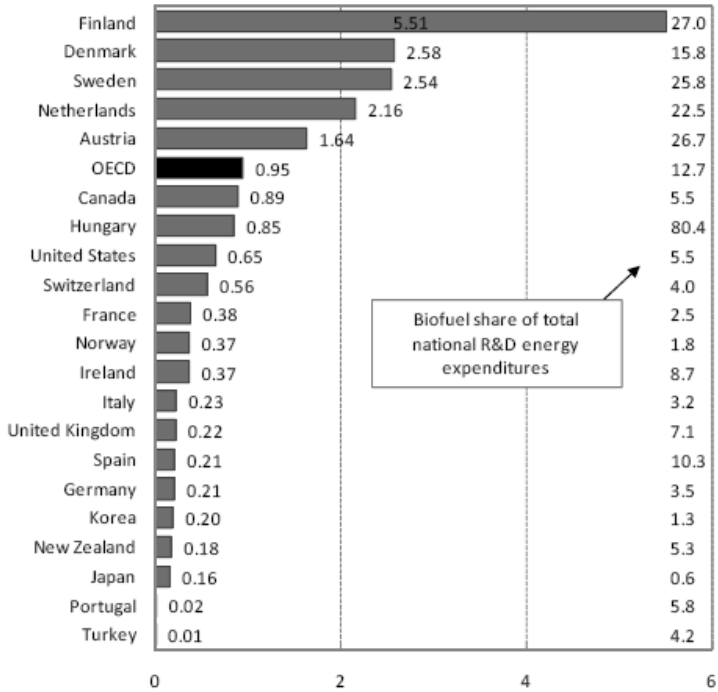
Impediment	Percent responding very significant
Lack of capital (debt or equity)	54
US regulatory requirements	30
Limits of available technology	30
Inability to qualify for federal grants	26
Inability to qualify for state grants	25
Lack of human resources	24
Poor public perception of bio-products	22
Inability to establish alliances	15
Patent barriers	10
Access to university technology	9

Source: Adapted from USITC (2008). Industrial biotechnology: development and adoption by the US chemical and biofuels industries. Investigation no. 332-481. USITC Publication 4020, July.

Far and away the most important impediment to industrial biotechnology R&D is perceived to be finance-related, in terms of lack of capital and of ability to qualify for grants. Given the top-down approach adopted by the United States, it is very likely that the situation is the same in most other parts of the world. For biofuels specifically, and industrial biotechnology more generally, funding of R&D is a global issue.

Although the United States dwarfs other nations in terms of the actual amounts spent on biofuel R&D, it is interesting to note that several Nordic countries rank highest for per capita government spending on such R&D (Figure 3.2); Finland leads the way, followed by Denmark and Sweden. In Finland and Sweden, the forest sector is relatively large and plays a vital role in both the traditional economy and their growing bio-economies.

Figure 3.2. Per capita government budgets for biofuel R&D, 2007



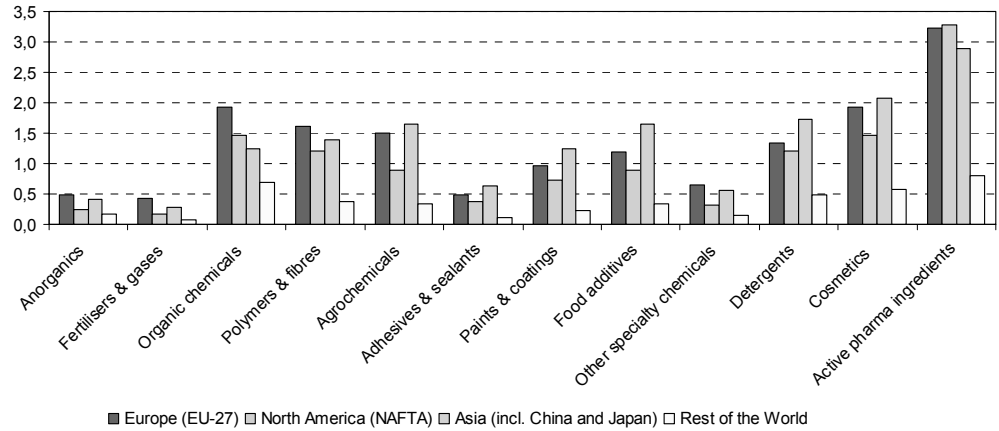
Note: Energy allocation data for Austria, France, Finland and the Netherlands are for 2006.

Source: OECD, based on data from the International Energy Agency, Energy Technology database R&D edition; and OECD, MSTI 2008/1 data for national populations in 2006 (latest available year for all countries), April 2009.

Bio-based chemicals

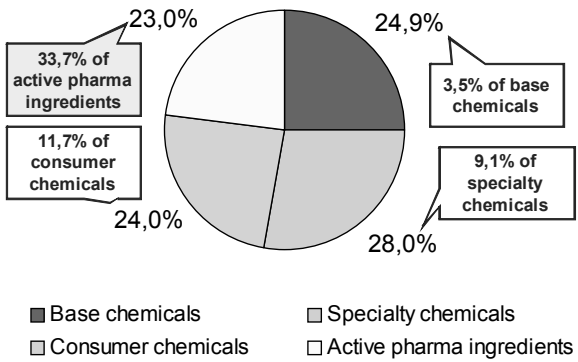
The list of chemicals that could potentially be produced via a bio-route is far too large to be defined at this early stage in the development of the bio-based economy. It is more relevant to look at sales volumes and the types of bio-based chemicals by sub-segments of the chemical industry. Global sales of products made by biotechnology processes in 2007 totalled approximately EUR 48 billion (Figure 3.3) or 3.5% of total chemical sales (excluding pharmaceutical products but including active pharmaceutical ingredients) (Festel, 2010). This approximately concurs with the data of NationMaster (Winters, 2010), which showed that less than 4% of US chemical sales are bio-based. The amount is predicted to increase to EUR 135 billion by 2012 (OECD, 2009). The breakdown by segment is given in Figure 3.4.

Figure 3.3. Biotechnology sales per sub-segment, 2007



Source: Discussion paper, OECD workshop on outlook on industrial biotechnology, Session II on industry structure and business models for industrial biotechnology, January 2010.

Figure 3.4. Bio-based chemical sales by segment, 2012



Source: Discussion paper, OECD workshop on outlook on industrial biotechnology, Session II on industry structure and business models for industrial biotechnology, January 2010.

By 2017, biotechnology sales are projected to have reached EUR 340 billion, with polymers and fibres replacing cosmetics to become the second largest sub-segment in sales behind active pharmaceutical ingredients (Festel, 2010).

Platform chemicals and integrated biorefineries

A platform chemical, as the name implies, is one which is produced in large volumes and is used to produce other chemicals through conversion technologies. It makes sense to identify the platform chemicals that form the basis of large-scale production for at least three reasons:

- Large-scale production will make it possible to create economies of scale. This will improve the competitiveness of biological as compared to petrochemical production.
- For the integrated biorefinery model to work, platform chemicals need to be identified so that the necessary production technology can be built at the refinery site.
- It is likely that production of bio-based chemicals will be driven by biofuel production, as in the case of the oil refinery, as this model offers much higher returns on investment.

Various attempts have been made to define the list of platform chemicals that will be required in the early integrated biorefineries. For example, Werpy and Petersen (2004) made a list for the US DoE of 15 target molecules that could be produced from carbohydrate raw materials. Table 3.5 gives a convenient categorisation of the core chemical products of lignocellulosic biorefineries according to their route of production.

Table 3.5. Platform chemicals that are potential targets for lignocellulosic biorefineries

Class	Chemicals	Production route
Lower alcohols	Methanol, ethanol, 1-butanol, isobutanol	Fermentation or biomass-derived syn gas
Diols	1,2-ethane diol, 1,2-propane diol, 1,3-propane diol	Fermentation or chemo-catalytically
Polyols	Sorbitol, xylitol	Hydrogenation of cellulose and hemicelluloses, respectively
Dicarboxylic acids	Acetic, lactic, succinic, 3-hydroxypropanoic	Fermentation

Source: Adapted from Sheldon RA (2011). Utilisation of biomass for sustainable fuels and chemicals: Molecules, methods and metrics. *Catalysis Today*.

Succinic acid is a very good example for the platform chemical concept. Succinic acid is considered to be an important platform chemical which can be used directly or as an intermediate in the manufacture of paints, plastics, food additives, and other industrial and consumer products (Bechthold *et al*., 2008). It is mainly produced by a chemical process from *n*-butane/butadiene via maleic anhydride, utilising the C4-fraction of naphtha in quantities of about 15 000 tonnes per year. However, fermentation-derived succinate has the potential to supply over 270 000 tonnes of industrial products annually (Zeikus *et al*., 1999). What is more, while ethanol fermentation produces CO_2, succinate fermentation consumes it. This makes bio-succinate production a very green technology.

The divide between commodity chemical and platform chemical is often blurred. For example, bioethanol and other lower alcohols are commodity chemicals for a variety of uses. However, they can also be used as precursors for the production of olefins, thereby creating a direct link to petrochemical refineries. Sheldon also argues that future biorefineries might realistically produce acrylic and methacrylic acids and caprolactam.

One class of chemicals missing from this list is the aromatics. The primary biological source would be the aromatic amino acids, derived from the protein fraction of biomass or produced by fermentation. These could also be a source of some aromatics such as styrene. Alternatively, butadiene produced from bioethanol could be converted to aromatics by known technologies.

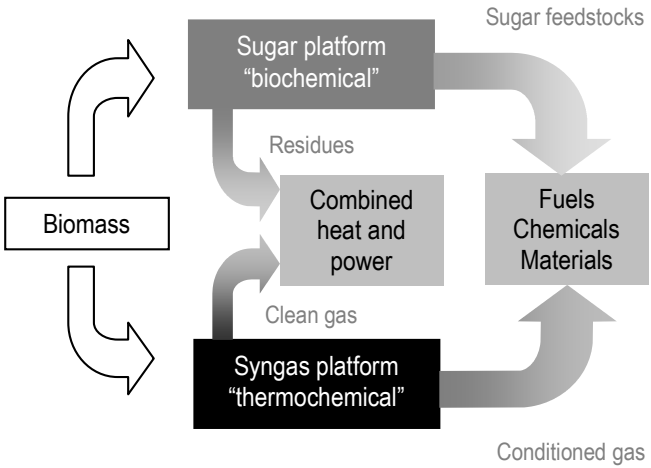
Two very large production commodity platforms not included are bio-based ethylene and propylene, discussed below in terms of their roles in the production of polyethylene and polypropylene. Bio-based ethylene and propylene differ from the platform chemicals in Table 3.5 in that the biological component is bioethanol, from which ethylene (Morschbacker, 2009) and propylene (Sakaki *et al*., 2009) are derived chemically. If such bio-based ethylene and propylene achieve large production status, bioethanol would be the ultimate biological platform chemical. Petrochemically derived ethylene is already the largest production organic chemical globally (Chemical and Engineering News, 2006).

Integrated biorefineries

Integrated biorefineries (Figure 3.5) have to be able to convert efficiently and simultaneously a broad range of industrial biomass feedstocks into affordable biofuels, energy and a wide range of biochemicals and biomaterials. These goals are met by integrating chemical and fuel production within a single operation (Bozell, 2008). In such an operation, high-value products become an economic driver that provides higher margins to support

low-value fuel, leading to a profitable biorefinery operation that also has an energy impact. This is how petrochemical oil refineries are operated: the 7% to 8% of crude oil dedicated to chemical production results in 25% to 35% of the annual profits of integrated petrochemical refineries.

Figure 3.5. An integrated biorefinery concept



Source: www.nrel.gov/biomass/biorefinery.html.

Table 3.6. Biomass sources and primary products in selected second-generation biorefineries in Europe

Location	Country	Biomass	Primary products
Karlsruhe	Germany	Straw	Synthesis gas
Freiberg	Germany	Dry wood, straw	Synthesis gas
Schwedt	Germany	Dry wood, straw	Synthesis gas
Südlohn-Oeding	Germany	Waste edible fats	Biodiesel
Embden	Germany	Waste edible fats	Biodiesel
Kleisthöhe	Germany	Waste edible fats, rapeseed oil	Biodiesel
Güssing	Austria	Wood chips	Producer gas, energy
Lappeenranta	Finland	Bakery, sweet factory waste	Bioethanol
Närpiö	Finland	Potato flake factory sidestream	Bioethanol
Harmina	Finland	Bakery waste	Bioethanol
Pitea	Sweden	Black liquor	DME
Värnamo	Sweden	Wood chips, straw pellets	H_2-rich gas
Schaffhausen	Switzerland	Grass	Gas, technical fibres
Utzenaich	Austria	Grass silage	Gas, technical fibres, proteins

Source: Adapted from Lyko H, Deerberg G and Weidner E (2009). "Coupled production in biorefineries – Combined use of biomass as a source of energy, fuels and materials". *Journal of Biotechnology* 142, 78-86.

However, if integrated biorefineries are to utilise a range of feedstocks efficiently (Table 3.6), this will require significant technology development and financial risk. The construction of biorefinery pilot and demonstration plants is not only costly, it also requires bringing together market actors along new and highly complex value chains. These include the diverse suppliers of biomass raw materials (*e.g.* farmers, forest owners, wood and paper producers, biological waste suppliers, producers of macro- and micro-algae), the industrial plants that convert the raw materials and the industries that provide them with the necessary technologies, and the various end users of intermediate or final products. Another key issue will be the sustainability and security of feedstock supplies.

Countries such as the United States, Brazil, China and others are increasing investments into research, technology development and innovation, and supporting large-scale demonstrators. Europe is behind other world players in this area and concerted action is needed for Europe to reach its 2020 targets. The US DoE is co-financing the commercial demonstration of an integrated bio-refinery system for the production of liquid transport biofuels, bio-based chemicals, substitutes for petroleum-based feedstocks and products, and biomass-based heat/power generation (European Commission, 2011).

Bulk chemicals

The selected bio-based products in Table 3.7 may be good candidates for gaining large market shares of bulk chemicals as their future production costs are expected to be comparatively low, whereas the current production capacity of petrochemical equivalents is high (Dornburg *et al.*, 2008; Hermann and Patel, 2007).

Table 3.7. Selected bio-based chemicals and petrochemical counterparts

Bio-based chemical	Reference petrochemical
Ethyl lactate	Ethyl acetate
Ethylene	Ethylene
Succinic acid	Maleic anhydride
Adipic acid	Adipic acid
Acetic acid	Acetic acid
n-Butanol	*n*-Butanol

Source: Dornburg V, Hermann BG and Patel MK (2008). Scenario projections for future market potentials of bio-based bulk chemicals. *Environmental Science and Technology* 42, 2261-2267.

Medium to high volumes of acetic and adipic acids, ethylene and *n*-butanol are produced from fossil resources, but only low volumes of ethyl lactate and succinic acids. Ethyl lactate is a solvent that could replace ethyl acetate on a large scale, and succinic acid could be used in the production of 1,4-butanediol, polyesters and tetrahydrofuran.

The extent to which these substitutions will occur in future depends on a variety of factors, but the crucial factors are petrochemical feedstock prices and fermentable sugar prices. Both are difficult to predict. Dornburg *et al*. (2008) concluded that to achieve high market potential for bio-based chemicals in Europe technology developments in industrial biotechnology must proceed, biofeedstock prices have to be lower than current sugar prices, and fossil fuel prices must increase. Dornburg *et al*. used a number of scenarios to illustrate their thinking. In the scenario in which all assumptions favour the market potential of bio-based chemicals, the price of fossil fuels is assumed to be USD 83 per barrel from 2020 onwards, an amount already exceeded several times by 2011. They also concluded that in terms of energy use, GHG emissions and land use for feedstock availability, lingo-cellulosics were to be recommended as the basis for producing bulk bio-based chemicals from fermentable sugar.

Fine or specialty chemicals

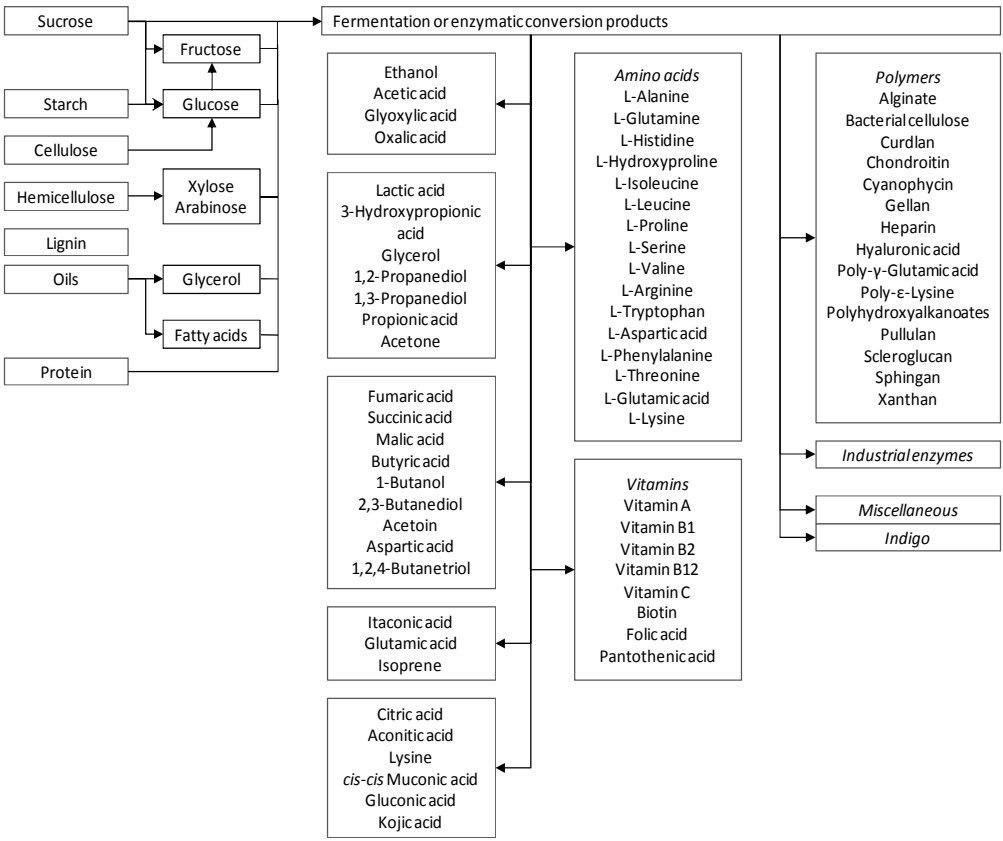
The difference between fine and speciality chemicals has always been hard to define. Here they are treated together. Pollak (2007) defined fine chemicals as "complex, single, pure chemical substances [...] produced in limited quantities (<1 000 metric tons per year) in multi-purpose plants by multistep batch chemical or biotech processes. They are sold for more than USD 10 per kilogram, based on exacting specifications, for further processing within the chemical industry."

Apart from its production volume, riboflavin (vitamin B2) fits the category of fine chemical. Several thousand tons are produced yearly and are consumed mainly as food and feed additives (Hümbelin *et al*., 1999). In recent years a number of producers have developed biotechnological processes to replace the more costly chemical synthesis of the compound. Besides the economic advantage, there are eco-efficiency benefits: the bio-technological process uses renewable sources, is more environmentally friendly and yields a product of equal or superior quality (van Loon *et al*., 1996). Some of these advantages (OECD, 2001; EuropaBio, 2008) have been quantified:

- 40% cost reduction.
- 80% reduction in the use of non-renewable resources.
- 50% reduction of volatile organic compounds.
- 66% reduction in emissions to water.

Figure 3.6 summarises the relationship between the production of platform, bulk and fine chemicals via bio-based routes. It gives an indication of the breadth of the bio-based chemicals market. The potential for bio-based fine and specialty chemicals is substantial if the technology and economics of integrated biorefineries can be perfected.

Figure 3.6. Chemicals obtainable from major biomass constituents by established or potential biotechnological processes



Source: EuropaBio (2009). SME Platform. Access to finance: a call for action. 27 May.

Bio-based chemicals: The policy gap

Biofuels have gained a number of incentives that range from production incentives (such as per gallon tax incentives for the production of biofuels) to loan guarantees and grants for the construction of biofuel biorefineries. However, there is very little in the way of similar incentives for renewable chemicals and bio-based products (Carr *et al*., 2010). Efforts to try to redress the balance have begun. For example, the US trade organisation BIO has been working on a proposal for a production tax incentive for renewable chemicals and bio-based products. According to BIO, existing programmes, such as loan guarantee and grant programmes, should also be open to facilities producing non-fuel bio-based products.

The situation in Europe is similar, in that, in contrast to bioenergy and biofuels, there is currently no equivalent European policy framework to support bio-based materials (Carus *et al*., 2011). Bioenergy and biofuels receive strong support not only for R&D, pilot and demonstration plants, but also during commercial production (quotas, tax incentives, green electricity regulations and more). Without comparable support, there may be under-investment by the private sector in bio-based materials. As bio-based chemicals are important for making integrated biorefineries economical, this appears to be a policy mismatch (see further discussion below).

Bioplastics

It is expected that overall plastics consumption will grow from the current 250 000 kilotonnes a year to about 1 million kilotonnes by the end of this century. Environmental concerns regarding conventional petrochemical plastics are well known: they lack biodegradability and generate high GHG emissions in their manufacture. Also, they are often single-use, light and bulky, and create a disposal problem. In fact, plastics accumulate in the environment at a rate of 25 million tonnes a year (Ojeda *et al*., 2009). Although they are inexpensive to produce, the projected consumption rates raise economic concerns: to meet the 1 million kilotonnes market demand would require about 25% of current oil production. As easily accessed sources of crude oil become difficult to find, competition for its use increases. Therefore, the reasons to search for alternative polymers are not only environmental.

Definition

In the bioplastics field, the term bioplastic, or biopolymer, is not uniformly defined in the literature. This can cause confusion and also has practical implications, for example for labelling and for the likely carbon

footprint of the material, and would be an area for policy analysis. Biopolymers are commonly regarded as biodegradable polymers. The most common definition is a combination of renewable resources and biodegradability (*e.g.* Lee *et al.*, 2003).

An example of a confusing definition is "bioplastics are either biodegradable, have bio-based content or both". When defining bioplastics, the terms biodegradable and bio-based should not be confused. A further potential source of confusion lies in the term oxo-biodegradable. The Oxo-Biodegradable Plastics Association (2010) stated that "oxo-degradation is officially defined as degradation resulting from oxidative cleavage of macromolecules, and oxo-biodegradation as degradation resulting from oxidative and cell-mediated phenomena, either simultaneously or successively". The source of these official definitions was guidance from the European Committee for Standardization (CEN) (2006).

A distinction should be made between biodegradable and bio-based. A material is considered bio-based if it, or part of the raw materials used for its manufacture, is renewable (this can be measured by standard techniques (*e.g.* ASTM D6866-10). For example, on 1 April 2011 it was announced that NatureWorks was approved to use the USDA's product label on its certified bio-based plastics under the department's BioPreferred programme. The bio-based versions of thermoplastics such as polyethylene and polypropylene have the greatest potential for market penetration. However, there is no difference in terms of biodegradability between a plastic that is a bio-polyethylene or a petrochemical polyethylene. To be biocompostable a bioplastic must biodegrade (break down into carbon dioxide, water and biomass); disintegrate (after three months of composting and subsequent sifting through a 2 mm sieve no more than 10% residue remains); and be of low eco-toxicity (the biodegradation must not produce any toxic material and the compost must sustain plant growth). It is important to recognise that compostability, which reduces the product to very small fragments, is not the same as, or as desirable as, biodegradability. Very small fragments of bioplastics tend to be chemically active, can attract other molecules and become toxic. As such they represent a danger to the environment.

Clear messages to policy makers and the general public are essential, and policy interventions need to be based on a clear, widely recognised understanding of the subject matter.

Market potential of bioplastics

Just five petro-polymers dominate the plastics market: low-density polyethylene (LDPE), high-density polyethylene (HDPE), polypropylene (PP), polyvinyl chloride (PVC) and polyethylene terephthalate (PET) make

up about two-thirds of the plastics market. Bio-based versions of some of these are beginning to be produced. The environmental credentials of some of these biopolymers come from either CO_2 capture and/or the fact that its building blocks are derived from renewable sugar rather than non-renewable oil. The genuinely biodegradable biopolymers are usually of microbial or plant origin.

Bioplastics from renewable sources, either biodegradable or non-biodegradable, were still a niche market in 2001, as their material and application development costs were far from competitive. However, in 2003 European consumption, while still a mere 40 000 tons, was double that of 2001 (Schwark, 2009). Data on the market for bioplastics are highly variable. In 2008 a number of market studies predicted that growth rates for the bio-based plastics would be 17% a year through to 2020, with significant upward growth potential. A comprehensive market survey of bioplastics (Ceresana Research, 2009) estimated that during 2000-08, worldwide consumption of biodegradable plastics based on starch, sugar, and cellulose – so far the three most important raw materials – increased by 600%.

According to a survey by Shen *et al.* (2009), the bioplastics industry expects production to grow by an average of 19% a year between 2007 and 2020 to reach production of 3.45 million tonnes annually by 2020. Current growth rates for bioplastics may be of the order of 30%; some companies are reporting 50%. Currently global bioplastics consumption is of the order of 1 000 kilotonnes, a mere 0.4% of total plastics consumption.

COPA (the Committee of Agricultural Organisation in the European Union) and COGEGA (the General Committee for Agricultural Cooperation in the European Union) have made an assessment of the potential of bioplastics in different sectors of the European economy:

- Catering products: 450 000 tonnes a year.
- Organic waste bags: 100 000 tonnes a year.
- Biodegradable mulch foils: 130 000 tonnes a year.
- Biodegradable foils for diapers 80 000 tonnes a year.
- Diapers, 100% biodegradable: 240 000 tonnes a year.
- Foil packaging: 400 000 tonnes a year.
- Vegetable packaging: 400 000 tonnes a year.
- Tyre components: 200 000 tonnes a year.
- A total of 2 million tonnes a year.

This analysis does not take into account recent developments in two large, politically powerful industries with global supply chains: automotive, with its constant need for weight and cost reduction (Pritchard, 2007), and consumer electronics (Ravenstijn, 2010).

For the bioeconomy, perhaps the most important question is the extent to which conventional petro-plastics can ultimately be replaced by bioplastics. Unsurprisingly, a definitive number is hard to find. One study (Shen *et al.,* 2009) estimated that the total *technical* maximum substitution potential of bioplastics for replacing their petrochemical counterparts was 90% of total polymers consumption (including fibres) as of 2007. The USDA has estimated that the upper limit for substitution of petrochemical plastics with bioplastics is 33%. There is however general agreement on the timescale: this will not happen in the near future.

Bioplastics and consumer electronics

Bioplastics have found uses in a variety of components of consumer electronics. They are used in connectors, PC housing, battery packages, chargers, mobile phones, portable music players and keyboards. Nokia and NEC were among the first to be involved in bioplastics, and today big industry names such as Fujitsu, Philips, Siemens and Sony are very active. Moreover, new bio-based polymers are becoming available as the demand for increased performance and new applications increases.

The thermoplastic compounder RTP Company is introducing a line of bioplastic compounds that use resins derived from renewable resources. Its bioplastic compounds contain 20-80% bio-content by weight. Prospective applications include automotive interior and industrial components, semi-durable consumer goods, and housings and enclosures for electronics or business equipment (Reinforced Plastics, 2009).

NEC has introduced a composite resin based on polylactic acid (PLA), a bioplastic, and fibres of the plant *Hibiscus cannabinus*. It is based on 90% biomass, and can be used to replace glass-reinforced polycarbonate in mobile phones (Ravenstijn, 2010). NEC was due to replace up to 10% of its polymer usage with biopolymers by the end of 2010. It has also been working on development of heat-retardant PLA composites for PC housings. In late 2009, it successfully developed and implemented a bioplastic with flame-retardant and processability characteristics that can be used in electronic devices. The new bioplastic includes more than 75% biomass components (polylactic acid, PLA) and can be produced using manufacturing and moulding processes that halve the CO_2 emissions of conventional processes used to make petrochemical-based flame-retardant plastics for use in casings

for electronic goods (*www.nec.com/global/environment/featured/bioplastics/index.html*).

Sony has reported developments in flame-retardant biopolymers for products ranging from portable audio devices, home video/audio units, televisions, mobile phones, camcorders and laptop computers. The Japanese government is supportive of the incorporation of bio-based components in products. Sony is both developing new materials that are environmentally more acceptable and responding to market demand.

In 2010 Fujitsu Siemens announced it would use a bioplastic based on cellulose acetate for the keyboard of a computer product. It is also injection moulding computer keys using blends of polycarbonate and PLA.

Mitsubishi Chemical Company has a fully bio-based plastic that has been successfully developed into functional optical films for flat panel displays. A demonstration plant is under construction with plans later for a commercial plant.

A few years ago these engineering applications of bioplastics and bio-based plastics were unheard of. Innovation is driving bioplastics applications well beyond the simple packaging applications that were once the norm. Notably, durability has become an important characteristic for these bio-based engineering plastic materials. The notions of biodegradability and compostability are undesirable in such applications; recyclability and renewability are more important.

Future outlook

Various predictions of growth in the literature refer to individual segments of the overall area of bio-based product development and market penetration. Table 3.8 presents US predictions of growth across the broad range of bio-based products in the chemical sector as of 2008.

Table 3.8. World bio-based market penetration 2010-25

Chemical sector	2010 (% of market)	2025 (% of market)
Commodity chemicals	1-2	6-10
Specialty chemicals	20-25	45-50
Fine chemicals	20-25	45-50
Polymers	5-10	10-20

Source: USDA (2008). US Bio-based products market potential and projections through 2025. USDA OCE-2008-1, February.

The manifestly different approaches of the United States and EU reflected differences in objectives. In the United States the central issue was energy security. The bio-based economy was declared a national security issue and was driven top-down by government. The Biomass Research and Development Act (2000) set out directions for national energy and agricultural policies to reduce dependence on imported petroleum. This has resulted in massive public spending on research. The results are there to see. The EU approach was based on keeping the EU chemicals sector competitive.

However, the US biofuels strategy has not meant that the chemicals sector has been ignored. Many milestone achievements have been made, *e.g.* Sorona, 1,3-PDO. The developments in chemicals have given the United States a head start, especially in intellectual property, and the potential to outcompete foreign economies.

The Asian chemical industry as a whole has overtaken the EU in terms of sales. The use of biofuels as transport fuel has good prospects in developing countries, most of which face severe energy insecurity and have large agricultural sectors to support production of biofuels from energy crops (Liaquat *et al.*, 2010).

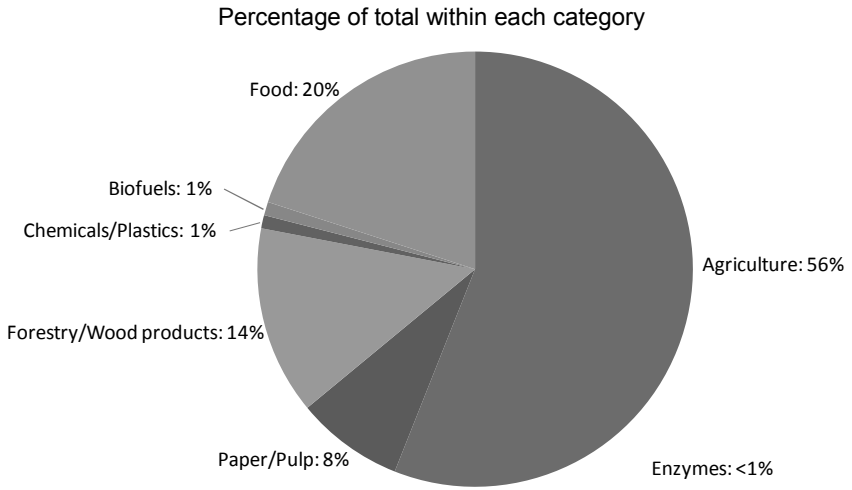
Green jobs

Every new job in the US chemicals industry can lead to 5.5 additional jobs elsewhere in the economy (Bang *et al.,* 2009). This, and recent US biorefinery openings, demonstrate that the current US bio-based products industry is already responsible for more than 40 000 American jobs (Biotechnology Industry Organization, 2010). Federal policy in the United States in support of biofuels has resulted in an additional 240 000 jobs and contributed USD 65 billion to GDP in 2008 (Carr *et al.,* 2010). The Brazilian ethanol programme provided nearly 1 million jobs in 2007, and cut 1975-2002 oil imports by a cumulative undiscounted total of USD 50 billion (Wonglimpiyarat, 2010).

Less than 4% of US chemical sales are bio-based. However, the USDA has projected a potential market share in excess of 20% by 2025 (USDA, 2008). If that growth rate can be achieved and sustained, it would create or save tens of thousands of additional jobs, even in the near term (Industrial Biotechnology, 2010b, Industry Report). Many jobs in the petrochemicals industry have been lost in OECD countries as the industry moved to be closer to the feedstock sources.

In the EU the integrated bioeconomy of 2009 was already worth EUR 2 trillion annually and employs over 21.5 million people (BECOTEPS, 2011). The breakdown of these jobs is instructive from the industrial biotechnology perspective (Figure 3.7).

Figure 3.7. Breakdown of jobs in the EU bioeconomy, 2009



Source: Adapted from BECOTEPS (2011). The European bioeconomy in 2030: Delivering sustainable growth by addressing the grand societal challenges. White paper of BECOTEPS (Bio-Economy Technology Platforms), an EU Framework 7 programme.

Quite clearly, industrial biotechnology still plays a relatively minor role in bioeconomy jobs in Europe. Jobs in enzymes play a small role, although Europe has a clear world lead in this sector, as some 70% of industrial enzymes originate in Europe (Potočnik, 2008).

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Chapter 4

Current high-visibility industrial biotechnology products

It has often been said that one of the reasons why investors are reluctant to invest in industrial biotechnology is the lack of tangible products and "blockbusters". This chapter describes some of the recent products that are emerging from industrial biotechnology. One of these has been predicted to be the first industrial biotechnology blockbuster in terms of sales. As the products become more visible, the investor climate should improve. It is worth noting that many of the products are components of everyday products, such as garments and tyres. Although consumers may not realise it, they purchase industrial biotechnology products in, for example, shirts which are a blend of cotton and bio-based textiles, and tyres containing bio-isoprene. Better recognition could greatly aid the market diffusion of bio-based products.

It has often been said that one of the difficulties facing industrial biotechnology is a lack of investors, both public and private. Compared to pharmaceutical biotechnology, industrial biotechnology lacks visibility: its products, and their value, are less clearly perceived. However, research in and commercialisation of industrial biotechnology have made good progress in recent years. This chapter aims to illustrate some major successes, but also to point to the breadth and variety of industrial biotechnology's future prospects. It is not meant to be exhaustive.

The biofuels sector has already had plenty of exposure and so will be discussed relatively little here. Very recent developments in US legislation (see Chapter 3) seem to make the future of biofuels a near certainty. Equally, the biochemicals sector is well established at full scale and will also receive less attention. In particular, production of amino acids and vitamins by fermentation routes are a major industry in its own right, and there are no serious synthetic routes for most of these products. Instead, the chapter concentrates on products that have a petrochemical route to production, but can be replaced by biological routes which are potentially easier to make, use less energy and water, produce less waste and have lower greenhouse gas (GHG) emissions.

For the bioplastics sector, the second largest renewable sector after biofuels, framework conditions – both legal and market – play a significant role in the market introduction phase. Unlike the renewable energy and biofuels sectors, this sector lacks supportive framework conditions. In individual EU countries the first initiatives to facilitate the introduction of bioplastics are however emerging.

Industrial biotechnology penetrates the thermoplastics market

Ethylene is the organic compound most produced in the world; in 2005 the combined US and European production exceeded 45 million tonnes (Chemical and Engineering News, 2006). The most obvious route to ethylene in a bioprocess is the conversion of bioethanol to ethylene via (non-biological) dehydration of bioethanol. This can be carried out using a range of catalysts and there are no technological hurdles to overcome. The question is price, specifically the availability of cheap sugar for fermentation to ethanol. This means that Brazil, with its long history of cane sugar bioethanol production, is likely to be the initial producing country.

The Brazilian petrochemicals and polymers group Braskem started to supply its first bio-based polyethylene (PE) products in 2010 (Smith, 2010). Braskem claims that the production of every tonne of its bio-based PE captures 2.5 tonnes of CO_2; the traditional petrochemical route results in emissions of close to 3.5 tonnes. However, it should be noted that there is no

difference in the biodegradability of bio-PE and petrochemical PE. Polyethylenes represent 64% of the plastic materials used for packaging and bottles, most of which are discarded after a single use (Sudhakar *et al.*, 2008).

Braskem's production facility has the capacity to make 200 000 metric tons of bio-based PE a year. It has already sold 70% of the capacity of this facility to major brand owners, including Tetrapak and Procter & Gamble. Of the initial output, 50% is earmarked for Europe, with 25% going to Asia and the remaining 25% to the Americas. Key markets include rigid and flexible packaging, as well as housewares.

Moreover, Braskem has claimed another significant breakthrough in the bioplastics sector with the development of a bio-based route to produce butene (Smith, 2008). This allows the development of a bio-derived LLDPE (linear low density polyethylene) and will open the market to applications in flexible film packaging.

Polypropylene (PP) production via a bio-route is more technically demanding. Braskem plans to invest USD 100 million to make 30 000 tonnes a year of propylene from ethanol by the end of 2013 (Tullo, 2010). The company will use the propylene to make polypropylene with the same properties as conventional hydrocarbon-derived polypropylene. It is claimed that its bio-based PP route captures 2.3 tonnes of CO_2 per tonne of polymer produced; petrochemical PP emits 1.8 tonnes of CO_2 per tonne of polymer produced.

Production of bio-based ethylene is now common. It also opens up the possibility of producing bio-based vinyl chloride (VC) in the short term. This implies that within ten years a significant part of the world's dominant thermoplastic materials (PE and PVC) could be bio-based (Haveren *et al.*, 2008). This depends on feedstock pricing, but would be an astonishing achievement on the road to the bioeconomy.

Sorona from bio-PDO

Poly(trimethylene terephthalate) (PTT) has several advantageous properties, such as good tensile behaviour, outstanding elastic recovery, and ability to be coloured with different dyes. The monomer for PTT is 1,3-propane diol (PDO). The bio-route to PDO is more energy-efficient than the petroleum route and reduces greenhouse gas emissions by 40% (Kurian, 2005).

The PTT polymer from bio-PDO (Sorona®, by DuPont) is easier to recycle owing to the absence of heavy metals in the product. As a fabric, Sorona® has several attractive features: it can be dyed at low pressures (thus

saving energy); the dyed fabric exhibits deeper shades and superior wash fastness; it is highly resistant to staining; it resists UV degradation; and has low water absorption and low electrostatic charging. Sorona® can be used in films, filaments, engineering components, resins and other applications in addition to fibres and fabrics. With the introduction of Sorona®, Dupont claims it has commercialised the most advanced polymer platform in over six decades. Sorona® has been tipped by Dupont to be the first non-pharma biotechnology blockbuster (sales in excess of USD 1 billion) (Decoding the DNA decoder - Cosmic Log. *msnbc.com*).

On 14 January 2010, DuPont announced that Toyota had adopted Sorona® as the material for the ceiling surface skin, sun visor and pillar garnish of its new SAI model. DuPont Sorona® fibres also were selected as materials for optional Toyota floor mats. Combined with a large percentage of eco-plastics made from plant-based materials, renewably sourced materials comprise approximately 60% of this car's internal surface area (DuPont News, 2010).

Greater value added can be obtained from sources far beyond conventional applications. Recent work on polymerisation of PTT with polyethylene glycol (PEG) has resulted in polymers with enhanced biocompatibility. These may have new applications in the fabrication of biomaterials, such as scaffold for bone cartilage, and in skin tissue engineering (Szymczyk, 2009). In such unexpected ways, raw materials of biological origin can lead to added value in new markets.

Bio-isoprene: sugar to rubber

Bio-isoprene is the result of research collaboration between Danisco-Genencor and Goodyear Tire and Rubber Company. Tyre companies use isoprene to produce synthetic rubber that is used to supplement natural rubber in tyres. It is a major component, accounting for as much as 27% of the content of new tyres. It is also used in a variety of other products, and world-wide production from petroleum feedstocks is of the order of 800 000 tonnes, about 60% of which is used in tyres.

This is a classic example of the drive towards sustainability. To produce one litre of petrochemically derived isoprene requires about seven litres of crude oil (Biofuels Digest, 2010). As the raw materials for bio-isoprene are plant-derived there is at least the potential for reducing (GHG) emissions. The enzyme isoprene synthase has only been identified in plants, but the expression of plant genes in production strains of micro-organisms remains a challenge. In this case, synthetic biology has allowed the construction of a gene that encodes the same amino acid sequence as the plant enzyme, but is optimised for expression in engineered micro-organisms. Moreover,

isoprene is a gas at low temperatures and bubbles out of the fermentation process. This allows recovery of the product in the gas phase, thus ameliorating often costly downstream processing which can render bioprocesses uneconomical.

However, the need for rational life cycle analysis (LCA) should also be borne in mind. It can be argued that bio-isoprene has a better environmental performance than synthetic isoprene, but neither is biodegradable. The technology will not be at full scale for several years, but prototype tyres were showcased in December 2009 at the United Nations Climate Change Conference in Copenhagen. Pilot production may be as little as a year away. Goodyear was awarded the "Environmental Achievement of the Year Award" for BioIsoprene technology in March 2010 (Goodyear News, 2010).

Toyota and green growth

Toyota has been developing bioplastics successfully for the last ten years, and was the first to make use of products made with polylactic acid (PLA) in 2003. Lactic acid has long been produced both by fermentation and chemical routes. Distillation of lactic acid for purification and polymerisation results in PLA, a biodegradable plastic material. Cargill Dow (now NatureWorks) opened a 140 000 tonnes a year PLA plant in 2001 (Griffiths and Atlas, 2005).

To improve recycling in the automotive industry, the Toyota Motor Corporation decided to include industrial biotechnology in its portfolio of businesses in 1996. Part of this decision was the introduction of bio-degradable plastic components in motor vehicles. In May 2003 the Toyota Raum was fitted with floor mats and the spare wheel cover made from PLA, a small but significant step (OECD, 2005).

Toyota completed a pilot plant of around 1 000 tonnes capacity in October 2004, and it became fully operational in May 2005 (Toyota Environmental and Social Report, 2005). The plant was built in order to conduct tests to verify that it met the cost levels and quality targets required for mass production.

In 2009 the Lexus 250h hybrid was introduced. Approximately 30% of the plastic used in the interior and trunk space is "eco-plastic". It is used in the seat cushions, on the door scuff plate, in the toolbox area and other parts of the car where oil-based plastics are traditionally used. This helps to reduce the HS 250h's plastic-based carbon dioxide emissions by nearly 20%. Moreover, 85% of the vehicle is fully recyclable. In the Toyota Sai hybrid, introduced in 2009, 60% of the exposed interior surfaces is covered with bioplastics, and a model to be introduced in 2011 will use bioplastics

for 80% of the interior surfaces (JCN Newswire, 2010). This is part of a plan to replace a total of 20% of oil-based plastics across the range of Toyota cars by 2015 and means an added demand for 360 000 tonnes of bioplastics. In a departure from PLA, the Lexus CT200h will use bio-PET as the liner material in the luggage compartment. Toyota has committed to buying 40% of the output of the Braskem plant in Brazil.

First-generation bioplastics lacked the engineering properties for advanced applications, but this is being addressed. Toyota is to use DuPont Zytel RS PA610 as a radiator end tank, which must withstand heat and road salt. The renewable carbon in the building blocks of Zytel RS product lines comes from sebacic acid, which in turn is derived from castor oil obtained from castor plants, which is not a food source (DuPont, 2010). Yet other bioplastics initiatives at Toyota include renewable components of vinyl to cover seats, dashboards and door interiors, working with Canadian General-Tower (Smock, 2010).

The automotive industry more generally is following Toyota's lead. For example, a composite plastic, usually polypropylene, reinforced with kenaf, is being delivered by Sustainable Fibre Solutions (SFS Pty Ltd) to BMW, Daimler Chrysler, Toyota, GM, VW and Nissan (Shelley, 2009). Sustainable Fibre Solutions, a joint venture between the Seardel Investment Corporation and the Industrial Development Corporation, is the first to successfully cultivate kenaf in South Africa (Sustainable Fibre Solutions Pty Ltd, 2010). A member of the hibiscus family (*Hibiscus cannabinus* L), kenaf is related to okra and cotton. In the United States the automotive industry has been less enthusiastic about bio-based materials as a category, but is very interested in specific bio-based materials that offer a price advantage or a useful performance characteristic (such as weight reduction or durability), or have significant and measureable environmental benefits.

In the Toyota example are many key components of green growth strategy and delivery of the bioeconomy:

- Globalisation: Toyota sources these materials from around the world. Moreover, the level of competition generated, and the fact that patenting in industrial biotechnology is facilitating innovation (Linton *et al.,* 2008), means there is still plenty of room for new companies to enter and plenty of scope for spillovers.
- Greenhouse gas emissions reduction: Bioplastics have an overall CO_2 capture whereas oil-derived plastics release CO_2.
- Social aspects: One of the objectives of using renewables is to stimulate rural economies through job creation in agricultural communities.

- Environmental aspects: Some of the bioplastics are non-biodegradable but recyclable, and others, in particular PLA, are genuinely biodegradable.
- Economic aspects: Toyota predicts that bio-PET will be cost-comparable with oil-based PET once high production volumes are achieved (Smock, 2010). Competition to supply bioplastics is already a feature of the market. Toyota sources PLA from Toray Industries and NatureWorks, having sold its own plant to Mazda and Teijin. Purac and Arkema have announced a collaboration in functional lactide-based block copolymers, which will enhance the thermo-mechanical and physical properties of polymers such as PLA, resulting in a wider range of applications opportunities. Futerro is a joint venture between Galactic and Total Petrochemicals to develop technology for PLA production from renewable vegetable resources using clean, innovative and competitive technology. Market uptake is clearly generating competition.
- Performance: No technology can be sold on its green credentials alone. The material must match up in performance and price as well. Bio-PET has performance parity with oil-PET. The stain resistance and other attributes of Sorona are as good if not better than those of competing products.

These outcomes are in line with the Biomass Nippon Strategy, set out by the Japanese government in 2002 (Kuzuhara, 2005). The strategy identified four reasons why Japan should tackle biomass utilisation as a national project:

- Prevention of global warming.
- Creation of a recycling-oriented society.
- Fostering of new strategic industries with a competitive edge.
- Stimulation of agriculture, forestry and fisheries, as well as associated rural communities.

Coca-Cola bio-PET: PlantBottle

Based on tonnage, about 55% of Coke's packaging is polyethylene terephthalate (PET). The design of PET bottles is close to optimum to limit weight; the most negative environmental impact is the manufacture of PET. The best solution would be to replace PET. Coke's PlantBottle does not quite do this: bio-PET is indistinguishable from oil-PET, but some 30% of the oil-derived materials are replaced by biomaterials. The building blocks of PET are monoethylene glycol (MEG) and terephthalic acid. In the

PlantBottle process, bioethanol is fermented to bio-MEG. According to Coca-Cola sources (Defosse, 2009), these bottles are the first beverage bottles that include content derived from renewable resources and can still be recycled in standard PET recycling streams (unlike, say, PLA). It was the intention of Coca-Cola to use 2 billion of these bottles by the end of 2010.

Preliminary LCA results are encouraging. As in other examples, the economics currently make sense if the bioethanol is produced in Brazil. In the longer term, lignocellulose conversion is the target feedstock to produce 100% bio-based PET. Coca-Cola foresees increasingly urgent replacement of commodity plastics with bioplastics in the coming years. Its attitude to price is that the consumer demands bio-materials and the pricing structure will change to accommodate this. Another factor to add to the green growth factors noted in the Toyota example is the critical role played by public perception and demand.

Spider silk may soon come of age

Spider silk is among the mechanically most outstanding biomaterials and can, under certain conditions, outperform some of the best high-technology materials such as nylon or Kevlar in terms of toughness (Vendrely and Scheibel, 2007). Spider dragline silk is exceptionally strong, five times stronger than steel by weight and three times tougher than man-made Kevlar (Xia *et al.,* 2010). While the biomedical market has traditionally been regarded as the market for spider silk products owing to the combination of excellent mechanical properties, biocompatibility and slow biodegradability, other applications have appeared. Recombinant silk fibrils could be used as nanowires or surface coatings. Spider silk fibres may be applied in technical textiles (for example in parachute cords, bullet-proof vests, aircraft composites) which demand high toughness.

Bringing spider silk to industrial-scale production using genetically modified production strains has proven extremely difficult. Now, however, AMSilk GmbH of Germany claims to have developed a process for producing biopolymers such as spider silk on an industrial scale. In March 2011 it secured EUR 5 million in funding to advance their commercialisation efforts for their first spider silk-based products (*www.amsilk.com/en*).

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Chapter 5

Business organisation and finance in industrial biotechnology

In the past industrial biotechnology has used traditional business models that may not be optimal for a high technology business that relies heavily on R&D. New ways of working are starting to emerge. This can equally be said of financing. At this stage there is an overwhelming need for large-scale production facilities and public as well as private investment are essential to underpin progress. At industrial biotechnology's current state of development, intellectual property is not concentrated and there is plenty of room for entry of new players. A great many companies are small SMEs, many of them spin-outs from universities. These companies often find survival difficult as it can be many years before they reach profitability. In many countries, strategies to help such companies survive are emerging.

The clustering phenomenon

Biotechnology as an industrial activity is still very highly research-dependent. Often the organisation that generates an idea does not have all the skills necessary to take that idea to eventual product roll-out. This is one reason why clustering became an important feature of the development of biotechnology.

There have been varying assessments of the conditions under which biotechnology clustering occurs. A useful summary was given by Chiesa and Chiaroni (2005), who identified four main driving forces of biotechnology development in nine developed countries:

- The availability of funds (*e.g.* venture capital, government funds).
- The presence and exploitation mechanisms of scientific research (van Geenhuizen and Reyes-Gonzalez, 2007).
- Industrial characteristics such as critical mass, integration and mechanisms to attract key managerial and commercial people.
- Supporting factors such as a legal framework, public acceptance and promotion.

This summary was not based specifically on industrial biotechnology, where other factors may need to be considered. Given the essential requirement of biomass, there is the potential for new small and medium-sized enterprises (SMEs) located in the rural environment in order to be close to the source of the biomass. The future location of biorefineries for cellulosic biofuels may well be close to the origins of the biomass to lower transport burdens. The arrival of the integrated biorefinery may also influence clustering behaviour, but a mismatch may exist between the industrial site and the site of academic and research excellence.

Industrial biotechnology companies

Biotechnology is an unusual technological field in that it draws heavily on university science, venture capital financing, the production and marketing capabilities of global pharmaceutical firms, and the skills in translational science developed by smaller, more nimble science-based start-ups (Ebers and Powell, 2007).

Industrial biotechnology companies can be categorised in terms of their size and the importance of industrial biotechnology to their business (Figure 5.1). Five types of companies with different characteristics can be

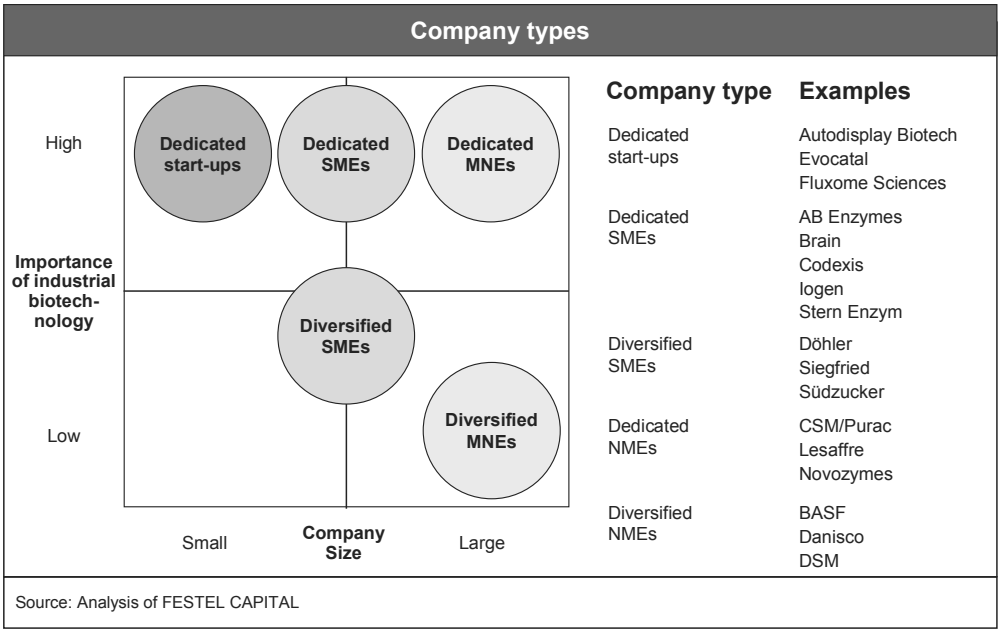
defined: dedicated start-ups, dedicated SMEs, diversified SMEs, dedicated multi-national enterprises (MNEs) and diversified MNEs.

Dedicated start-ups largely focus on R&D and on developing and commercialising specific technologies and their applications. Start-ups are likely to contribute significantly to the further technological development of industrial biotechnology (*e.g.* Evocatal, Fluxome Sciences, Direvo Industrial Biotechnology, Eucodis Bioscience).

Dedicated SMEs are moving beyond an early focus on R&D to establish production facilities and market their products (*e.g.* Brain, Codexis). These companies are the core of further technological and commercial development of an independent industrial biotechnology sector.

Diversified SMEs are in established industrial sectors such as the chemicals or food industry, serve already developed markets with highly specialised products, and introduce biotechnology processes and products into their markets to benefit from growth opportunities, to reduce costs or to fulfil regulatory requirements (*e.g.* Döhler, Siegfried). It is expected that these companies will be important in driving the commercial development of industrial biotechnology.

Figure 5.1. Types of industrial companies in the industrial biotechnology area



Source: Discussion paper, OECD workshop on outlook on industrial biotechnology, Session II on industry structure and business models for industrial biotechnology, January 2010.

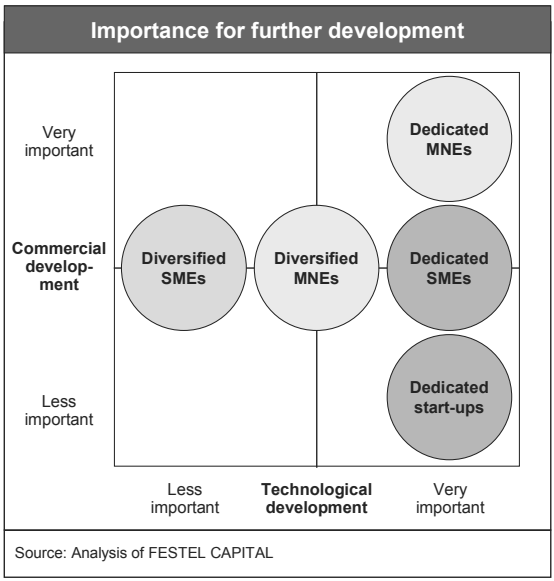
Dedicated MNEs are a group dominated by companies with a long history in the area of natural products (*e.g.* CSM/Purac, Lesaffre). These companies commonly make use of well-established technologies (not usually high technology), have optimised processes over many years, and supply traditional markets (*e.g.* starch, yeasts). Industrial biotechnology is one cornerstone of their technology portfolio and they are increasingly moving towards more sophisticated products and processes. This group has a sub-group of high-technology companies such as Novozymes. These companies are also expected to play a significant role in the technological and commercial development of industrial biotechnology.

Diversified MNEs are mainly established companies from the chemical industry (*e.g.* BASF, DSM), agri-industry (*e.g.* ADM, Cargill) or the food industry (*e.g.* Danisco). Their strengths include a broad and integrated technology portfolio which complements industrial biotechnology processes, such as purification technologies, a depth of further technical resources and significant financial resources.

Dedicated and diversified MNEs are by far the most important groups in terms of sales, customer networks and available R&D budgets. They have the resources to commercialise products worldwide. Figure 5.2 presents the relative roles of the different company types for the further development of industrial biotechnology. As a rule, dedicated companies contribute primarily to technological development, whereas commercial development is mainly driven by dedicated MNEs. These distinctions help to better understand the industry structure/dynamics and suggest three target groups which may require different policy approaches.

- Dedicated start-ups and SMEs may benefit from incentives to foster growth based on R&D-based innovations such as the YIC [young innovative company] scheme in France and Belgium (EuropaBio, 2007).
- Diversified SMEs may benefit from incentives to enable the use of industrial biotechnology in established production processes.
- Dedicated and diversified MNEs may benefit from incentives to support market introduction and penetration of industrial biotechnology products.

Figure 5.2. Relative importance of different company types for further development



Source: Discussion paper, OECD workshop on outlook on industrial biotechnology, Session II on industry structure and business models for industrial biotechnology, January 2010.

An important related group is non-profit governmental or semi-governmental institutions focused on research and education (*e.g.* universities and research institutions). They provide new or improved basic technologies for the industrial biotechnology area and often work closely with industrial companies. As with other high-technology areas, a key challenge is improving the transfer of technology from academia to industrial application.

Business models and growth strategies in industrial biotechnology

So far, industrial biotechnology has mainly made use of established business models, but others are gradually beginning to emerge. It could be argued that the particular dynamics of biotechnology are ill suited to traditional models. In particular there is a very obvious paradox. The molecular biology technologies that drive product innovation move very quickly, but actual product generation is relatively slow, *i.e.* the innovation cycle by no means moves at an even pace. The business model is critical: it is perhaps the most important consideration for venture capitalists that look to commit funds to companies.

Established business models

Producers

"Producers" develop their own technologies or buy/license them and focus on production over the whole supply chain from raw materials to distribution. Organisationally, this type of company is likely to be typical of the vertically integrated company (Luukkonen, 2005). Diversified SMEs and dedicated and diversified MNEs adopt this model. Many service-oriented dedicated SMEs are also currently moving towards this business model as it offers more opportunities for growth. A key disadvantage is the high capital costs needed to build up production facilities. The example of biofuel producers (especially biodiesel producers in Europe) shows that there is a significant risk with this model if a period of strong investment leads to overcapacity in the market. Excess capacity in first-generation biofuels is a problem in the United States as well, for both ethanol producers and biodiesel producers. In the biofuels market, the United States has not yet achieved consumer-/demand-led market growth.

Service providers

Many dedicated industrial biotechnology start-ups and some dedicated SMEs are "service providers". These companies offer their particular know-how predominantly as services to support other companies. These companies are often profitable and achieve some growth, but have sub-critical size and access to finance can be limited. The key disadvantage of this model is that the intellectual property (IP) generated normally belongs to the client; it offers very limited growth or value creation potential through development and commercialisation of the company's own IP, unless it has developed and retains ownership of a platform technology. Exploitation of company-owned IP is necessary if the company is to achieve further growth. However, the risk is also limited as maintaining this business model implies relatively low capital requirements.

Emerging business models

There are a number of emerging business models, such as the "IP creator" and the "integrated process developer", that focus on the development of IP and licensing. These IP-oriented business models work to develop the company's own portfolio of technologies and products, which are then sold or licensed out. A suitable network and co-operation strategy is required to ensure the successful commercialisation of the IP.

Connect, a San Diego-based organisation (*www.connect.org*), has proposed a new business structure for commercialisation. It has carved out a new niche for "product definition companies" that specialise in late-stage research in order to identify potential products. The product development companies would license discoveries from research institutions and raise the money to advance the research to the product development stage. They would then sell the research to large companies, such as pharmaceutical or chemical companies, which would complete the development process. This type of company has no expectation of actually making a product and thus removes large costs and risks from its operations.

Another driving force for new and hybrid business models will be the increasing importance of developing countries. A good example is the emergence of Shanghai as a centre for biotechnology in China. Despite state-directed promotion of biotechnology R&D, the main competitive edge of Shanghai's growing biotechnology industry lies in low development costs compared to developed countries and production expertise. Shanghai concentrates 68% of R&D expenditure on product/process development, 26% on applied research, and only 6% on basic research, as compared to 60% for development, 22% for applied, and 18% for basic research in the United States (Miller *et al.,* 2011). The patent data indicate that Shanghai is process-innovative, but not product-innovative. However, recent German evidence indicates that process innovation has a more significant effect on job creation than product innovation (Lachenmaier and Rottmann, 2011). Inadequate protection of intellectual property, lack of venture capital investment, and the tightening supply of highly qualified knowledge workers are likely to shape business models.

IP and industrial biotechnology

The biotechnology industry is characterised by rapid growth, complexity and comparative youth. Participants tend to attach a great deal of importance to IP. This is an industry that, collectively, submits a large number of difficult, highly technical patent applications. Patent examiners therefore have difficulty paring down broad claims and weeding out applications that do not meet statutory patentability criteria (OECD, 2005). In 2005 the OECD considered that there was little evidence that an anti-commons problem had arisen in the biotechnology industry. However, it is an industry in which such a situation might arise in future owing to a growing number of patents and a larger number of participants.

From 1975 to 2006 the US Patent and Trademark Office (USPTO) issued over 20 000 patents relating to industrial biotechnology. The number issued annually climbed through the 1980s, peaked in 1999, declined

through to 2005 and rebounded in 2006. The trend mirrors the capacity of the USPTO to process applications. A major report addressing patenting in industrial biotechnology was published in 2008 (Linton *et al.,* 2008). Two of the key findings of the study were:

- Patents in industrial biotechnology are not concentrated in the hands of a small number of owners. New owners are steadily appearing and the number of patents held by industry leaders is relatively small. This is good news as regards competition and confirms the earlier OECD findings.
- Over 70% of biofuel and chemical company representatives responding to a survey reported that patent barriers are among the least significant impediments to R&D and commercialisation of industrial biotechnology products and processes.

A significant trend in biofuels patenting has been observed recently (Thompson, 2011). Patent applications filed prior to the beginning of 2009 focused on new biofuel starter materials and streamlined processes. In 2011 there seems to be a shift to patenting in known biofuel materials and improving either the material and/or the process. Further, biofuel processes involving algae are gaining patenting momentum in the transition from the laboratory to commercialisation and scale-up, and many patent applications are directed to the utilisation of waste materials to lower the footprint of biofuel production. Thompson considers that these developments promise to make 2011 a good year for those in biofuels and the green technology businesses.

At this stage, then, concentration of IP is not an issue for industrial biotechnology. However, a phenomenon that is a concern is the situation of some of the patent offices around the world. Small technology companies create sustainable market advantage in several ways, one of which is the exclusivity gained from patenting. The monetisation of IP is also a major way for small biotechnology companies to raise capital (Pisano, 2010).

However, the patent filing and award systems are failing to keep up. The average review period in the United States was 27 months in 2003; in 2009 it had soared to 35 months (Belz, 2010). The US Patent and Trademark Office introduced a three-track system to replace the old system in 2011. Asia is filing a larger number of patents than before, and for the first time in 2009 more patents were issued by the Japan Patent Office than by the USPTO. Chinese patenting is also growing rapidly. The problem in the USPTO appears to be a lack of adequate funding (Pegram, 2011).

Smaller companies express concerns over the publishing of patent applications on the Internet 18 months after filing when the actual granting of the patent takes years. This allows competitors to see valuable details of applications without the protection of a granted patent.

The problem at the European Patent Office is longstanding and well described. Each nation has its own agency, and the costs of translation are substantial. There has long been a call for a single agency and a single language, but this has not occurred. New initiatives are afoot in 2011 to try to break the deadlock (Morningside Translations, 2011).

Another concern regarding patenting is changes in the United States regarding patent eligibility (Morley and Tung, 2011). A US Supreme Court decision dealing with business methods patents may have spillover effects into biotechnology patenting, raising the possibility that industrial process patents may no longer be "patent-eligible".

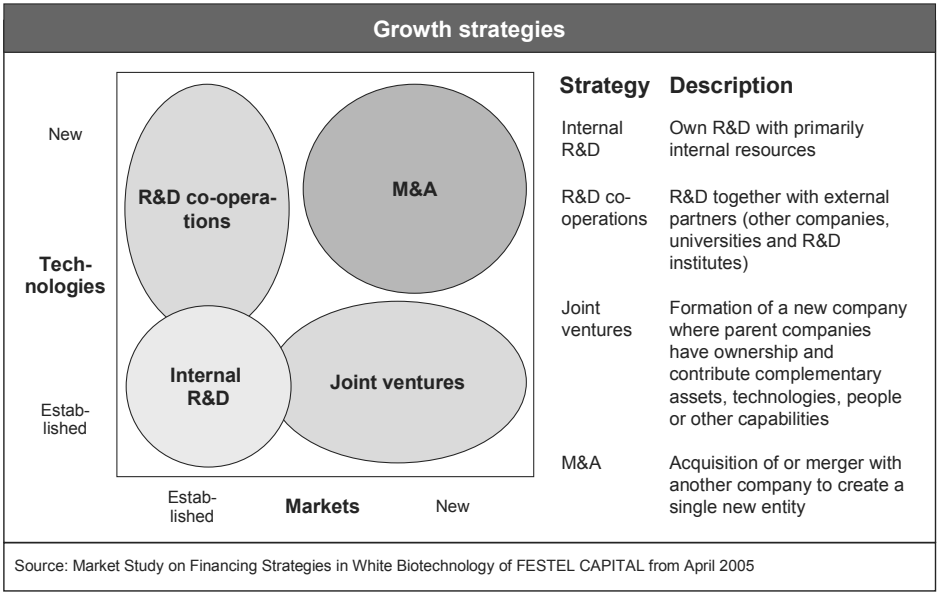
Growth strategies for industrial companies

As with other types of biotechnology, industrial biotechnology companies have available to them four different growth strategies, each with its advantages and disadvantages, along the two dimensions established/new markets and established/new technologies, as shown in Figure 5.3.

- Internal R&D: own R&D with primarily internal resources.
- R&D co-operation or alliances: R&D together with other companies, universities and R&D institutions.
- Joint ventures: formation of a new company with another company to use complementary assets, technologies, people or other capabilities.
- Mergers and acquisitions (M&A): acquisition of, or merger with, another company to create a new single entity.

For industrial biotechnology start-ups and SMEs, the preferred strategy is organic growth based on internal R&D for established markets and technologies. Start-ups are crucial to technology-dependent sectors, both as a key source of breakthrough innovations and as a catalyst for the commercial success of new innovative technologies.

Figure 5.3. Growth strategies for industrial biotechnology companies



Source: Discussion paper, OECD workshop on outlook on industrial biotechnology, Session II on industry structure and business models for industrial biotechnology, January 2010.

R&D co-operation or alliances are also an important growth strategy for industrial biotechnology companies, and a large proportion of them have such arrangements. These are of particular importance to industrial biotechnology as they ensure the transfer of research results and technology from universities and research institutions to market-oriented SMEs and MNEs. As a result, however, the SME that carries out the R&D assumes a great deal of risk owing to the high-risk nature of R&D. At the same time, uncertainty and risk should make large companies more inclined to contract out R&D to SMEs (Sharp, 1985).

Joint ventures are mainly used to open new markets and to obtain access to emerging markets such as China and India. They are not yet common in industrial biotechnology. However, as the industrial biotechnology sector matures, such partnerships are likely to grow in importance.

Another growth strategy with increasing importance in industrial biotechnology is M&A transactions, notably between MNEs and SMEs/start-ups (*e.g.* the sale of Biopract by DSM) or between SMEs (*e.g.* acquisition of Jülich Fine Chemicals through Codexis).

Financing and investment models for industrial biotechnology

Financing trends

A key issue affecting the amount and type of financial investment available to industrial biotechnology companies is the investment community's degree of familiarity with industrial biotechnology. The global biotechnology investor community has relatively little exposure to this sector compared, for example, to medical biotechnology. There are generally insufficient funds to support innovation in industrial biotechnology (Hasler, 2010). However, industrial biotechnology has seen some significant venture investments in the last few years, especially in the United States, but most of the investment is mainly focused on biofuels. This is not surprising given the US focus on bioethanol and the high capital intensity of biofuel production.

Engagement of financial investors

Financial investors, such as private equity companies, have played an important role over the past few years in the implementation of industrial biotechnology in the chemicals sector. Investor transactions have increased strongly and make up around 30% of transaction volume, and investors increasingly adopt "buy-and-build" strategies in order to create increased value. For example, Equity Partners, a subsidiary of JP Morgan Chase, becomes a majority shareholder in companies it acquires, and its financing allows the investee company to achieve growth in interesting future technologies in the industrial biotechnology area. Another example is Cornerstone Capital in Frankfurt, which offers buyout financing and growth financing to the chemical industry. Cornerstone Capital has a special focus on industrial biotechnology as a growth option in the chemical industry.

Project-oriented financing

Project-oriented funding is becoming more important, especially in the area of renewables, such as bioenergy projects. However, given its narrow focus, project financing is not a suitable vehicle for industrial biotechnology in general.

Founding angel activities

Founding angels, together with appropriate research partners, found start-up companies to further develop research results. They focus on bridging the finance gap between academic research and commercialisation of the research results. This relationship may then move on to commercialisation of the technology in conjunction with an industrial partner. The

founding angel model is already being successfully implemented in the United Kingdom and the United States, mainly in the field of nanotechnology. It is now being used in some investments focused on industrial biotechnology in Germany and Switzerland.

Capital requirements

Capital requirements for R&D and infrastructure, by region

The total yearly capital requirements are around EUR 3.3 billion for R&D and EUR 6.9 billion for infrastructure. On a sector level active pharmaceutical ingredients require the most capital for R&D and have the second highest capital requirements for infrastructure. Base chemicals require the largest investments in infrastructure as the large volume production in this sector is very capital-intensive. Specialty chemicals require large investments in R&D to support the wide range of potential applications. Consumer chemicals require the least capital for R&D and for infrastructure. On a regional basis Europe requires the most capital in both R&D and infrastructure with more than 30%, followed by North America, Asia Pacific and the BRICs (Brazil, the Russian Federation, India and China).

Capital requirements for start-ups and SMEs

The total amount of required financial capital estimated for European start-ups and SMEs over the next few years is EUR 1.4 billion. This comprises EUR 200 million to fund existing European industrial biotechnology start-ups through their next phase of development; EUR 122 million for the initial financing of new start-ups; and EUR 1.1 billion to finance the growth of existing SMEs.

Financial sources

Non-traditional financial sources

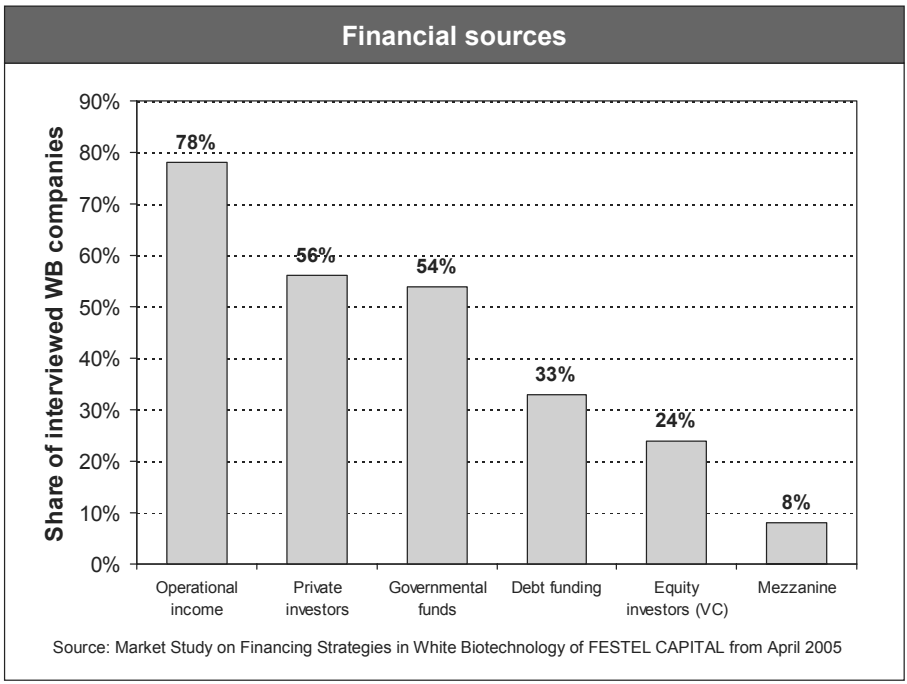
Non-traditional financial sources most relevant to industrial biotechnology companies include mezzanine financing, project financing and private equity financing. The attractiveness of these sources is viewed differently by different actors in the field: industrial biotechnology start-ups/SMEs, MNEs, and private and institutional investors. Private and institutional investors see mezzanine and private equity financing as attractive sources, whereas start-ups and SMEs have a strongly positive view of private equity financing (including venture capital, VC). Industrial biotechnology SMEs have little experience with mezzanine and project

financing. Private equity financing is the main and preferred source of funding for these companies.

Financial sources for start-ups and SMEs

Operational income is the most important financing source for industrial biotechnology start-ups (Figure 5.4). Financial resources offered by private investors are rather small (often not exceeding EUR 0.5 million) and insufficient for further growth. Venture capital offers far larger resources, but to date few industrial biotechnology start-ups have received funds (between 15% and 20%). Many VC managers have little understanding of the differences between industrial and other types of biotechnology; this results in an inappropriate evaluation of the value of start-ups. VC managers also claim that the service-oriented business model, to which many industrial biotechnology companies adhere, fails to offer the desired returns. Timing has a huge impact on the exiting internal rate of return (IRR). The long time periods required before industrial biotechnology start-ups begin to see revenues is therefore not conducive to the VC mode of funding.

Figure 5.4. Financial sources for industrial biotechnology SMEs and start-ups



Source: Discussion paper, OECD workshop on outlook on industrial biotechnology, Session III on financing and investment models in industrial biotechnology - research methodology and first results, January 2010.

Investors and entrepreneurs must arrive at an estimate of the market value or "valuation" of a technology start-up. The valuations that investors place on start-ups will influence the proportion of equity shares disbursed to raise enough funds to ensure firm growth and survival. Both entrepreneurs and investors consider valuation an important metric, one which determines their equity proportion and their financial return from invest into the venture. Therefore, understanding the factors affecting new ventures' valuation is an issue of substantial importance (Zheng *et al*., 2010).

Debt funding and an initial public offering (IPO) are less relevant for industrial biotechnology start-ups owing to their low equity basis and the fact that most lack the critical size for an IPO.

Government funds can help to overcome funding problems, but are predominantly allocated to basic research projects rather than product development, and provide at best 25-50% of the research costs. Nevertheless, about one-third of start-ups view government funding as an integral part of their financing strategy and use this to strengthen and enhance their technology base.

Start-ups in EU accession countries may also benefit from EU structural funds which provide access to larger volumes of funds and are not restricted to basic R&D. They may also benefit from specific incentives offered by several European countries. Start-up companies in these countries are exempt from taxes and social security charges on salaries, and as long as they reinvest a certain amount of their revenue in R&D they can operate under a lower average tax burden and can carry forward their losses until they reach profitability.

Market failures and consequences

Lack of investors for start-ups

Generally, there is a large equity gap during the critical start-up growth phase as government or private investors provide only small amounts of funds. Industrial biotechnology currently appears rather unattractive to investors, owing to their lack of experience with the sector and the few encouraging examples. This situation should change because, as this report highlights, such examples are emerging, especially in the biopolymers field. Attracting VC will remain a challenge in the short and medium term. Many industrial biotechnology start-ups must therefore rely on operational income, limiting the scale and pace of possible growth.

Lack of investors for pilot plants

There is a clear need for more pilot plants to allow industrial biotechnology developers to demonstrate technical proof-of-concept. Despite government subsidies and financing, investors are struggling as a result of the credit crisis, which is limiting the availability of debt capital. Private debt is crucial as many government grants and loan guarantees require private-sector cost sharing. The lack of private debt underscores the general lack of funds available for industrial biotechnology.

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Chapter 6

Biotechnology policy – Developments, implications and conclusions

A range of supply- and demand-side policies, from biomass production to waste and by-products, have been deployed to develop the biofuels industry. It is important to balance supply and demand incentives, but this balance is not easily achieved. As biofuels globalise, there is a need for internationally agreed standards and to enable free trade and stimulate markets and the use of life cycle analysis (LCA) to verify sustainability. There is as yet no policy arsenal for bio-based chemicals and bioplastics comparable to that available for biofuels. However, the integrated biorefineries of the future will probably depend on their production alongside high volume, low margin transport fuels to make refinery economics viable.

Industrial biotechnology is much more than liquid fuels. The value of biochemicals (other than pharmaceuticals) could increase from 1.8% of all chemical production in 2005 to between 12% and 20% by 2015 (OECD, 2009a). However, bio-based chemicals have not enjoyed the wealth of supportive policy measures liquid biofuels have received. This is equally true of bioplastics, if they are treated as a separate category. The case for increased policy support for bioplastics is especially critical as the number of applications is growing with the number of new materials, and blending with petro-plastics is starting to produce new generations of engineering plastics. A particularly encouraging phenomenon is the extent of industry pull for bioplastics, with some of the most famous multinational enterprises (MNEs) now using them in their products.

Another area for policy action is industrial biotechnology research and development (R&D), where the policy instruments are likely to be quite different. R&D is dominated by universities and research institutes and dedicated and diversified small and medium-sized enterprises (SMEs). Biotechnology SMEs often fail to attract investment for a variety of reasons, yet growth can only be achieved through innovation as biotechnology is an area highly dependent on research.

Policy options for biofuels, bioplastics and bio-based chemicals do however share some characteristics. All require a stable supply of feedstocks, so that factors that affect feedstocks, *e.g.* price, variety, pre-treatment, land-use, competition from crude oil, transport logistics and international supply chains, affect all of industrial biotechnology.

Short- and long-term policy instruments

When considering policy instruments potentially available to encourage the development of industrial biotechnology, it is important to distinguish among those that are principally short-term in nature, providing temporary assistance and subject to change at short notice, from the more durable policies that are in place for the longer term.

Short-term policy instruments

Access to finance and feedstocks during the global financial crisis

Perhaps the biggest hurdle to moving industrial biotechnology from the laboratory to full scale is the gap in investment funding (Shott, 2010). Yet, as European Commissioner Máire Geoghegan-Quinn noted when announcing support of EUR 6.4 billion for research and innovation, to be allocated by the end of 2011, "Investment in research and innovation is the only smart and lasting way out of crisis and towards sustainable and socially equitable growth." (cited in Fletcher and Bastin, 2010)

Recent studies in several OECD member countries have shown that many biotechnology companies faced a tough financial climate, even before the current financial crisis (USITC, 2008; EuropaBio, 2009). For small companies, a long and costly development process may warrant special financial support. In particular, lifecycle assessment (LCA) studies and intellectual property (IP) servicing are very heavy financial burdens for industrial biotechnology SMEs to bear, and EuropaBio issued a stark warning regarding the financial dilemma of European biotechnology SMEs (EuropaBio, 2009). Four points from that publication demonstrate the vital importance of financial barriers:

- In May 2009, around 87% of biotechnology SMEs worldwide were in the pre-profit phase, a natural consequence of their business model. In the last five years, the trend has been for the larger players to place greater reliance on R&D performed by emerging companies. These externally initiated programmes now represent as much as 30% to 50% of the pipeline in many major companies. But this business model also transfers the risk of R&D upstream to small innovators and their funding sources. This business model anticipates years of negative cash flow, and future liquidity is needed via a public offering, licensing or partnering. There is a clear tendency, particularly in the cleantech industry, towards funding later-stage companies (Hasler, 2010).

- More than one in four small biotechnology firms have less than six months cash in hand, and 45% of the publicly traded biotech SMEs have less than one year's cash available. These firms rely on private equity sources for continuous growth funding, but the financial crisis has made access to capital very difficult.

- At that time, the IPO financing model (public market) did not exist, and it is not clear when it might resume.

- Venture capital (VC) is one of the primary sources of risk investments in biotechnology start-ups, but VC investment declined by almost 57% in 2008 compared to 2007. Even more worrying is the fact that half of this decline was in the month of October 2008 alone. All forms of investment (including VC) raised by bio-technology firms decreased by 54% for the first nine months of 2008, compared to the previous year.

Subsidies, grants, mandates and other financial incentives

While subsidies and mandates underpinned the development of Brazil's successful ethanol industry and lie at the heart of US ethanol policy, their cost efficiency in achieving public policy goals in the long term remains to be demonstrated.

Demand-led policies

Accompanying the introduction of mandates are the demand-side policies that have been adopted in Brazil, the United States and China, nations that promote biofuels. Other demand-side policies focus on the sustainability agenda (including green public procurement) and are often implemented as a mix of public procurement procedures (*e.g.* the USDA BioPreferred programme, *www.biopreferred.gov*), legislation and direct financial incentives.

Long-term policy instruments

Strategic R&D support

Industrial biotechnology is a relatively new and thus immature discipline. There are major areas of knowledge still to be explored. Basic or strategic research is essential to develop the fundamental knowledge base. If industrial biotechnology is to realise its expectations and contribute to future competitiveness and industrial sustainability, the commitment to underpinning R&D should be long-term and, in the most favourable climate, guaranteed. On 21 July 2010 the European Commission announced EUR 6.4 billion of funding for research and innovation, its biggest ever funding package, to stimulate smart growth and jobs (The Burrill Report, *www.burrillreport.com/article-2618.html*). Top priority is given to SMEs, which represent almost 99% of all European businesses. They will receive close to EUR 800 million in areas such as the knowledge-based bio-economy. SME participation must reach 35% of the total budget for a number of topics.

Promoting flexible pilot plants as pathways to biorefineries

It is important to foster synergies among the various participating sectors, *e.g.* by stimulating public-private partnerships. This co-operation must extend downstream to demonstration projects that facilitate the development of flexible, research-oriented pilot plants to validate the concept of integrated and diversified biorefineries. One of the challenges for commercialisation of industrial biotechnology is the expense of the production facilities. For universities and SMEs demonstrating a process

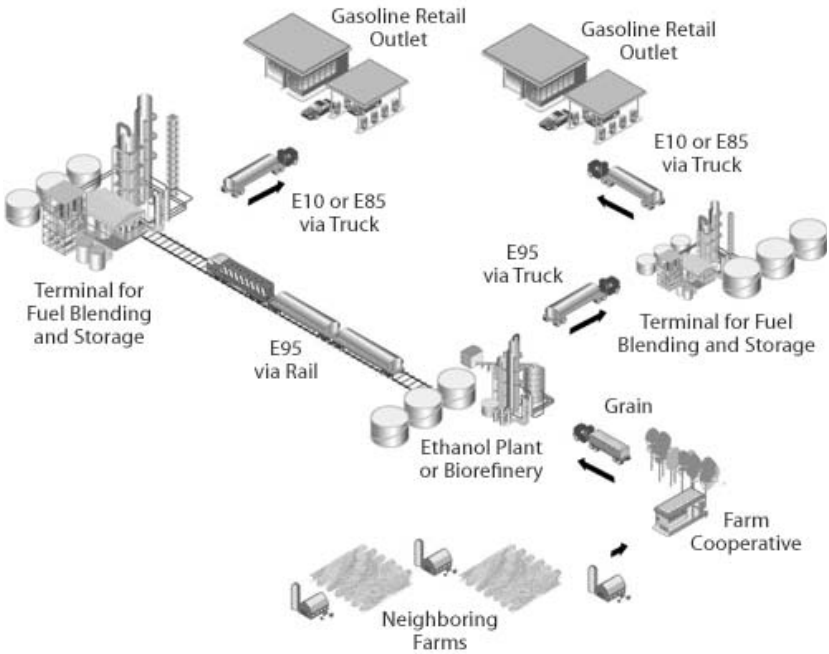
even at pilot scale is often beyond their financial means. As of 2009, over 100 pilot and demonstrator plants were either in operation or being built in the EU (Skibar *et al.,* 2009). The US DoE has invested heavily in pilot and demonstrator plants in support of biofuels development.

Infrastructure interdependencies and capital investment

There are major infrastructure constraints to the expansion of industrial biotechnology, especially for biofuels and other chemicals (Figure 6.1), as well as complex interdependencies among chemicals, fuels, vehicles and infrastructure (Batten, 2008). It is vital to develop long-term policies that ensure timely investment in infrastructure networks to avoid future bottlenecks.

In the current US market, dominated by first-generation ethanol, products travel extremely large distances. Fuel is typically produced in large agricultural areas, but is consumed in areas of high population density. The implications for the funding of infrastructure are massive. Rail, barge and truck transport in the United States is at or near capacity constraints (Lundy, 2008).

Figure 6.1. Logistics of a rail and truck distribution system for bioethanol



Source: US DoE (2008). Ethanol Distribution. *www.afdc.energy.gov/afdc/ethanol/distribution.html*.

Biomass security

Practical steps must be taken to facilitate the move towards bio-processing in manufacturing. One necessary prerequisite is the assurance of a secure, varying, sustainable and affordable supply of biomass. This will require a special combination of policy instruments: financial incentives, innovation and long-term supply agreements. Here the necessity of building international supply chains will be critical.

Current policy trends

Policy trends and challenges by sector

Bio-based chemicals

In the chemicals industry, use of fossil-based raw materials is often exempted from environmental taxes. This creates weak incentives to increase the use of renewable feedstocks (Hatti-Kaul *et al.,* 2007). A crucial issue, still to be addressed, is the expansion of existing policy instruments that favour the increased use of renewable, CO_2-neutral feedstock in this sector.

It is noteworthy that no co-ordinated policy strategy targeting renewables has been adopted to maintain the EU's position as a world leader in chemicals production. However, nearly all major EU members offer, to varying degrees, dedicated funding for public-private partnerships that undertake industrial biotechnology R&D. The SusChem Technology Platform initiative introduced in mid-2004 will also expand R&D investment and enhance European competitiveness in various industry sectors, including industrial biotechnology.

Bio-based chemicals pose a major challenge for policy makers because of the need to address the complete value chain of intermediate products in a cradle-to-grave perspective (Hatti-Kaul *et al.,* 2007). Such chains are generally much longer than those based on fossil feedstocks, although the products containing such biochemicals are environmentally benign in comparison with the products made from fossil feedstocks. Nowadays, the environmental impact of all chemicals needs to be evaluated from a lifecycle perspective.

Bio-based plastics

Two different concepts underlie the term "bioplastics":

1. Compostable plastics certified according to EN14995 (Europe), ASTM D-6400 (USA) or ISO 17088 (other countries). These are based on renewable or non-renewable resources and the focus is on functionality, *e.g.* compostability or biodegradability.

2. Bio-based plastics produced on the basis of renewable resources, with a focus on their raw materials. Rather than using fossil carbon in manufacturing conventional plastics, bio-based polymers use carbon from renewable resources such as sugar, starch, vegetable oils or cellulose in their production. Increasingly, the products may be a blend of bio- and fossil-derived. Bio-based polymers are not biodegradable and compostable in all cases.

In contrast to the situation of biofuels and renewable energies, there is currently no EU-wide framework for action to support the use of renewable raw materials (*European Bioplastics*, 2008). Nor is there an international framework of any consequence. Because of this, the bioplastics sector suffers from a lack of tax incentives, supporting regulations, skilled researchers or investment in public sector R&D in comparison with biofuels. Development costs are high, and production does not yet benefit from economies of scale.

Three positive developments are to be noted:

- The Japanese government's Biomass Nippon Strategy legislated in 2002 that 20% of all plastics consumed in the country are to be sourced renewably by 2020 (prompting Toyota, NEC and others to accelerate R&D into bioplastics).

- New regulations in the German Packaging Directive cover packaging made from bioplastics. As such, bottles produced from at least 75% renewable resources are exempt from the compulsory deposit for single-use drink bottles. Exempting a single-use bottle from the deposit system gives the brand owner a EUR 0.25 pricing advantage over its deposit-carrying competitors on the supermarket shelf. The scheme is not expected to compromise the existing high level of recycling.

- The OECD is developing, with the support of member and non-member countries, a new international instrument setting out principles for sustainability assessment of biomaterials, including bioplastics.

Other policy possibilities for bioplastics are:

- Political objectives concerning future utilisation: percentage of market/consumption share at a given period of time, measures to support implementation.
- Tax legislation, *e.g.* reduced value-added tax, environmental tax, investment support.
- Preferential treatment of products in public procurement programmes.
- Simplified special regulations in waste legislation.
- Treatment of bioplastic secondary raw materials as renewable energies (electrical and thermal energy recovery).
- Opening of community recovery systems for biowaste ("biobin") for certified compostable plastic products.
- Provision of equity and venture capital to small and medium-sized businesses.
- Government R&D programmes for the co-financing of industry and university projects.
- Activities related to communication and market introduction (Ghanadan and Long, 2011).
- Agricultural policy: promotion of cultivation of renewable resources on fallow (set-aside) or other fields.

Biofuels

As the major biofuels policies are explored elsewhere in this report, only summary comments are included here. Government policies play an important role in determining the commercial attractiveness of biofuels production and trade in many countries, especially in the leading producers of ethanol, Brazil, the United States and China. This is hardly surprising given the promise of benefits in several areas of interest to governments, including agricultural production, greenhouse gas (GHG) emissions, urban air quality, energy security, trade balances, regional development and new economic opportunities for developing countries.

Governments currently support biofuels via subsidies, mandates, tax incentives, tariffs and other trade barriers. Quantifying and assessing these policies to facilitate an evidence-based assessment of policy effectiveness is necessary, but remains difficult because of the huge array of policies in place at various levels of government. It is also crucial that policies are

tailored to support the development of the most advantageous biofuels and discourage production of poor performers (International Energy Agency, 2008). Policy makers could offer different levels of support to different biofuels. The capacity of biofuels to advance multiple policy goals simultaneously should be considered when designing incentive mechanisms. An integrated approach combining rural development, climate change, and energy provision is warranted when formulating the policy framework for second-generation biofuels (Carriquiry *et al*., 2011).

Some emerging policy trends

A key question pertaining to emerging policy trends is how industrial biotechnology can contribute to broadening the opportunities for sustainable development. There is huge potential for linking new policy approaches to industrial biotechnology to policy initiatives on sustainable development.

Composting of bio-based plastics

The properties of biodegradability and compostability are due to the molecular structure of polymer materials; they do not depend on the raw material. The implementation of a separate, high-quality composting system for the treatment of organic waste could boost market development of biodegradable and compostable plastics.

Biodegradable plastic products that fulfil the requirements of EN 13432, the European Committee for Standardization's rigorous standard for bioplastics (CEN, *www.cen.eu*), can contribute to an efficient biowaste management system. For example, compostable bin liners or biowaste bags can bind organic waste, while creating a homogeneous mixture with organic waste (no separation of the plastic material from waste necessary) that can be diverted from landfill. For the environmentally safe application of biodegradable polymers and biocomposites, it is important to prove that the degradation products do not have any ecotoxicological effect. To meet the criteria of biodegradability, these materials also have to be non-toxic in order to comply with EN 13432 (Rudnik *et al*., 2007). Composting is very cost-efficient and the concept is easy to understand for consumers.

At present, very few EU members have nationwide industrial composting systems in place and operating. In the Netherlands EN 13432 certified packaging is allowed to enter the composting system, thus diverting it from landfill. Although several EU members have composting measures, there is no clear policy support for the composting of biodegradable and compostable products. Today the bio-based and biodegradable plastics industry must face the challenge that the use as fertiliser of compost derived from these products is not permitted, even when the products comply with

the strict criteria of the harmonised EN 13432 standard (in Germany and in France). The EU should strive to harmonise regulations on composting and the use of compost as fertiliser.

R&D mismatches

There may arise a serious mismatch between the level of private-sector investment in industrial biotechnology R&D and the potential market opportunities for the sector and for convergence with agriculture. The future economic contribution of biotechnology is believed to be greatest in industrial applications, with 39% of the total potential gross value added (GVA). Yet only 2% of biotechnology R&D expenditures were spent on industrial applications in 2003, whereas 87% went to health applications (OECD, 2009a). This mismatch represents a massive challenge for policy makers in terms of the need to spend more heavily on R&D.

Demand-led innovation

Two classes of demand-side initiatives are of growing importance for the optimal uptake of industrial biotechnology.

The lead market initiative and industrial platforms

Europe's Lead Market Initiative (LMI), adopted in December 2007 by the European Commission, aims at fostering the emergence of markets with potentially high economic and societal value. It has identified six lead market areas to serve as pilot markets for the approach and for the implementation of its action plans. They are: eHealth, protective textiles, sustainable construction, recycling, bio-based products and renewable energies. This said, there remains a possible major weakness, namely the effective integration of supply- and demand-side policies.

The LMI intends to deliver a supply- and demand-side policy mix that works in unison. The envisaged added value of the initiative is to develop a prospective, concerted and tailored approach to regulatory and other policy instruments, such as legislation, public procurement, standardisation, labelling, certification, and complementary instruments.

Demand-side policies linked directly to sustainability

According to Cunningham (2009), examples of demand-side policies focused on the sustainability agenda include green public procurement, energy-efficient construction and transport, power generation projects using renewable energy sources, biofuels and infrastructure for waste management. Several European countries have introduced green public procurement policies. Instruments such as green public procurement are often implemented

as a mix of public procurement procedures, legislation and direct financial incentives.

The Swedish bioethanol situation offers an example of public procurement influencing market uptake. Sweden is reported to have the largest bioethanol bus fleet in the world, with over 600 ethanol-operated buses in service. In 1994 the first three flex-fuel cars (powered by both ethanol and petrol) were imported. At the same time, the BioAlcohol Fuel Foundation (BAFF), founded in 1983 as the Swedish Ethanol Development Foundation (SSEU), began lobbying other municipalities to invest in ethanol. It took ten years to establish the first 100 E85 pumps, and today these pumps are erected at the rate of close to 100 every two months. At present there are about 1 400 E85 pumps throughout Sweden, not many fewer than in the entire United States. Sweden has about 147 000 flex-fuel cars (*www.sekab.com/default.asp?id=1844&refid=1958&l3=1949*).

Sweden has produced a range of other consumer-oriented, demand-side policies supportive of biofuels to complement the supply side:

- A SEK 10 000 bonus to flex-fuel vehicle buyers (over EUR 1 000, and over USD 1 500 as of 20 June 2011).
- Exemption from Stockholm congestion tax.
- Discounted auto insurance.
- Free parking spaces in most of the largest Swedish cities.
- Lower annual registration taxes.
- A 20% tax reduction for flex-fuel company cars.

The most recent acceleration of growth of the E85 fleet is the result of the National Climate Policy in Global Co-operation Bill passed in 2005. The Swedish government has an ambitious target to eliminate oil imports by 2020. The Swedish approach to using biofuels to reduce dependence on oil relies on incentives to change the direction of fuel consumption, rather than setting mandates or benchmarks (Kroh, 2008).

On the supply side, Ford Sweden and Saab have become leaders in flex-fuel ethanol cars, and Volvo currently markets several ethanol-operated models (SEKAB website). This is an example of supply- and demand- side policies operating simultaneously. Mowery and Rosenberg (1979) concluded that both were necessary for innovation. The relationship between supply- and demand-side policies to stimulate innovation is detailed in the OECD's *Demand-Side Innovation Policies* (OECD, 2011).

Sustainability indicators and assessments as supporting tools for policy makers

Addressing sustainability concerns beyond GHG emissions is now a major challenge for biofuels and other bio-based products. The lack of any widely accepted scheme to assess and confirm sustainability credentials, and a shortage of relevant statistics, are major barriers to consumer and government confidence.

To support the transition towards a bioeconomy, OECD countries aim to develop common ways of assessing the lifecycle environmental and economic effects of bio-based products. A recent OECD workshop on best practices in assessing the environmental and economic sustainability of bio-based products (OECD, 2009b) made a start on this challenging task. The workshop took stock of existing approaches to the sustainability assessment of bio-based products and identified the key elements of "best practice" assessment methodologies.

Lifecycle analysis (LCA), product carbon footprint (PCF) standards and standardisation

Although biotechnology has helped sectors such as the chemicals industry to lower the levels of greenhouse gas emissions associated with their products, measuring sustainability requires a much broader set of assessments (O'Connell *et al*., 2009). Because of the interdependencies in processes involved in growing, harvesting, manufacturing, distributing and disposing of a product, sustainability requires a lifecycle ("cradle-to-grave") systems analysis encompassing the whole value chain.

LCA is a structured, comprehensive and internationally standardised method used to undertake this analysis. It quantifies all relevant emissions and resources consumed and the related environmental and health impacts and resource depletion issues associated with any goods or services. The essential value of LCA studies is that they help to avoid resolving one environmental problem while creating others, an unwanted shifting of burdens that reduces an environmental impact at one point in the life cycle while leading to an increase at another point.

Several LCA standards have been developed in parallel (*e.g*. ISO 14067, 2009; PAS 2050, 2008). For example, PAS 2050 was developed as a method for assessing consistently the lifecycle GHG emissions of goods and services. The product carbon footprint (PCF) is a derivative of the more comprehensive LCA, which is described in the international standards ISO 14040(2006)/14044 (2006). A PCF is the total set of GHG emissions caused by a product and is therefore a sub-set of the ecological footprint.

The approach is enshrined in the volume mandates set by the US Energy Independence and Security Act (EISA) (2007), which also required the US Environmental Protection Agency (EPA) to apply lifecycle greenhouse gas performance threshold standards to ensure that each category of renewable fuel emits fewer greenhouse gases than the petroleum fuel it replaces.

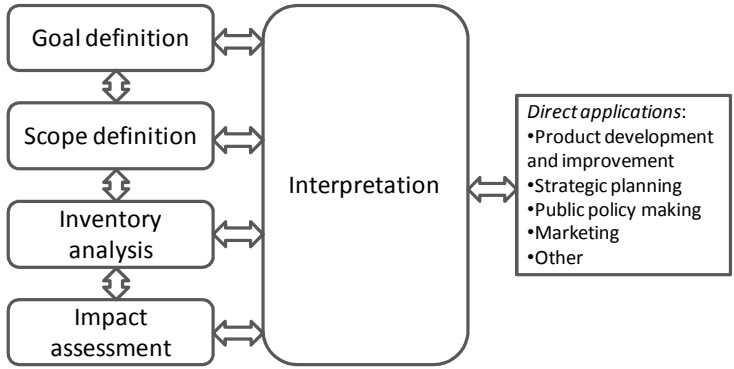
However, with a variety of standards comes the danger of discrepancies in LCA and PCF results. Discrepancies between LCA and PCF methods could also cause confusion, waste resources and hinder the acceptance of PCF results (Bioproducts Working Group, 2010). A single, globally accepted harmonised standard is desirable to maximise the credibility, consistency and practicality of PCF. This harmonisation will require international policy action.

Any approach adopted must consider multiple inputs. For example, the BEES (Building for Environmental and Economic Sustainability) (Cooper *et al*., 2009) analytical technique considers multiple environmental and economic impacts over the entire life of a product. Considering multiple impacts and lifecycle stages is necessary because product selection decisions based on single impacts or stages could obscure others that might cause equal or greater damage.

The USDA BioPreferred programme uses the 2006 BEES Stakeholder Panel importance weights to synthesize its 12 environmental impact scores into a single decision-enabling score (Duncan *et al*., 2008). Global warming, weighted at 29%, was judged most important, yet not so important that decisions can be made solely on the basis of this impact. Other important concerns include human health (13%) fossil fuel depletion (10%), air pollutants (9%), water use (8%), ecological toxicity (7%), eutrophication (6%), and habitat alteration (6%). Also of interest are the identified impact areas of concern assigned the lowest weights: smog formation (4%), indoor air quality (3%), acidification (3%), and ozone depletion (2%).

The European Commission recently published a guide to improve harmonisation (the International Reference Life Cycle Data System, ILCD, 2010). The ISO 14040 and 14044 standards provide an indispensable framework for LCA (Figure 6.2). This framework, however, leaves the individual practitioner with a range of choices, which can affect the legitimacy of the results of an LCA study. The ILCD was created to support consistent, robust and quality-assured life cycle data and studies. Moreover, it provides a common basis for coherent SCP (sustainable consumption and production) instruments, such as ecolabelling, ecodesign, carbon foot-printing, and green public procurement.

Figure 6.2. Framework for lifecycle assessment



Source: Originally from ISO 14040 (2006). Environmental management - Life cycle assessment – Principles and framework; modified from International Reference Life Cycle Data System (ILCD) (2010). Handbook – General Guide for Life Cycle Assessment - detailed guidance. First edition March 2010. EUR 24708 EN, Publications Office of the European Union, Luxembourg.

Lignocellulosic ethanol production will be a key area for the deployment of LCA in future. Various authors have already employed LCA on lignocellulosic feedstock, and discrepancies in their approaches lead to uncertainty and inaccuracy. If not addressed, this will diminish the credibility of LCA testing (Singh *et al.,* 2010).

As early as 2000, Mitchell (2000) identified over 25 computer models of bioenergy systems, including lifecycle cost models, and advocated a decision support tool to help practitioners. It identified a number of difficulties that hinder the successful development of decision support systems:

- The underlying concepts and relationships were not fully developed or understood.
- There were too few reliable data across the range of possibilities.
- Models were being built by people trying to understand the relationships rather than for people who use the model in practice.

Ayoub *et al*. (2007) proposed a general bioenergy decision system (gBEDS) as an effective tool in planning for expansion of bioenergy production. Their model, developed with Japan's specific conditions in mind, included environmental, economic and social decision support. Specifically for bioenergy applications, Elghali *et al*. (2007) described a multi-criteria decision analysis framework and decision-conferencing approach for assessing the sustainability of potential short-term projects and long-term scenarios. It was predicted that subsequent practical use of the framework would enable guidance on the development of technologies and supply

chains which recognises social and environmental impacts and acceptability as well as socioeconomic barriers to development.

Very recently the basic framework for a decision support tool to evaluate biofuel production pathways has been described; its purpose is to provide decision makers with a structured methodology. The tool integrates the most important aspects along the entire value chain (*i.e.* from biomass production to biofuel end use), namely the technical, economic, environmental and social aspects (Perimenis *et al*., 2011).

Given the plethora of new bioplastics and biocomposites now in production, and given that many of the products are not single-use but are intended to be durable engineering materials, the LCA issues are even more important than for biofuels. Harding *et al.* (2007) compared LCA for a bioplastic with two of the most common petrochemical plastics, polypropylene (PP) and polyethylene (PE). In all categories of the LCA, the bioplastic was superior to PP. However, the eutrophication impact of PE production was 500% lower than that of the bioplastic, partially because of the agricultural component of the bioplastic production.

Fresh in people's memory is the failure of bio-indigo to compete in LCA with chemically produced indigo (Saling *et al.,* 2002). It failed on some environmental as well as cost parameters. To date biotechnology indigo has not entered the marketplace.

For international comparability and credibility, harmonised LCA is thus a policy issue that needs to be addressed across the spectrum of industrial biotechnology products: biofuels, bioplastics and bio-based chemicals. As the supply chains globalise, the limitations of non-harmonised LCA will become more apparent.

Comparative bio-based chemicals and bioplastics policy: a common regime?

It is quite clear that on a global basis biofuels have a very large policy advantage over bio-based chemicals and bioplastics. What is not clear is whether this is justified. Certainly, production volumes for biofuels are currently much larger than those for chemicals or bioplastics, and it could be argued that on this basis alone, liquid biofuels should be a special case. However, this view may be flawed for at least the following reasons:

- Integrated biorefineries will have a much better return on investment if they are allowed to produce high-value, low-volume chemicals alongside low-value, high-volume biofuels (rather like an oil refinery). Without policy intervention, this important stream of products from integrated biorefineries might not emerge, and the added value from chemicals and plastics will not be obtained.

- Bio-based chemicals and bioplastics production are aligned with international efforts to meet climate change targets (Bang *et al.*, 2009).
- Their production would take pressure off finite crude oil supplies.
- Biofuels are part of the solution during the transition to other energy solutions, but it is likely that biomass will continue to be important for replacing petrochemicals and plastics after the fuels themselves have been superseded (Nuffield Council on Bioethics, 2011).

It is useful to compare some policy measures that have helped the development of biofuels in the United States and elsewhere and would also stimulate bio-based chemicals. First are some of the specific measures applied in the United States (based largely on Winters, 2010).

One is early-stage support in tax policy through a variety of incentives to stimulate capital investments for large infrastructure projects and commercialisation. There is little doubt that biofuels development has greatly benefited from such measures or that bio-based chemicals lack a strong investment climate.

The goal of the US Advanced Energy Manufacturing Tax Credit (MTC) is to expand domestic manufacturing industry for clean energy, thereby supporting the larger goals of stimulating economic growth, creating jobs, and reducing greenhouse gas emissions (White House Press Office, 2010). It provided a 30% tax credit for investments in 183 manufacturing facilities for clean energy products and was predicted to directly generate 17 000 new jobs, as well as a further 41 000 jobs through matched investment of USD 5.4 billion by the private sector. It excluded bio-based chemicals projects. Similar measures, if applied to bio-based chemicals in other countries, where the investor climate for non-biofuels industrial biotechnology is less well developed, could also have stimulatory effects. The measures need not be as generous as there is already significant investment in integrated biorefineries.

Another example is the Tax Relief, Unemployment Insurance Reauthorization, and Job Creation Act of 2010 (Library of Congress, 2010) which extended the volumetric ethanol excise tax credit (VEETC) of the American Jobs Creation Act of 2004; the credit pays blenders USD 0.45 for every gallon of ethanol blended with gasoline until the end of 2011. A production tax credit for biodiesel producers equal to USD 1.00 per gallon regardless of the feedstock used to produce the biodiesel (Mueller *et al.*, 2011) is valid until the same date. In addition, a tax credit for small biodiesel producers equal to USD 0.10 per gallon is currently allowed for the first 15 million

gallons of production. Again, similar credits for bio-based chemicals would unlock investment.

Continuing support through R&D tax credits would help bio-based chemicals manufacturers to continue R&D investment through the early years of product development when costs are high owing to the lack of economies of scale.

Government funding such as grants, loan guarantees and other public finance schemes that are directed to next-generation bio-based chemicals would provide the stimulus (and also private sector buy-in) for the critical areas of new feedstocks and conversion technologies. The large programmes of the US Department of Energy (DoE) and the US Department of Agriculture (USDA) for biofuels have not been open to bio-based chemicals. Yet, as Ross Maclachlan, President, CEO, Lignol noted, "My view is that we are not seeing any heavy-hitting legislation right now that puts real money or mandates in place to encourage or require the use of renewable chemicals, even though the use of bio-based chemicals will displace 'a barrel of oil' just as easily, or even more so, than will renewable fuels" (cited in Shaw *et al*., 2011).

Where appropriate, efforts also should be made to create incentives for bio-based chemicals in climate change and carbon limitation legislation. If a bio-based product is proven through LCA or PCF (or other indicators) to be superior to its petrochemical counterpart with respect to GHG emissions, this should be taken into account in offsets. This would help drive investments and stimulate the industry to investigate further CO_2 reduction opportunities.

Public procurement programmes, such as the often-cited USDA BioPreferred voluntary labelling and procurement scheme, have the potential to be major market drivers for bio-based chemicals.

The EU initiative to enhance the market capitalisation of bio-based chemicals contains similar policy recommendations (*e.g.* Schintlmeister and Jonsson, 2009). The Lead Market Initiative (LMI) Ad-hoc Advisory Group for Bio-based Products made various recommendations on required action:

- Legislation promoting market development, including total CO_2 equivalent emissions offsets, indicative or binding targets, and tax reductions for sustainable bio-based products.
- Product-specific legislation, *e.g.* allowing bio-based plastics to enter composting, recycling and energy recovery schemes.
- Legislation relating to biomass to guarantee quantity and quality of feedstocks at good prices.
- Encouragement of green public procurement for bio-based chemicals.

- Standards, labels and certification that help verify claims such as biodegradability and bio-based content can promote market uptake.
- Financing of research, and continuing efforts to build demonstration plants through public-private initiatives.

International thinking is therefore converging as regards bio-based chemical policy. This raises another critical issue: to globalise this business will require international harmonisation similar to initiatives to create international quality standards for biofuels.

Table 6.1. Suggested policies and measures to promote wider use of renewable raw materials (RRM)

Policy measure	Objective
Medium- and long-term R&D and demonstration	Increase applications and economic performance, increase range of additives to improve engineering parameters
Standardisation	Harmonise standards (*e.g.* composting)
Public procurement	Enable commercialisation, create economies of scale
Limited fiscal and monetary support (*e.g.* reduced VAT rate)	Enable commercialisation, create economies of scale
Include in climate and product policy	CO_2 credits for manufacturers/users
Adaptation of waste legislation and waste management	Improve infrastructure for separate collection (financial incentives for consumers)
Inclusion in agricultural policy	Secure stable supply of biomass feedstocks
Public awareness	Widen understanding of benefits

Note: RRM is a synonym for bio-based materials. Apart from bio-based polymers the group of RRMs comprises bio-based lubricants, solvents and surfactants.

Source: Adapted from Crank M, Patel M, Marscheider-Weidemann F, Schleich J, Hüsing B and Angerer G (2005). Techno-economic feasibility of largescale production of bio-based polymers in Europe ed. O Wolf. European Science and Technology Observatory. European Commission Technical Report EUR 22103 EN.

Policy recommendations for bioplastics present distinct similarities to bio-based chemicals policy. The issue is perhaps more urgent for bioplastics owing to the large number of new molecules, blends and applications that are emerging. As an example, policy measures that could be applied to bioplastics are summarised in Table 6.1.

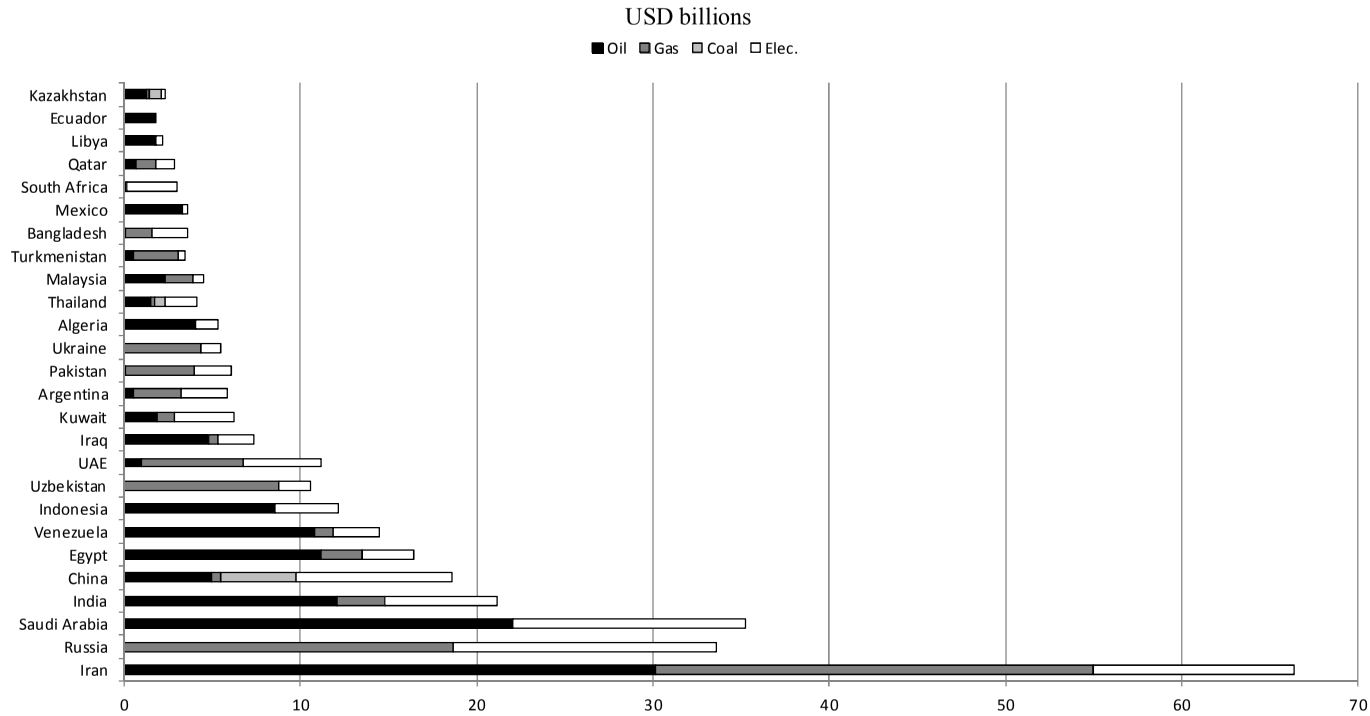
Given such similarities, there may be some justification for treating bio-based chemicals and bioplastics in the same policy regime, for the following reasons.

- Some of the companies that make bio-based chemicals and bio-plastics might be expected to make both, *e.g*. BioAmber makes both succinic acid and polybutylene succinate plastic.
- The supply and value chains are very similar. Essentially, bioplastics extends the value chain of bio-based chemicals.
- They share the same feedstocks.
- Given recent advances in bio-based plastics and biocomposites, it is inevitable that a significant proportion of bio-based chemicals will become platforms for the production of plastics. Ultimately, in fact, many paths lead back to bioethanol.
- National administration of grants, loan guarantee programmes and taxes would be simplified by having one common regime instead of two.
- Company administrations would similarly be simplified and streamlined.
- Bioplastics manufacturers would be eligible for extra manufacturing incentives because of their core processes, *e.g.* injection and blow moulding. These could also extend to petrochemical injection and blow moulders with the introduction of the use of bioplastics in their manufacturing facilities (as would seem inevitable).

It is immediately apparent that the policy measures for all of the major products of industrial biotechnology (fuels, chemicals and plastics) are related, and that much of the intellectual work has therefore been done. It is now a matter of implementation to bring chemicals and plastics to the market. The problems are generally smaller for chemicals and plastics as fuels are far bulkier and have much higher production volume products. As a result the transport infrastructure problems of biofuels are much less of an issue, perhaps not even an issue, for chemicals and plastics.

One interesting area that should be investigated is the competition for biomass feedstocks. Biofuels, of course, require much greater quantities of biomass, and their impact on land use is commensurately larger. But the potential benefits of material use in terms of employment and value added are significantly higher for chemicals and plastics than for the use of biomass for energy (Carus *et al.*, 2011). As of today, however, the EU for example, has set a target of 20% of renewably sourced energy by 2020. This will lead to increased support for biofuels, whereas there is at present almost no support for the use of biomass for chemicals or plastics. Without public support, there will be little private support.

Figure 6.3. Fossil fuel consumption subsidies, 2009



Source: IEA (2010), *World Energy Outlook 2010.*

Fossil fuel subsidies are another factor

Competition for crude oil for plastics is an issue because future demand for plastics will require an increasing proportion of the world's crude oil. This will happen at a time when increasing demand coincides with depletion of inexpensive crude oil reserves. This points to yet another area of disadvantage for industrial biotechnology products – fossil fuel subsidies. Globally these amounted to USD 312 billion, with oil products accounting for almost half of the total in 2009 (Figure 6.3). Fossil fuel subsidies are inefficient and lead to a range of detrimental economic distortions. One of the major outcomes of the G20 Summit in Pittsburgh in 2009 was an agreement ultimately to phase out nearly USD 300 billion in global subsidies for fossil fuels (White House Press Office, 2009). It has been estimated that eliminating fossil fuel subsidies in a number of non-OECD countries would cut global GHG by 10% or more by 2050 (Burniaux and Chateau, 2011). From the industrial biotechnology perspective, it would also be a large contribution to the levelling of the playing field.

The White Paper, *Bio-based Chemicals and Products: A New Driver of US Economic Development and Green Jobs* (Biotechnology Industry Organization, 2010), touched on the possibility that bio-based chemicals and bioplastics could revolutionise and revitalise the chemicals and plastics manufacturing industry in the United States and throughout the world. These are very large ambitions. They cannot be achieved by lopsided policy that strongly favours liquid fuels.

Conclusions

This report draws out the somewhat schizophrenic nature of industrial biotechnology: in the three sectors, biofuels, bio-based chemicals and bioplastics, there is a great deal of promise for full-scale replacement of a significant portion of crude oil as a feedstock. Crude oil is often seen as the source of many ills, but its partial replacement should not be seen solely in terms of environmental benefits and energy security. Crude oil should be seen as a precious, non-renewable and diminishing resource that it would be well to use wisely in future.

A number of challenges stand in the way of bringing this promise to fruition. It is difficult for industrial biotechnology to attract R&D funding, and the problems facing industrial biotechnology SMEs have been highlighted. The difficulties of securing sufficient biomass without wide price fluctuations, the building of pilot and demonstrator plants, the globalisation of the business, and the distribution logistics are all well recognised.

Only one of the three sectors, liquid biofuels, has a maturing policy environment, especially in the United States with its top-down approach. It is also evident that many other developing and developed countries have adopted biofuels policy; this may eventually be beneficial in setting up international supply chains. Effective policies include regulation and the drive towards mandated targets. There is now an emerging need for concerted, harmonised policy around standardisation and lifecycle analysis.

Bioplastics is likely to be the next sector to require strong policy intervention. On the one hand, projected plastics consumption shows a worrying competition with transport fuels for crude oil. On the other, the growing list of molecules and of applications and the uptake by multinationals indicate that bioplastics are on their way to success from a very modest starting point. At present, however, there are no extensive, coherent policy strategies for bioplastics.

Bio-based chemicals may appear to be the sector that presents the least urgency. Because many biochemicals cannot be easily made by a synthetic chemical route, their market position is safe. However, it is evident that the wider bio-based chemicals sector, which implies bio-content but not necessarily production by a biocatalytic route, is expanding. This suggests that policy intervention should be seen as equally urgent. There can be no better example than bio-based ethylene, formed from bioethanol. It is being taken seriously, especially in Brazil (Morschbacker, 2009). Ethylene is the most produced organic chemical in the world. The bio-based route would compete not only with the petrochemical route, but also with biofuels for a share of production of bioethanol, and would therefore, of course, also be competing for a share of biomass.

Ultimately all three sectors will be interdependent owing to the need for common raw materials and supply chains. This makes the economics of the integrated biorefinery potentially more attractive. Perhaps policy calls for similar integration.

A further objective of this study has been was to highlight some recent products that are bringing bioplastics and bio-based chemicals to the attention of consumers and investors. Two examples are bio-isoprene for tyre production and Sorona®, a bio-based fabric. There is a perception that industrial biotechnology products are unattractive, and this has consequences for investment and market penetration. Investors are attracted by blockbuster products, and the lack of visibility of these sectors helps explain the lack of investment. Additionally, the general public knows little about industrial biotechnology products, so it is difficult for them to gain market share. However, as high-visibility products such as bio-isoprene and Sorona®

reach the market, this can only enhance the reputation of industrial biotechnology generally. Public perception is an issue of the highest priority.

Ongoing globalisation creates its own particular policy needs. Secure global supply chains may come to dominate policy for industrial biotechnology. Europe wishes to maintain its competitiveness in the chemicals industry, and industrial biotechnology is a priority strategy for achieving this. But lack of availability of land in Europe for the production of biomass will create reliance on sourcing elsewhere. Europe will be strong on sustainability issues, and unless clear sustainability standards are set and met elsewhere, the EU may lose out. It is clear that China will take a leading role in the future development of industrial biotechnology as its energy consumption increases further. In the context of globalisation, the need for harmonised policy has been discussed. So far, the United States has a head-start with many products and protected IP. These and other globalisation issues will inevitably create tensions and perhaps market failures.

There has never been a period of greater interest in industrial biotechnology. The range of new products and R&D projects is exciting. Innovative policy measures, especially in biofuels, and evidence of national and regional commitment to the future of industrial biotechnology is there to be seen. Although it has traditionally suffered in terms of funding, compared to, say, pharmaceuticals, public funding has improved and public-private projects are under way. It goes without saying, though, that to achieve its full potential, there is a lot to be done. Long-term, flexible policy is required to make industrial biotechnology achieve its potential.

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Annex A

OECD workshop on the outlook on industrial biotechnology

13-15 January 2010
Vienna, Austria

Programme

Workshop Chair: Mr Marvin Duncan, Chairman of the OECD Task Force on Industrial Biotechnology

Workshop Facilitator: Mr Joel Velasco, Chief Representative in North America of Brazil's Sugarcane Industry Association (UNICA), Washington DC.

13 January 2010 - Day 1

Welcome by the OECD and the Austrian delegation

Introductory remarks and outline of the day

SESSION I: TRENDS IN TECHNOLOGY AND APPLICATIONS

Objective: To get an overview of current technological trends in industrial biotechnology and to understand what policy could do to support technological advances.

Presentation of the paper "Industrial Biotechnology: Trends in Technology and Applications"

Mr Manfred Kircher, Chairman of CLIB2021, Germany

Commentary session

Mr Alois Jungbauer, University of Natural Resources and Applied Life Sciences, Austria

Group discussion

Questions to be addressed:

R&D trends and indicators

- What are the current industrial biotechnology R&D achievements and priorities in academia and industry by sector? How can we evaluate their impact on industrial biotechnology?
- How can technological developments in industrial biotechnology be best measured? What are the available indicators and data sources? Are these indicators available, accurate and comparable between OECD countries?
- What barriers, if any, impede the translation of R&D into marketable technologies and products? How can one evaluate the efficiency of translational research in industrial biotechnology? What kind of indicators could be used for this purpose?
- What R&D priorities could be foreseen in the near future for both academic and industrial research activities (5-year period of time)? Is there any economic evidence to support the vision? Are there any foreseeable and justifiable benefits (*e.g.* delivery of public goods; industrial growth and sustainability; environmental sustainability) while fixing such priorities?
- Co-ordination of R&D programmes among main actors.
- Are the IB R&D priorities and activities co-ordinated between academia and industry? Is such co-ordination necessary?
- Are there any examples of successful co-ordination and its impact on the delivery of valuable technologies/products and examples when the absence of co-ordination negatively affected the IB translational research?

Synthesis of main discussion points and closing of the day

Mr Joel Velasco, Chief Representative in North America of Brazil's Sugarcane Industry Association (UNICA), Washington DC

Presentation of the Austrian Centre for Industrial Biotechnology (ACIB)

Mr Alois Jungbauer, University of Natural Resources and Applied Life Sciences, Austria

14 January 2010 – Day 2

SESSION II: STRUCTURE OF THE INDUSTRY AND BUSINESS MODELS

Objectives: To identify the new industrial biotechnology structural trends and to map the current and emerging business models in this sector.

Introductory remarks and outline of the day

Presentation of the paper "Industry Structure and Business Models for Industrial Biotechnology - Research Methodology and First Results for Further Discussion"

Mr Gunter Festel, CEO, Festel Capital, Switzerland

Commentary session

Mr Teppo Tuomikoski, Programme Manager, Tekes, Finland

Group discussion

Questions to be addressed:

Structural trends in industrial biotechnology

- What are current trends and changes in structure of industrial biotechnology?
- What factors drive the engagement of industrial biotechnology actors while developing the IB business models?
- Sector-specific structural differences and measurement indicators
- Are there any differences in the IB structure depending on the application area? What are the regional differences? How do "small" countries position themselves in global industrial biotechnology?
- What indicators and data sources are available to measure the development of industrial biotechnology? How does globalisation influence these trends? Are indicators available for most of the OECD countries? How accurate and comparable are the data?
- Business models for industrial biotechnology.
- What are the current and emerging business models for firms?
- Do existing models constrain industrial capacity for developing/performing R&D or absorbing next-generation technologies?

Synthesis of main discussion points

Mr Joel Velasco, Chief Representative in North America of Brazil's Sugarcane Industry Association (UNICA), Washington DC

SESSION III: TRENDS IN FINANCING AND INVESTMENT

Objective: To review the sources of financing for industrial biotechnology firms; to review investments in R&D and infrastructure; to discuss market failures and, finally, to discuss how the industrial biotechnology sector will weather the current financial crisis.

Presentation of the paper " Financing and Investment Models in Industrial Biotechnology- Research Methodology and First Results for Further Discussion"

Mr Gunter Festel, CEO, Festel Capital, Switzerland

Commentary session

Mr Martin Austin, Managing Director, TransformRx, Basel, Switzerland

Group discussion

Questions to be addressed:

Investment trends in industrial biotechnology

- What are the main trends in industrial biotechnology financing and investment?
- What is the impact of the current financial crisis and globalisation on the availability of finance and investment for the industrial biotechnology sectors?
- What makes industrial biotechnology an attractive sector for investors and which aspects discourage investment?

Measuring investment in industrial biotechnology

- What parameters/indicators could be used for measuring financial and investment trends in industrial biotechnology?
- Are these indicators available, comparable across countries and accurate?
- Public policy and investment in industrial biotechnology.
- Where might public interventions be warranted and why (what incentives are there)?
- What recommendations could be made to guide the governmental programmes supporting IB?
- What are the main elements of the policy environment – in OECD and non-OECD countries – which influence financing for, and investment in, industrial biotechnology? Where might changes in policy be warranted?

Synthesis of main discussion points and closing of the day

Mr Joel Velasco, Chief Representative in North America of Brazil's Sugarcane Industry Association (UNICA), Washington DC

15 January 2010 – Day 3

SESSION IV: TRENDS AND CHALLENGES FOR PUBLIC POLICY

Objective: To assess mismatches between countries and challenges for public policy.

Introductory remarks and outline of the day

Presentation of the paper "Industrial Biotechnology: Policy Trends"

Mr David Batten, Senior Economist and International Analyst, Transport Bio-fuels Stream, CSIRO Energy Transformed Flagship, Australia

Commentary session

Mr Dirk Carrez, Public Policy Director, EuropaBio

Group discussion

Questions to be addressed:

Policy trends for industrial biotechnology

- What policy areas should be given priority while developing and supporting industrial biotechnology?
- What are the main policy trends and challenges in supporting industrial biotechnology?
- What is the role of different actors in IB-related policy development?

Policy tools for industrial biotechnology

- How are the identified public policy challenges addressed; are there "best practices"? How could the efficiency and impact of such policies be measured?
- What are the foreseeable roles of national bio-based economies in the global bioeconomy? In other words, could be there "winners" and losers"? What are the foreseeable national economic niches (in industrial biotechnology) in the global bioeconomy?
- Are there any national strategies which address industrial biotechnology-related issues in a system integrative way (*e.g.* policy coherence between agro-, industrial, environment and health related policy frameworks)?

Synthesis of main discussion points

Mr Joel Velasco, Chief Representative in North America of Brazil's Sugarcane Industry Association (UNICA), Washington DC

Closing of the workshop

Austrian Delegation and OECD Secretariat

Annex B

OECD workshop on building an efficient bioeconomy through industrial biotechnology

St. Petersburg, Russian Federation, 28-29 October 2010

As a follow-up to the Vienna "Outlook on Industrial Biotechnology" workshop in January 2010, a further workshop entitled "Building an Efficient Bioeconomy through Industrial Biotechnology" was held in St. Petersburg, Russian Federation, on 28-29 October 2010. This meeting was hosted by the Russian Federation Ministry of Science and Education.

The delivery of green growth has high priority on the policy agendas of OECD member and non-member countries. Reviewing the industrial biotechnology innovation systems of these countries provides an excellent opportunity to evaluate the contribution to such growth of this highly innovative and complex industrial sector. However, while the bioeconomy-related issues of OECD countries already have been studied in some depth, those of the BRICS countries (Brazil, Russian Federation, India, China and South Africa) have been less well addressed.

The broad objectives of the workshop were to exchange experience in setting and implementing policy agendas to support the development of national bio-based economies and to develop a set of practical recommendations on how the barriers can be overcome and common issues be addressed.

Presentations were made on experience in Brazil, China, the Russian Federation and Germany. The current stage of development of industrial biotechnology varies greatly among countries as do market opportunities. These variations rely on factors such as: internal resources; environmental issues and pressures; R&D capacity; size/scale of production plants; competitiveness of biotechnologies used; and governmental support and engagement. For example, whereas China sees significant involvement of the government in the development and governance of industrial biotechnology, the Russian Federation seems to offer limited public policy support.

Some key messages from the workshop were as follows.

1. Each country faces a different set of challenges for developing the bioeconomy. These challenges strongly depend on the country's resources and history.
2. Identifying common themes in countries and establishing overall guidance can help address these challenges.
3. Gathering reliable data and statistics that will allow measuring the impact of bio-based products is crucial to promoting the development of industrial biotechnology. The establishment of data sources upon which to base metrics for validating the environmental benefit/cost benefit for consumers of bio-based products is required. For example, it is necessary to develop metrics to measure the environmental benefits and costs of fossil energy and bio-based energy products and to convey that information to policy makers and consumers in understandable language.
4. A public-sector regulatory function will be needed both to ensure the integrity of the developing bioeconomy and to build/sustain consumer confidence. Bio-based products, if they are to capture market share, will need to perform as well as, or better than, their fossil energy-based or chemical-based competitors, be less costly, and provide enhanced environmental performance.
5. Development opportunities for the bioeconomy in individual countries will depend on the resource base available. All countries can become effective players in the bioeconomy by identifying niches for development opportunities that play to their competitive advantages. The identification of core competencies within each country will in part rely on regional development studies.
6. Political championship is a factor to take into account in the promotion and support of industrial biotechnology development.
7. The bioeconomy is international in scope and constructive international partnering will be important to its development. Constructive dialogue among scientists, public policy makers, industry and consumers is necessary to promote broad understanding of, and support for, the developing bioeconomy.
8. Selective use of turn-key technologies combined with original research can accelerate implementation. Scientific discovery, especially in biology and engineering, will underpin and enable new product development. There is a need to expand the role of researchers beyond simply the reporting of research findings.

9. A holistic understanding of the bio-based value chain is necessary in order to identify opportunities available to individual countries and firms. An expanded understanding of supply chain integration and co-operation leading to new models is important.

10. Bio-based product development, scale-up and commercialisation may require public-sector investment for a limited period of time. Private investment may be augmented by government funding for scale-up before adoption by commercial firms.

11. Overall, developing the bioeconomy will both require, and provide opportunities for, creative public/private sector co-operation.

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