Industrial or White Biotechnology

A driver of sustainable growth in Europe

Working document from EuropaBio and ESAB to be used as input for the Industrial Biotechnology section of the European Technology Platform for Sustainable Chemistry

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Foreword

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It is with great pleasure that I accepted the invitation to write the foreword to this document on Industrial (or White) biotechnology which is one of the three pillars supporting the Sustainable Chemistry (SUSCHEM) platform. This topic is of particular importance to the Commission as this sector is an important part of its Framework Programme 7 proposal.
The Commission, with the strong endorsement of the Council and Parliament, has identified life sciences and biotechnology as the next wave of the knowledge-based economy (after information technology). Europe "owns" a clear long-term European Strategy and Action Plan in support of the sector[1]. We see Industrial biotechnology as the application of modern biotechnology for the sustainable and eco-efficient industrial production of chemicals, materials and energy. It is based on the knowledge revolution that has taken place in the life sciences over the last two decades including genomics and bioinformatics, and exploits the renewable resources of agricultural and forestry production. Industrial biotechnology will not only impact the chemical industry itself but also other sectors such as energy, paper and pulp , polymers , enzymes, textiles and leather, animal feed, metals and minerals as well as waste treatment. Industrial biotechnology is seen as a major contributor to meeting Europe's Lisbon objectives and a driver of sustainable development.

Many Member States have already indicated the interest they attach to this area as several of them have recently launched national initiatives: in Austria, Belgium, Finland, Germany, the Netherlands, Sweden, and the UK, which will complement the Community action.
It is the interaction of life sciences and chemistry that will lead to innovative products and processes such as biodegradable plastics made from maize and biodiesel from oil seed rape. In the fine chemical sector up to 60% of products may use biotechnology processes by 2010. Air and water pollution could be reduced, energy use and raw material input lowered.
In the near future "biorefineries" will gradually and partially replace fossil-fuel based refineries in our countryside. They will utilize renewable resources grown on our abundant farm lands and they will not emit "greenhouse" gases or generate toxic wastes. They will reduce our dependence on finite and increasingly costly, fossil fuel reserves. And perhaps most importantly, they will meet our twin objectives of industrial competitiveness with societal acceptance. This is not an unrealistic scenario: in the US, the first of these integrated bio-refineries for the production of bio-degradable plastic are up and running!
But this potential will only be realized when there is full cooperation and consensus thinking between all societal stakeholders. It is vital that we engage in dialogue, to share the facts and information as well as to discuss the opportunities and also the concerns. Industrial biotechnology will only be applied when the economic and regulatory conditions are favourable in Europe. The progress that is being made in other OECD countries and in particular, the USA, Canada and Japan should be a challenge for Europe. In order to stimulate global companies to invest in this field here in Europe we must deliver a clear vision and road map of the way ahead. That is why the Commission has strongly supported the establishment of this sector as part of a Technology Platform, including such stakeholders as industry, academia, NGO's, and regulators to develop a clear vision statement and Strategic Research Agenda for Europe.

[1] "Life Sciences and biotechnology - A strategy for Europe", COM(2002)27

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Executive summary

Industrial or White Biotechnology is the application of biotechnology for the processing and production of chemicals, materials and energy. White biotechnology uses enzymes and micro-organisms to make products in sectors such as chemistry, food and feed, paper and pulp, textiles and energy. White Biotechnology could provide new chances to the chemical industry by allowing easy access to building blocks and materials that were only accessible before via intricate routes or not at all. White Biotechnology will have a considerable impact by using biomass as an alternative to fossil resources for the production of biochemicals such as biofuels and biopolymers. The use of renewable raw materials as alternative feedstock will reduce consumption of the limited fossil resources and lower European dependence on imports. Consequently this could contribute to our meeting of the Kyoto protocol targets for reductions in carbon dioxide emissions because of a more favorable CO_2 balance. At the same time, this technology may also boost the rural economy by providing new markets for agricultural crops and through the development of integrated biorefineries in farming areas. It needs to be guaranteed that raw materials can be bought at the cheapest price all over the world.

White biotechnology processes can help to make industrial manufacturing processes more environmentally friendly. They are performed in a contained environment, and have the potential to produce high yields of specific products with low energy use and minimal waste generation. The potential of white biotechnology is very promising and it is expected that white biotechnology will be a key technology contributing to the achievement of the Lisbon strategy to make Europe the most competitive and dynamic knowledge-based economy in the world. Also EUs major trading partners recognize the importance of white or industrial biotechnology for their industrial base and have already put in place well-funded long-term strategic plans. In the light of this, the following vision for white biotechnology has been established.

The stakeholders recognise that this Vision will only become a reality with the appropriate enabling political and economical environment stimulating research and innovation, entrepreneurship, product approval and market development. Such a supporting environment will help the industries to switch and produce eco-efficient products - when economically feasible - and benefit from the broad potential of white biotechnology to the European industry. In this type of activity it is of paramount importance to carry out extensive and careful life cycle analysis of the new developments and to compare it with alternative ones, since only a real eco-efficient technology can be implemented in a sustainable fashion.

Our vision for industrial or white biotechnology in 2025:

- **An increasing number of chemicals and materials will be produced using biotechnology in one of its processing steps. Biotechnological processes are used for producing chemicals and materials, otherwise not accessible by conventional means, or existing products in a more efficient and sustainable way.**
- **Biotechnology allows for an increasing eco-efficient use of renewable resources as raw materials for the industry**
- **Industrial biotechnology will enable a range of industries to manufacture products in an economically and environmentally sustainable way.**
- **Biomass derived energy, based on biotechnology, is expected to cover an increasing amount of our energy consumption.**
- **Rural biorefineries will replace port-based oil refineries wherever it is economically feasible.**
- **European industry will be innovative and competitive, with sustained cooperation and support between the research community, industry, agriculture and civil society.**
- **Green Biotechnology could make a substantial contribution to the efficient production of biomass raw materials.**

The action plan necessary to achieve this vision includes:
- The development of a strategic research agenda and road map.
- The removal of technical, economic, regulatory and implementation barriers.
- The involvement of the society in decision making via stakeholder dialogue.

1. Introduction to industrial or white biotechnology

Industrial or white biotechnology is making an increasingly important contribution to the development of a sustainable, bio-based economy. Industrial Biotechnology is the application of biotechnology for the processing and production of chemicals, materials and energy. It uses enzymes and micro-organisms to make products in sectors such as chemistry, food and feed, paper and pulp, textiles and energy. White Biotechnology could provide new chances to the chemical industry by allowing easy access to building blocks and materials that were only accessible before via intricate routes or not at all. White Biotechnology could have a considerable impact by using biomass as an alternative to fossil resources for the production of biochemicals such as biofuels and biopolymers.

Although healthcare ("red" biotech) and agriculture ("green" biotech) have dominated so far, "white" biotechnology is likely to become as important. Conventional processes in chemical and textile industries will be transformed, and biofuels will make an important contribution to our overall energy needs. Use of biotechnology to replace existing processes could make many industries more efficient and environmentally friendly and contribute towards industrial sustainability. Waste will be reduced, energy consumption and greenhouse gas emissions will be lowered and greater use will be made of renewable raw materials.

Instead of relying on high temperature and energy-intensive processes, white biotechnology achieves the same results using biological catalysts – enzymes – operating mostly at low temperatures. Feedstocks can be derived from fossil resources or be typically agricultural materials such as starch, converted first to simple sugars and then transformed into a wide range of end products via fermentation. To achieve this, a sophisticated range of scientific disciplines, including biochemistry, microbiology, genomics, proteomics, bio-informatics and process engineering is brought together under the umbrella of white biotechnology.

The basis of any biotechnological process is the use of enzymes or whole cell systems (typically micro-organisms). Mankind has made use of them for many hundreds of years in processes we consider traditional: using yeasts to make bread, beer or wine or lactic acid bacteria to produce yogurt, for example. These examples rely on using selected strains of naturally-occurring micro-organisms, but biotechnology now gives us the tools to improve their performance or modify biosynthetic pathways to make new products. A simple example, now well-established in the food industry, is the use of a pure form of the enzyme chymosin, made by bacterial fermentation, to produce the majority of our hard cheeses. Prior to this, the same cheeses were made using rennet, a material extracted from calves' stomachs, which contains exactly the same enzyme in an impure form.

Genetic modification (also known as recombinant DNA technology) allows micro-organisms to be tailored to give higher yields of particular chemicals, or even to produce new ones if genes are transferred from other organisms. Increasing the efficiency of the reaction allows more and more scope for replacing established conventional processes by cleaner, lower-temperature fermentation, in a contained environment. The highly specific nature of individual enzymes means that chemicals can be produced in a purer form, and biological processes not only require fewer chemical inputs, but also result in smaller and more manageable waste streams. Especially for non-food uses, Green Biotechnology could make a substantial contribution in the efficient production of agricultural raw materials such as cereals which, in contrast to oil, have become cheaper as farming yields have increased.

White biotechnology, although already successfully established in some sectors, is still in its infancy. Significant challenges still lie ahead if its power is to be fully harnessed to the needs of industrial sustainability while maintaining European industry's global competitiveness. The European chemical industry is still the biggest in the world, and has identified biotechnology as a key factor needed to maintain its future growth, innovation and competitiveness. The impact of this approach on this and other industrial sectors is considered in a later chapter.

There are a number of factors which should give us confidence in the future success of industrial biotechnology in Europe, including:

- European scientists currently lead the world in this field (ref 1).
- Europe has the world's largest chemical industry.
- The concept of sustainable development is more advanced in Europe than elsewhere.
- The recent expansion of the EU will provide a large increase in agricultural biomass suitable as an industrial raw material.
- Established white biotechnology products such as detergent enzymes have been generally accepted by society.

However, both the USA and Japan – currently Europe's major competitors in the field of white biotechnology – have clear intentions to expand their activities in this area and have committed significant funds to this. The US for instance is spending nearly ten times as much as Europe in this field. Also China and other emerging economies are making rapid progress in the area. The EU, on the other hand, has largely overlooked the importance of industrial biotechnology when setting research priorities, leaving an opportunity for our major economic competitors to take the lead. Europe is also characterized by a fragmented approach across the different Member States, every country having its own programme and initiative, with little or no EU-level coordination. This paper proposes a clearer and more focussed vision for European research in this vital field.

2. White biotechnology: socio-economic challenges

There are some important global trends which will drive changes in our technology base over the coming few decades, and nowhere are these more important than in Europe. The key challenges are:

- Limits to the quantities of fossil resources extractable at an economically-acceptable cost.
- Continuing increases in energy use, particularly in the transport sector.
- Continued world population growth over the next half century.
- Increasing societal awareness of the need to make structural changes to industry to ensure sustainable economic growth.

The result is a growing demand for improved security of supply and increased energy efficiency. For both goals, white biotechnology has a big role to play.

a. Raw material supply

Fossil resources – coal, oil and gas – are currently both the world's major sources of energy and the primary raw materials for chemicals manufacture. Our dependency has increased over the years as the European economy has grown, but this has caused few problems while prices have been generally low. Although economically exploitable reserves of oil (the primary feedstock for the chemical industry) have remained at a reasonably constant level as new discoveries are made and new extraction technologies brought into use, these reserves are not infinite. Concerns about security of supply have also contributed to recent large price increases. The economic facts of life dictate that more attention should be given to alternatives.

The alternative to conventional fossil feedstocks is biomass: agricultural raw materials such as cereals which, in contrast to oil, have become cheaper as farming yields have increased. Weight-for-weight, agricultural raw materials are generally less than half the cost of fossil fuels. Some, such as straw (which accounts for about half the biomass in a field of cereals) have a market value of only about 10% of that of oil. All are grown in large quantities in Europe. Better utilisation of these raw materials would bring great benefits in terms of security of supply and European self-sufficiency, as well as reducing net carbon emissions. On top of this, green biotechnology could make a substantial contribution in the efficient production of raw materials.

But biomass cannot at present be used to produce the full range of petrochemicals. The processes simply have not been developed or do not yet compete with the highly efficient ones developed and refined over the last century. This could change as the powerful tools of industrial biotechnology are brought to bear. Micro-organisms have the potential to turn crops into the full range of products made by today's chemical industry. Biotechnology is key to the transition to a more sustainable industrial and economic development in the longer term. However, it is necessary to carry out extensive Life Cycle Analysis in order to find out which strategy is the most eco-efficient. Biotechnology will be implemented at large industrial and commercial scale, if the products show an added-value and/or the processes prove to be advantageous to the known technologies.

b. An increased demand for raw material and energy

Not only are fossil resources finite, but the demand for them continues to increase. About 80% of available raw materials and energy are consumed by the affluent 20% in the developed world. The developing world – particularly China and India with their huge populations and rapid economic growth – will consume an ever-greater proportion. This will be driven by development, but also by population growth. The best predictions at present suggest a growth of the world population from the estimated 6.4 billion to around 9 billion in 2050.

With present living standards, this implies an increase of nearly 50% in use of raw materials; with the hoped-for development included, this would be many times more. White biotechnological processes – partially developed in Europe - would be a key factor in making the lives of the world's expanding and developing countries better in a sustainable and environmentally-friendly way.

c. The need for greater innovation and efficiency

Economies grow by producing existing goods and services more efficiently and by developing new ones. One driver of innovation is new technology, which often allows products to be made which simply were not possible previously. This has been true of electronics, where a continuous process of innovation has underpinned a large part of global economic expansion in the last few decades. It will be equally true of white biotechnology, where we can foresee the introduction of new biodegradable plastics, biofuels, nutraceutical food ingredients and novel pharmaceuticals.

Technological innovation can also drive efficiency improvements. Biotechnology can reduce energy use, improve utilisation of raw materials, and lead to lower waste. Biotechnology can not only create processes which result in less waste; in many cases it can use the waste itself as a raw material for further value-added processing.

Furthermore, Industrial Biotechnology can drive innovation within the chemical and related industries and open the doors to a range of new materials not accessible – or only with great difficulty and effort – through conventional methods. This will assist in reaching the Commission goals of transforming the European industry into the most dynamic knowledge-based industry in the world.

d. The demand for greater sustainability

Sustainability is a term which, in broad terms, covers the need to reduce our environmental impact and assure a prosperous future for generations to come. In other words: social, environmental and economic benefits should go hand in hand. White biotechnology could generate new employment, while reducing the impact of industry on the environment and creating further economic value. As we have already seen, industrial biotechnology can contribute to greater efficiency and reduced waste. It can also eliminate the use of some toxic or dangerous ingredients. However, one of the major long-term benefits will be its contribution to the programme of reductions in carbon dioxide emissions.

CO_2 levels in the atmosphere have been rising year-by-year, and it is believed this increase is largely due to Mankind's burning of fossil fuels. Carbon dioxide is present at low levels in the Earth's atmosphere, is produced by most living creatures during respiration and is essential for plant growth. However, it is also a major contributor to the so-called "greenhouse effect" and its increasing level is believed by many scientists to be driving a general increase in temperature, which will have potentially damaging effects.
Industrial biotechnology could allow for the increased use of renewable raw materials to replace fossil fuels, and could make a significant contribution towards the emissions-reduction targets agreed by the EU under the terms of the Kyoto protocol.

e. The changing consumer behaviour

Affluent European consumers are increasingly making purchasing decisions based on ethical, moral or environmental considerations. Such buying patterns also give signals to retailers and manufacturers that factors other than quality and price are important.

As environmental awareness grows, the demand for products from clean, green manufacturing processes will grow. This makes the products of industrial biotechnology even more attractive: they will be seen by many as premium products rather than like-for-like alternatives.

3. The impact of biotechnology on industry and agriculture

Biotechnology already has an established place in the food and pharmaceutical industries. In other sectors, there has been hardly any penetration sofar. However, the biological sciences have great potential to make both incremental efficiency improvements and to bring about radical change in a wide range of sectors. Some of the more important ones are discussed below.

a. The chemical industry

Global chemical production in 2004 amounted to 1,736 billion. The enlarged EU accounted for more than one-third of this, at 580 billion, making Europe the world's largest producer of chemicals, ahead of both the USA and Asia (ref 2).

In order to maintain this leading position, the industry has committed itself to biotechnology as one of the key technological pillars driving innovation, growth and future competitiveness. By identifying or modifying specific enzymes, setting up screening programmes and genetic modification, complex molecules for speciality chemicals will be produced relatively easily and in high yield. Biotechnology will even offer the possibility of making molecules impossible to produce through conventional chemical synthesis.

In other cases, the advantages will be in terms of efficiency rather than novelty. Lower cost raw materials can be converted in low-temperature, energy efficient processes using enzymes or micro-organisms to high-value end products with minimal generation of waste. There are few opportunities to use renewable raw materials in the current processes. Nevertheless, these processes have been developed and refined over a century or more and have reached a high degree of efficiency. In contrast, industrial biotechnology is still in its infancy and process development is at a relatively early stage. As the use of biological processing increases and experience accumulates, efficiencies will be further improved, accelerating the move away from conventional synthesis.
However, the use of Life Cycle Analysis tools to determine the most sustainable technology have to be applied, so that the new technology has chances to survive a large scale industrial implementation.

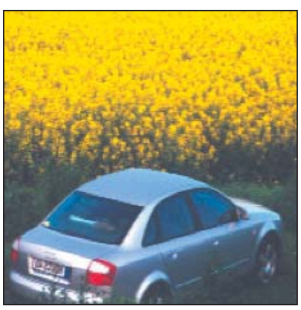
Of course, these developments will be in parallel with improvements to chemical catalysts and separation techniques, and greater recycling, but it is anticipated that biotechnology's contribution to the chemical sector will become increasingly important. According to a McKinsey study (ref 3) Industrial Biotechnology is expected to make significant inroads in all areas of the chemical industry by 2010, but particularly in the fine chemicals sector. They estimate that biological process will, at the end of the decade, account for between 10 and 20% of production across the whole industry, from a current level of 5%. For the polymers and bulk chemicals sector, the penetration of biotechnology is estimated at 6-12%, but for fine chemicals the figure is predicted to be between 30 and 60%. Continued growth of industrial biotechnology is expected beyond 2010. McKinsey estimate the current value of chemical products produced using biotechnology to be at least $50 billion and believe this could rise to $160 billion by the end of the decade.

These figures are impressive, but the exact rate of growth will depend on a number of factors. The relative prices of oil and agricultural raw materials, combined with the speed of technological progress, will be the major determinants. However, of equal importance will be the political will to support and develop this new technology base.

Biotechnology in action: bio-plastics

Most plastics are made by chemical synthesis, but biotechnology is now beginning to play a significant role in the sector. For example:

- Mitsubishi Rayon has incorporated an enzymatic process step at the beginning of their polyacrylamide production process. They use an immobilised bacterial enzyme (nitrile hydratase) to produce acrylamide from an acrylonitrile feedstock. The acrylamide is then polymerised using a conventional chemical process. This is one of the first examples of biological processing in the bulk chemicals industry. Not only does it eliminate the use of sulphuric acid, but if gives higher yield, less waste and lower energy costs. To add to these advantages, product quality is also better. More than 100,000 tonnes are produced annually by this route.
- Cargill started the production of poly-lactic acid (PLA) under the Natureworks™ name, by fermentation of cornstarch. Although having properties comparable to conventional polymers, which make it suitable for use in the packaging and textile industries, PLA is completely biodegradable. After use, cups and other articles can simply be composted with organic waste. Annual production has now reached 140,000 tonnes.
- DuPont manufactures a copolymer of 1,3-propanediol (PDO) and terephthalic acid under the Sorona® name. Sorona® has been produced using propanediol synthesized from petrochemical feedstock. Recently, DuPont and Tate & Lyle formed a joint venture to commercialize the production of PDO from glucose using a modified bacterium. A large-scale fermentation facility will be completed in 2006, and it will have a capacity of 90,000 tonnes of PDO annually. Bio-PDO is produced more economically than petrochemical PDO, it can be produced at higher purity - and in turn yields a superior polymer, and it reduces dependence on non-renewable resources



b. The pharmaceutical industry

Europe is also the world's leading region for manufacture of pharmaceuticals, accounting for 37.5% of global production, worth some €160 billion (ref 4). The USA and Japan produce 30% and 20% respectively of world pharmaceutical output. Biotechnology has a large part to play in this industry in general and in Europe's successful position in particular. Continued fostering of the key science and technologies underpinning the sector is essential if the leading position is to be maintained.

There are a number of ways in which biotechnology is used in the industry, in particular:

1. So-called Advanced Pharmaceutical Ingredients (APIs) are key building blocks for the synthesis of sophisticated drug molecules. One of the key reasons to favour a biological route for production is that many of the products come in either "left-handed" or "right-handed" forms (so-called chiral molecules), only one of which is physiologically active. Enzymes will selectively produce only the active form, whereas chemical synthesis typically produces a mixture which is difficult to purify.
2. Antibiotics (a global market worth 20 billion) are made almost exclusively by fermentation using specially-selected micro-organisms. Antibiotic molecules are so complex that conventional chemical synthesis has never been a realistic alternative. In some cases, semi-synthetic antibiotic molecules are made by chemical modification of the molecules produced by fermentation, to give improved performance. Even these modifications are now increasingly being performed using biotechnology, giving both economic and environmental benefits.
3. Biological processes are also key to the production of other major drugs. For example, the ACE inhibitor Captopril™, used to treat high blood pressure, is produced from two building blocks, each produced by fermentation (in one case by a yeast, in the other by a bacterium). Only the final step of linking the two intermediates is carried out using conventional chemistry.
4. Finally, complex bio-molecules such as antibodies, peptides and proteins are increasingly being used in medicine, and many of these are produced by culturing cells derived from micro-organisms, plants or animals.

c. The food, drinks and feed industries

This sector is one of the most important for Europe, employing over 2.6 million people (the third largest industrial employer) and having a turnover of 666 billion in 2001. The food and drinks industry processes over 70% of the crops grown in the EU (ref 5).

Fermentation has been used to produce food and drinks for many centuries – beer, wine, bread and yogurt in particular – so it is not surprising to find that this sector still has the greatest use of biotechnology. In particular, enzymes are now widely used in the processing of fruit juice, cheese, wine, edible oils and animal feed. In the case of the starch industry, production of a range of sweeteners is entirely carried out by enzymatic processing.

Other common food ingredients are also produced in this way, for example the artificial sweetener aspartame is made from two amino acids produced by fermentation, and erythorbic acid (an antioxidant) is made directly by fermentation. Other amino acids are produced in a similar way on a large scale: in particular glutamic acid, used as a taste enhancer in the form of mono-sodium glutamate has a production volume of more than one million tonnes annually, comparable with many important petrochemicals. In the animal feed industry the amino acid lysine is produced by fermentation, and work is underway to develop a similar process for methionine. Both are used as nutritional supplements in feed.

d. The pulp and paper industry

World-wide, 340 million tons of paper is produced from either virgin pulp or recovered paper. This is by far the largest use of renewable raw materials for consumer products. In the industrial context, biotechnology has been used at an early stage in the pulp and paper industry in order to clean effluents and combat microbial growth and microbial traces in products. In more relevant times, enzymes have been used to prepare wood chips before making chemical pulp, to assist in the bleaching of chemical pulp (xylanases)and reducing some of the problems when using recycled fibres in papermaking (dewatering). Non-toxic control of microbiological growth in internal water systems is another area where biotechnology is used.

Seen in a wider context, biotechnological tools have up till now not represented a real breakthrough. Proposed advantages in the areas of reduced energy consumption in producing mechanical pulp, bleaching of pulp and pulp refining still need to prove themselves in the industrial context. Nevertheless, progress in the areas of enzyme assisted processes and improved product qualities are likely to be a reality for example in the areas of fibre-surface modification and embedded functionalitites in paper surfaces or fibre composites. For these reasons, it is very important that the pulp and paper industry closely follows and takes advantage of the developments within the biotechnological field.

e. The textile industry

In the field of textiles, there are many applications of biotechnology, both existing and in development. Current uses of enzymes are for various finishing or modification processes of fibres and fabric, including:

- "Stone-washing" of denim.
- Brightening or toning down colours.
- Reducing pilling and improving the drape and feel of materials.
- Removal of peroxide after bleaching.

All these processes are cheaper or more environmentally friendly than the conventional chemical treatments.

Other processes are either newly introduced or still in development. For example, cotton scouring (the removal of non-cellulose components) is normally done with a series of chemical treatments. However, the recent introduction of an enzymatic process allows the scouring to take place at a lower temperature and gives a considerable reduction in waste water. Other developments in the pipeline include the use of enzymes on materials to improve dimensional stability, give flame-retardant properties, improve the dyeing process, prevent odour build-up and reduce bacterial growth.

A more fundamental application of biotechnology comes in the production of the polymers which are the basis of textile fibres. Cargill (NatureWorks) has launched a fibre – Ingeo™ – made from poly-lactic acid, with cornstarch as the raw material, and DuPont has an improved polyester fibre called Sorona™ on the market. Although currently made from two chemically-synthesised monomers, by 2006 it is planned that one of the monomers (propanediol) will be completely made from corn starch by fermentation. Making this biological route efficient and economic has been made possible by the modification of a single micro-organism to produce the monomer in a one-step fermentation process.

f. The detergents industry

Detergents are widely used by both consumers and industry, and after use they are discharged directly into waste water. When first introduced, these detergents contained high levels of phosphate, which was capable of polluting surface water. However, more recently, this phosphate has been successfully replaced by a product of biotechnology: citric acid. This is effective, fully biodegradable, non-toxic, low-cost and produced from renewable raw materials by fermentation.

The other major application of biotechnology in detergents is the use of enzymes. Detergents now account for about one-third of the total market for enzymes. Their use enables clothes to be cleaned effectively at much lower temperatures than were the norm ten or twenty years ago, thus saving considerable amounts of energy. Proteases – which attack protein-based stains such as blood or egg – are the most widely-used laundry enzymes, but amylases (to dissolve starch) and lipases (to remove fat) are also used. Further improvements are being made by enzyme manufacturers to increase the effectiveness of their ingredients at even lower temperatures, giving the prospect of yet more energy savings.

Another important class of detergent ingredients are surfactants, mainly produced from petrochemical feedstocks. Bio-based alternatives are available, which are more environmentally friendly and give better washing performance. However, they are currently more expensive than the conventional alternatives, so further development is required before they can become the preferred ingredient for the mainstream market.

g. The starch industry

The starch industry extracts starch from cereal grains and potato and processes it into products that are used as ingredients and functional supplements in food, feed and non-food applications. There are more than 600 different starches and starch derivatives, ranging from native starches to physically or chemically modified starches, liquid and solid sugars.

In terms of figures, the European starch industry annually processes 12.5 million tons of cereals and 10 million tons of potatoes, with an output of 9 million tons of starches and starch derivatives. The annual turnover amounts to about 7 billion euros and the industry invests approximately 150 million euros in R&D per year. The European starch industry sells 45% of its total production (3.6 million tons of starch equivalents) in non-food applications where starch products are used as binding agent, moistening/plasticiser agent, thickener, carrier, sweetener, gelatinising agent and nutritive substrate. Traditional non-food applications include, amongst others: paper and board, textile, adhesives, pharmaceuticals and cosmetics.

Given that starch is renewable and biodegradable, it is the most perfect raw material for the green and sustainable use of agricultural products. The industry has long been using enzymatic technologies for starch hydrolysis, technologies that are driving the development of white biotechnology. Today the starch industry is already involved in the manufacture of bio-products and plays a pivotal role in the development of green chemistry, as an alternative to fossil-fuel-based products, in the following sectors:

- Fermentation: for the production of citric acid, lactic acid, amino acids, organic acids, enzymes, yeast and ethanol;
- Chemicals: for the production of surfactants, polyurethane, resins, and biodegradable plastics (polylactic acid) for the packaging and textile industries, that compete with other polyesters on the market as well as fine chemicals and pharmaceuticals;
- Detergent industry: uses starch products for the production of biodegradable, non-toxic and skin friendly detergents; and
- Other "green" applications of starch products include binders, solvents, bio-pesticides, lubricants, bio-colorants and flavours etc.

Thanks to its state-of-the-art enzymatic technologies and to the renewable nature and variety of its products, the starch industry is already contributing to a better and more secure environment. In the future, it has strong potential to contribute towards the greater development of green chemistry products in Europe.

h. The energy sector

Biofuels are the focus of growing interest for transportation. Despite the significant efforts to reduce energy consumption in industry and home, travel by road and air continues to rise. Even though engines are becoming increasingly efficient, use of petrol, diesel and jet fuel is rising, seemingly inexorably. In the case of road transport, bio-ethanol and bio-diesel are beginning to have a significant impact on the mix of fuels in some countries. Mixed with conventional fuels, they can not only be used in standard engines without modification, but also improve combustion and reduce air pollution.

Ethanol (or ethyl alcohol) is produced in far larger quantities than any other fermentation product: 26 million tons in 2002. Of this, nearly two-thirds was used as fuel. Brazil leads the world, producing 8.7 million tons of bio-ethanol for fuel, followed by the USA with 5.7 million tons. The European Union, in contrast, made only 1.6 million tonnes in the same year, but has recently set ambitious new targets. By 2010, 5.75% of both petrol and diesel will comprise biofuels, rising to 20% in 2020 (ref 6).

The ethanol is currently produced from easily-fermentable agricultural materials such as sugar cane (in Brazil), sugar beet or cereal grains (in the USA and Europe). But there are vast quantities of waste materials such as straw, corn cobs or even waste paper available, and research is underway to modify micro-organisms to use these as an efficient substrate, or to make enzymes which can cost-effectively break down cellulose to easily-fermentable glucose. Success here would greatly improve the overall economics of ethanol production.

Bio-diesel is produced from vegetable oil (typically rapeseed oil in Europe) using a process of chemical modification. A biological process based on lipase enzymes would be a great improvement.

Biomass can also be fermented to produce methane (an efficient and established technology) or hydrogen (still in the development stage). Either of these could be a partial replacement for natural gas.

i. The agricultural sector

In the long term, white biotechnology is likely to have a great impact on European farming. This is because the farmland of the future could produce not only food and feed as it does currently, but also chemicals, industrial raw materials and fuels. A recent OECD report (ref 7) came to the conclusion that plant and animal wastes could become viable alternatives to fossil raw materials. However, this transformation will require encouragement by governments. The technology and its application has to be economically feasible.

European agriculture suffers from overproduction and requires a high proportion of the overall EU budget to subsidise it sufficiently for farmers to make a living. There are several factors leading to overproduction and/or low prices, including:

- Increasing yields due to improved varieties and management.
- Integration of the ten new Member States, whose large agricultural sectors are likely to become much more productive in the coming years.
- A relatively static population, with reduced food energy needs.
- More imports at world prices.

As the industrial biotechnology sector grows, increasing amounts of biomass will be needed as a fermentation feedstock. More sophisticated technologies will be developed to handle materials such as straw, which are currently largely wasted. At the same time, new crops may be grown to supply biorefineries with new feedstocks to produce new and value-added products.

Such developments will clearly, over time, have the potential to absorb all the crops we can grow, and to utilise all the agricultural waste which currently has no value. This could transform the lives of farmers by making their businesses profitable at world market prices without subsidies.

This would not only improve the economics of the biological production processes by providing raw materials at lowest cost, but also provide much-needed jobs in a generally depressed rural economy.

4. The environmental impact of White Biotechnology

White biotechnology will continue to make inroads in some sectors for economic reasons. However, in many cases the main driver for change will be the reduced environmental footprint of biological processes. As the “polluter pays” principle becomes more established, effluent streams add costs to a process rather than being a purely external factor. Of course, the processes themselves still have to be efficient and economic, but often both cost and environmental benefits come together.

The OECD, in a recently-published report on biotechnology and sustainability (ref 8), analysed a number of case studies across a range of sectors, including all those reviewed so far plus mining and metal refining. These studies confirm that biotechnology can reduce both costs and the environmental footprint of industrial processes. Some cases showed a reduction of 10-50% in capital and operating costs, while in others water and energy use decreased by 10-80% and the use of non-aqueous solvents was drastically reduced or eliminated. The achievement of such environmental benefits at the same time as reducing costs is a clear win-win situation, and there will be many other opportunities as technologies continue to develop and be applied.

As well as improving the efficiency and environmental performance of existing processes, examples are reported which show that biotechnology has enabled the development of new products whose properties, cost and environmental performance could not have been achieved using petrochemical feedstocks and conventional chemical processing. Taken as a whole, this report shows convincingly that biotechnology can fulfil the need for greater environmental protection without jeopardising economic growth. Indeed, in many cases, the ability to reduce costs will prove a positive boost to economic performance. The continued penetration of biological processing across a wide range of industrial sectors will provide a sound basis for progress towards a more sustainable production base.

The Öko-Institute in Germany, together with EuropaBio and other partners, has also collected a number of case studies in a report published in 2003 (ref 9). They quote, for example, the following:

- The move to bioprocessing for production of vitamin B_2 resulted in a 40% cost reduction and only 5% of the previous level of waste.
- A similar change to a biological production process for antibiotics combined the original ten-stage process into a single step, giving a 65% reduction in waste, using 50% less energy and halving the cost.
- Use of enzymes for textile processing reduced energy needs by 25% and gave 60% less effluent.
- Production of bioplastics derived from cornstarch reduced the inputs of fossil fuels by 17-55% compared to the conventional alternatives.
- The use of biofuels and conversion of chemical processes to use agricultural feedstocks gives significant reductions in net carbon emissions.

This ability of biotechnology to provide environmental benefits while reducing costs and so improving competitiveness has been recognised by the European Commission. In the 2002 Environmental Technologies Action Plan (ref 10), industrial biotechnology is acknowledged as having major potential. But this recognition of the potential has to be translated into action if the pace of change is to increase and the long-term sustainability of European industry is to be guaranteed (ref 11).

Our major competitors are also aware of biotechnology’s importance. For example, similar reports have also been published in the USA (refs 12 and 13). In “New biotech tools for a cleaner environment”, the implications of greater use of biotechnology for sustainable production and environmental improvement are discussed in detail. The conclusion is that large reductions in energy use, fossil fuel raw materials and both waste and carbon dioxide emissions are possible. In their own words “Industrial Biotechnology has the potential to greatly improve pollution prevention, control and innovation strategies and could revolutionize current manufacturing and environmental protection strategies… Industrial Biotechnology is creating a new industrial revolution where man and DNA are working hand in glove to green the industrial landscape”.

Such a vision is laudable. However, if this is put into practice by our major trading partners while we fail to grasp the nettle and take the step from fine words to reality, Europe will have failed to tackle both environmental protection and industrial sustainability in a coherent way.

5. International dimensions

a. US strategy

The United States sees the development of industrial biotechnology as a key strategic objective. The intention is to move towards a bio-based economy, where production and use of energy and industrial products has been fundamentally changed. Initially, the key driver was energy security, to reduce America’s dependence on the supply of crude oil from unstable regions of the world. However, the commitment entered into for one reason has now opened up a range of other possibilities, and the US has now shifted its focus to include bio-based chemicals manufacture and the creation of a domestic bio-industry. The main targets at present are power generation, biofuels for transportion and bioproducts. Specific targets for biomass use are enshrined in the Biomass R&D Act 2000, as summarised in the table below:

Share of production from biomass	2001	2010	2020	2030
Power generation	2%	3%	4%	5%
Biofuels for transportion	0.5%	4%	10%	20%
Bioproducts	5%	12%	18%	25%

These are not targets to be left on the shelf: the USA has a clear commitment to their achievement. There are two key elements which make their success almost certain:

1. High-level political commitment and broad R&D support.
2. Promotion of market pull by financial incentives and standard setting.

Political commitment has emerged quite rapidly in the last ten years, primarily due to high-level debates about the country’s increasing dependence on foreign oil. The first major policy initiative to emerge from this debate was President Clinton’s Executive Order of 1999 (ref 14), setting a goal of tripling the use of bio-based products and energy from biomass by 2010 and establishing a permanent council to develop a detailed research programme to be presented annually as part of the Federal budget. Legislation was then introduced, including the Biomass R&D Act 2000 already referred to, to create a focus on producing energy and value-added products from a wide range of agricultural and forestry residues.

Continued commitment has taken this a step further with the recent publication of a “Roadmap for Biomass Technologies in the United States” (refs 15 and 16). This was an initiative coordinated by the government-sponsored Biomass R&D Technical Advisory Committee, a body bringing together a wide range of stakeholders (including academia, industry, government, farmers and NGOs) to provide guidance on how to make the aspirations a reality. While describing the great potential for the use of biomass to produce both energy and a range of products, the report also highlights the challenges and presents a plan for a focused, integrated and innovation-driven R&D effort. It also covers ways in which societal approval can be gained, by public outreach programmes, and gives examples of market incentives likely to be necessary. Finally, it provides policy recommendations to remove barriers (including existing regulatory obstacles) which could impede the industrial use of biomass in the USA.

This planning has been backed by an impressive spend on research and development. Starting with a focus on interdisciplinary research and applied R&D, the programme now includes a range of public-private partnerships and large-scale demonstration projects. In 2003, the US Department of Energy (DoE) spent $125 million on biomass utilisation research, and the Department of Agriculture (USDA) contributed a further $259 million.

In addition, the DoE is spending nearly $100 million in support of biorefinery demonstration projects. These will integrate the conversion of biomass into fermentable sugars and their subsequent use to produce value-added products. At the same time, the necessary logistics of collection, storage, transport etc are being studied. The US government is working closely with industry on these initiatives, involving agro-industrial and chemical companies such as Cargill, Dow and DuPont and specialist biotechnology companies including Genencor, Novozyme and Diversa. Finally, the DoE has recently commissioned a report entitled "Industrial bioproducts: today and tomorrow" (ref 17), highlighting both the huge opportunities offered by biorefineries and the obstacles to be overcome.

This effort is already paying dividends: the demand for corn-derived chemical products is predicted to grow at an annual rate of over 13% and total bioproduct production is expected to reach 30 million tonnes annually by 2020.

While the government continues to provide a high level of backing for industrial biotechnology research, it also supports market development via a range of incentives. For example, the 2002 Farm Bill mandates federal procurement of bio-based products when they are available and are equivalent to fossil-based alternatives (the "buy bio" programme). This is being facilitated by the setting of procurement standards and targets for federal government purchase of bio-based fuels, power and bioproducts. Other standards (e.g. the renewable fuels standard) will provide market pull, and farmers are given incentives to grow crops for industrial use.

The US bio-ethanol industry is continuing to grow at a rate of over 10% annually, aided by tax breaks to petrochemical companies which blend ethanol with their petrol. The country now produces over seven million tons of bio-ethanol annually, 92% of which is used as fuel. It is mainly produced from corn, and now consumes 7% of the domestic maize harvest.

All the signs are that this is a long-term commitment by the USA to develop a large, sustainable, biomass-based sector of the economy by development and application of the tools of industrial biotechnology.

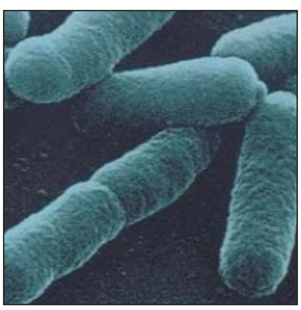
b. Industrial biotechnology in Japan

The Japanese were amongst the earliest adopters of industrial biotechnology, due no doubt to the familiarity of processing with micro-organisms in a country with a long tradition of making fermented food. They have established a world-class fermentation industry, particularly in specialised markets such as amino acids. However, Japanese companies were also among the first to use biocatalysts, and Mitsubishi Rayon was the first company to introduce enzyme technology to produce acrylamide. This is produced in a purer form using only 20% of the energy of the conventional chemical synthesis, and the technology is now in use all around the world. Other Japanese companies, for example Kaneka, pioneered the manufacture of pharmaceutical building blocks using industrial biotechnology.

Overall, Japanese bio-industry was estimated to have a turnover of $15 billion in 2003, 26% being in the chemicals sector. Clearly, Japan has a strong position in industrial biotechnology. However, the country does not have a strong agricultural base and does not have the capacity to supply home-grown biomass to industry at a competitive price to fuel future growth in the bio-processing sector. This is an important consideration, because most agricultural products are bulky and costly to transport. This may tend to focus growth in bio-processing in Japan towards higher-value, niche sectors rather than bulk chemicals and biofuels.

An action plan covering biotechnology strategy guidelines was published by the government-sponsored Biotechnology Strategy Council in 2002 (ref 18). This deals with three strategic strands:

- Achieving health and longevity
- Food safety and functionality
- A sustainable society



In the next years to 2007, Japan aims to double its funding of biotechnology research and triple the number of researchers involved. A significant proportion of this will be directed towards industrial biotechnology: in contrast to the situation in Europe and the USA, Japan puts significantly more research money into biotechnology for health-oriented foods, fine chemicals, the environment and power generation than for healthcare biotechnology.

c. The situation in China

China has a similar tradition to Japan of producing fermented food, although not on the same scale. On the industrial side, production using biological processing is increasing, albeit from a low base. The China Centre for Biotechnology Development estimates total sales of products from biotechnology to be $1.2 billion. However, China has great potential for future expansion of this sector. Not only does it have the required agricultural infrastructure, but its economy is growing rapidly.

The government is investing in major research in biotechnology, coordinated by the Ministry of Science and Technology. On the production side, there has recently been significant addition of large-scale fermentation capacity for bulk chemicals such as citric acid and ascorbic acid, largely for export. A number of large-scale bio-ethanol plants have also been built; the ethanol is to be mixed with petrol for the rapidly-growing market for cars. The Jilin plant, commissioned in 2003, is the world's largest, with a production capacity of 600,000 tons a year.

Although currently far behind Europe, the USA and Japan in use of white biotechnology, China's rapid growth and huge agricultural base are likely to make it a very significant player in the sector in years to come.

d. Other developing countries

Most developing countries simply do not currently have the resources to develop and use industrial biotechnology on their own. But, in the longer term, it is these countries which may be some of the greatest beneficiaries. Many of them have a large agricultural base which could become much more productive in the future. Biomass from this could be the feedstock for a range of new industries, by-passing completely the way industry developed in Europe, and avoiding many of the environmental problems associated with this. Extra world demand for agricultural produce – driven by population growth, increasing affluence and greater use of biomass by industry – will also tend to drive up commodity prices and directly benefit developing country farmers.

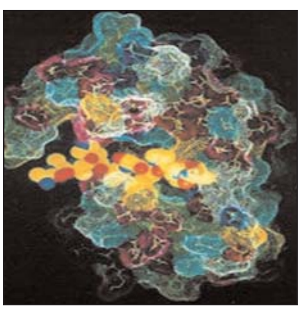
Expanding and developing countries rely almost totally on renewable resources for both energy and materials, but their efficiency of utilisation could be improved considerably and their harvesting made more sustainable. For example, in addition to the numerous benefits in terms of health and labour, replacement of individual wood fires by energy generated more efficiently from biomass in local power stations would reduce the current level of deforestation.

Greater self-sufficiency in energy and industrial raw materials would encourage economic growth and reduce many countries' vulnerability to currency fluctuations and supply problems for imports. If Europe continues to develop its strong base in industrial biotechnology, it will be in a good position to share technology with developing countries.

6. Current European policy and strategy

Recently, Commissioner Potočnik and the new European Commission have given a lot of importance to "Knowledge for Growth": to the interplay between education, research and innovation, and to the need for adequate regulatory, financial and other conditions. To quote him: "*Our main, if not only, factor of competitiveness in a globalising economy is knowledge. Not knowledge for the sake of knowing. But putting knowledge to work to create economic success and address challenges*" (ref 30).

Also, a number of policy initiatives have been taken which support white biotechnology in a broad sense. Underpinning everything is the so-called Lisbon agenda; the commitment by the European Council at their meeting in Lisbon in March 2000 to the objective of making Europe the most competitive and dynamic knowledge-based economy in the world, capable of sustained economic growth, with more and better jobs and greater social cohesion. This is a laudable aim, which can only be achieved by focussing on and supporting key growth sectors – including industrial biotechnology – as our major trading partners are already doing.



Building on this commitment, a number of more detailed policy statements have been produced:

- The "European Strategy for Sustainable Development" of June 2001 (ref 19) focuses on the development and wider use of new environmentally-friendly technologies.
- The "6th Environmental Action Programme" in 2002 identified key environmental improvement targets (ref 20).
- A report published at the same time on "Environmental Technology for Sustainable Development" (ref 21) coupled with an

"EU Action Plan for Environmental Technologies" sets out specific proposals. The Action Plan specifically mentions white biotechnology as a key example of a promising technology which can contribute to sustainable manufacturing.

A key policy document for the sector is the January 2002 publication "Life Sciences and Biotechnology – A Strategy for Europe" (ref 22), which sets out a 30-point action plan. This strategy is wide-ranging, covering biotechnology in healthcare and agriculture as well as industry and addressing ethical, regulatory and economic aspects. The potential for biotechnology to deliver more efficient processes using renewable raw materials, and thus decouple economic growth from environmental impact, is clearly recognised. The strategy has grown out of the acknowledgement by the European Council at the Lisbon and Stockholm summits that biotechnology is one of the key enablers of future competitiveness in a knowledge-based economy. It was endorsed by the Member State heads of government at the Barcelona summit earlier in 2004.

The challenge now is to translate this strategic commitment into a workable and well-supported plan which can deliver the benefits of biotechnology to important industries – including chemicals, pharmaceuticals, agriculture and waste treatment – to enable them to make a contribution to Europe's sustainable future competitiveness.

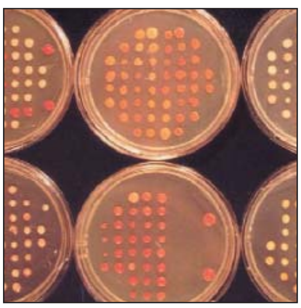
One important pillar of the plan must be support for research and development. The most important instrument for this is the series of Framework Programmes. The previous Framework Five (FP5) devoted considerable attention to industrial biotechnology. Unfortunately, the current FP6 makes little explicit mention of industrial biotechnology, and therefore fails to provide a coherent framework to encourage their development. Only two of the seven thematic areas are relevant: area 3 (nanotechnologies and nanosciences, knowledge-based multifunctional materials and new production processes and devices) relates to bio-processing, and area 6 (sustainable development, global change and ecosystems) focuses on clean energy and energy efficiency. This lacks the focus and coherence of the US approach, and we can only hope that it will be corrected in the forthcoming Seventh Framework Programme.

7. European Industrial Biotechnology: a Vision for 2025

Europe faces a number of key challenges and opportunities. Continued economic growth for the benefit of the former block of 15 existing Member States is made even more important by the need to integrate the 10 new Members and bring their citizens' living standards up to the Western European average. This goal can only be achieved by employing the strategy of the new European Commission "Knowledge for Growth": to shift rapidly into a knowledge-based society in which the knowledge is used in order to gain economic growth and increase the competitiveness of the European Industry. This should happen by respecting the environment and ensuring a sustainable development for the European society. Industrial Biotechnology can provide both: unprecedented economic growth based on innovation and an environmentally benign technology.

For these reasons, there has to be a transition from a society based on the ever-increasing use of fossil resources to a more sustainable one where renewable resources make a growing contribution to our energy and material needs. Industrial biotechnology is a key underpinning technology which can make this possible. **The development and use of industrial biotechnology is essential to the future competitiveness of European industry and provides a sound technological base for the sustainable society of the future.**

In our vision, Europe will have made substantial progress towards a bio-based society by 2025. In particular, the European chemical industry will regard biotechnology as an essential part of its process development toolkit, thus significantly enhancing its technical competence and competitiveness. **By the year 2025, an increasing number of chemicals and materials will be produced using biotechnology in one of its processing steps. Biotechnological processes are used for producing chemicals and materials, otherwise not accessible by conventional means, or existing products in a more efficient way.**



Biotechnology will also be used for the conversion of agricultural feedstocks into a wide variety of fine and bulk chemicals, bioplastics, biofuels, pharmaceuticals etc. At the same time, these biological processes will result in significant cost reductions, lower waste and energy use and a major reduction in our dependence on increasingly expensive, imported petrochemical feedstocks. **In other words, biotechnology will allow for an increasing eco-efficient use of renewable resources as raw materials for the industry.**

In the future, and especially for non-food uses, **Green Biotechnology could make a substantial contribution in the efficient production of agricultural raw materials** such as cereals which, in contrast to oil, have become cheaper as farming yields have increased.

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The change of raw materials and process technologies will also change our industrial landscape. **Rural biorefineries will replace port-based oil refineries wherever it is economically feasible.** These factories of the future will integrate agriculture and a part of the transformed chemical industry, converting biomass into a range of value-added products. Integration may even progress to the point where the biorefineries produce food, (bio)chemicals and energy from a single feedstock. Agriculture in their hinterland will be supported and the rural economy developed. European agriculture will be less dependent on subsidies, and roughly one-third of its output will be used for non-food applications.

Industrial safety will be improved: **industrial biotechnology will enable a range of industries to manufacture products in an economically and environmentally sustainable way.**

Last but not least, the EU is very dependent on imported oil and gas for power generation. As recent experience has shown, the price of both can be very volatile and, in the longer term, can only increase as demand for finite amounts of economically extractable fossil resources continues to grow. Biofuels will comprise an increasing percentage of the fuel our cars run on, and renewable resources will be used to generate an increasing amount of "green" electricity. **By 2025, Biomass derived energy, based on biotechnology, is expected to cover an increasing amount of our energy consumption** (ref 23).

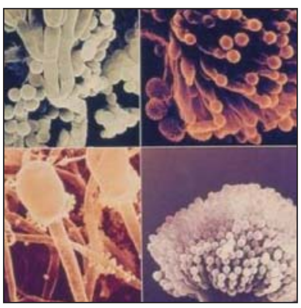
In 2025, the manufacturing industry will still be a cornerstone of a dynamic and prosperous European economy. Industry will have become more globally competitive while reducing its environmental footprint. European society will have made significant progress towards long-term sustainability, while strongly reducing its dependence on fossil resources. **European industry will be innovative and competitive, with sustained cooperation and support between the research community, industry, agriculture and civil society.**

This vision will only become a reality with the appropriate enabling political and economical environment stimulating research and innovation, entrepreneurship, product approval and market development. Such a supporting environment will help the industries to switch and produce eco-efficient products – when economically feasible - and benefit from the broad potential of white biotechnology to the European industry.

In sharp contrast to this positive outlook, if Europe does not commit itself to develop this new technology, our current major trading partners and rapidly-developing economies such as China will forge ahead with investments in industrial biotechnology. They will out-compete Europe, which will gradually become an economic backwater, to the detriment of its citizens' prosperity and quality of life. The aspirations of the Lisbon agenda will have been empty rhetoric.

In summary:

- Europe faces multiple challenges: while maintaining and improving our competitive position in the global market place, economic growth must be balanced by the need to care for the environment, improve quality of life and assure the prosperity of future generations.
- We envisage a future where these challenges of transition to a sustainable society are met by large-scale development and application of white biotechnology. The tools of biotechnology will be used to reduce the use of hazardous substances, minimise energy consumption and waste generation and reduce our dependence on fossil resources.
- To achieve this vision, certain specific actions are essential:
  - Development of a strategic R&D agenda and roadmap with a clear focus on industrial biotechnology.
  - Removal, as much as possible, of barriers to introduction of biotechnology in industry, whether technical, economic, regulatory or societal.
  - This transition must be facilitated by ongoing constructive stakeholder dialogues to ensure that society as a whole is fully engaged in the decision making process.



8. Developing a Strategic Research Agenda

White biotechnology is a relatively new discipline and therefore immature: there are major areas of knowledge still to be explored. This presents a bottleneck to greater exploitation, but also offers a tremendous opportunity for further research. As a first step on the road to increased industrial use of the biological sciences, a strategic research agenda covering both basic and applied science is needed. Both are essential: basic science to develop our fundamental knowledge base, and applied science to use this knowledge to introduce innovative products and processes.

Industrial biotechnology is by nature a multi-disciplinary area, comprising biology, microbiology, biochemistry, molecular biology, chemistry, process engineering etc. This can be a strength, since combining knowledge from different scientific disciplines can create unexpected synergies. However, it can also be a weakness if the various disciplines remain fragmented and unconnected. Good contacts and coordination, including the formation of multi-disciplinary project teams, are therefore essential if industrial biotechnology is to be a real driver of innovation and sustainability in Europe.

The strategic research agenda must include the following main research areas:

- **Novel enzymes and microorganisms:** The search for novel enzymes and microorganisms from specific or extreme environments, whether by direct isolation or mining of metagenomes, will create an expanding range of biological processes for industrial use.

- **Microbial genomics and bioinformatics (systems biology):** Understanding the activities of microorganisms requires more knowledge about their genetics. With good genome mapping, we would be in a better position to identify desirable or more efficient metabolic pathways, and adapt them to manufacturing processes.

- **Metabolic engineering and modeling:** As our understanding of microbial metabolism improves, there will be more opportunities to modify bacteria, yeasts, and other fungi to produce new products and increase yields.

- **Biocatalyst function and optimization:** Techniques such as protein engineering, gene shuffling, and directed evolution will enable the development of enzymes bettersuited to industrial environments. These tools also allow for the synthesis of new biocatalysts for completely novel applications.

- **Biocatalytic process design:** The use of industrial biotechnology processes in industrial environments, possibly integrated with conventional chemistry, requires particular attention to biocatalytic process design. The creation of engineering knowledge in industrial biotechnology is a prerequisite to its successful introduction in industry.

- **Innovative fermentation science and engineering:** Processes will continue to be improved, as knowledge of microbial physiology and nutrition is combined with better understanding of bioreactor performance and improved equipment design.

- **Innovative downstream processing:** Once made in a bioreactor, products have to be efficiently recovered and purified if the product quality and economics are to be acceptable. Downstream process design is therefore an integral part of successful innovation.

The research agenda should certainly include two important key aspects:

- **Performance proteins and nanocomposite materials:** The combination of proteins and inorganic materials, often with specific nanoscale geometry, offers new and innovative product areas such as self-cleaning, self-repairing, and sensing products. This is a good example of a new and fertile scientific interface which must be explored by multidisciplinary teams.

- **Integrated biorefineries:** At a manufacturing scale, there has to be an efficient integration of the various steps, from handling and processing of biomass, fermentation in bioreactors, any necessary chemical processing, and final recovery and purification of the product. The level of sophistication and control built up over many years in the chemical industry needs to be achieved also in biorefineries.

Once the strategic research agenda has been developed and agreed by the stakeholders, it needs to be supplemented by an action plan based on the following principles:

- **Long-term planning and continuity of research funding**: If white biotechnology is to fulfil its promised contribution to Europe's future global competitiveness and industrial sustainability, the commitment to underpinning R&D must be long-term and guaranteed. In this respect, the lack of explicit focus in the area in the sixth Framework Programme is very disappointing. Scientific expertise has to be built up and nurtured; it cannot be turned on and off at will. Far greater emphasis on industrial biotechnology in the seventh and subsequent Framework Programmes, in line with similar commitments by our trading partners, is therefore essential.
- **Coordination of European and national objectives and policies**: Too much research is currently carried out in an uncoordinated way by Member States. If we are to achieve the maximum return on research funds and not duplicate effort, national programmes should be run as part of the over-arching European research agenda.
- **Promote inter-disciplinary cooperation and overcome fragmentation**: Given the multi-disciplinary nature of industrial biotechnology R&D, it is vital that the various activities are not left as isolated research "islands". Bringing together groups of chemists, biotechnologists, engineers etc into clusters will provide critical mass, allow them to share support facilities and encourage cooperation and synergy. Such clusters can then, over time, grow into global centres of excellence.
- **Facilitate technology transfer**: High quality research is of little value if it does not contribute towards innovation and economic growth. All possible steps should be taken to facilitate good working partnerships between universities and industry, including the setting up of public-private partnerships.
- **Focus on overcoming bottlenecks in the technology**: Despite rapid progress in some areas, exploitation of new technologies can often be delayed by bottlenecks in a few key areas. Good overall coordination of the programmes should allow early identification of these problem areas and permit the focus of expertise into concentrated, ambitious projects in order to remove the bottlenecks.

9. Developing an Action Plan to encourage Implementation

As with any new technology platform, there are barriers to the effective deployment of biotechnology in industry. These fall into four main categories: technical, economic, regulatory and technology transfer.

- **Technical barriers**: By this we mean that the technology is relatively immature, and therefore at a disadvantage when compared with, for example, conventional chemistry. It is more difficult to assess the benefits of implementation, and risks are higher, or at least appear so. There is also the problem of biomass availability. Although physically available, we currently lack systems for collecting, handling and storing agricultural materials for non-food use.
- **Economic barriers**: High capital investment is often required for new processes, and this may be a disincentive, even when operating costs are lower. Manufacturers may find it preferable to continue to run conventional processes, using an existing plant which is fully depreciated. Incentives such as corporate tax advantages or investment tax credits are therefore needed to encourage switching. There also needs to be a high degree of certainty that there will be a market for the products from the new processes. Another barrier is the high price of some raw materials because of the Common Agricultural Policy. Developments such as the planned reform of the sugar regime should help in making European-grown commodities available at world market prices.
- **Regulatory/policy barriers**: Regulation can often be a barrier, either when new products have to be fitted within existing legislation for which they are not fully compatible, or when stringent, precautionary regulation makes compliance unfairly costly. A more balanced risk/benefit approach to regulation, rather than a purely risk-centred philosophy, would be beneficial for both industry and society. On the intellectual property front, the lack of an affordable harmonised European patent system is a severe disadvantage for European science and innovation. Finally, active supporting policies should also be encouraged: obligations to use biodegradable packaging or for processes to meet certain environmental criteria, for example. In this respect, development of a unique and generally-accepted eco-efficiency assessment tool would be of great benefit.
- **Technology transfer barriers**: Introducing new technologies to established industries can be very difficult, not only because of the barriers already mentioned, but also because of lack of awareness and expertise. This could be overcome by improving the qualification of the scientific-technical staff and increasing interdisciplinarity in education. Companies

that have successfully integrated industrial biotechnology into their operation may organise visits to demonstrate success. Also basic knowledge about biotechnology must be inserted as part of the curriculum of chemistry, environmental sciences, engineering, physics, but equally so in the social sciences.

10. Organising a dialogue with society

Experience with other areas of technology – genetically modified crops and animals for example – shows that it can be difficult for society as a whole to accept innovations. And yet, increasingly, it is difficult for Europe to decide to reject a technology or product which is accepted elsewhere and becomes a normal component of international trade. Even in the case of genetically modified crops, millions of tonnes of GM soy are imported annually to feed European farm animals.
On an objective level, we know that industrial biotechnology has great potential to solve some of the difficult problems facing modern societies: environmental degradation, climate change, reliance on imported oil and gas, etc. However, we cannot assume that the average citizen will necessarily be comfortable with widespread use of biological processes by industry, particularly in instances where genetically modified micro-organisms are used (although in contained environments). In order to assure society's consent, society must be involved in an open dialogue at an early stage.

Education is an important factor. It is desirable that future generations should be more scientifically literate as science forms the basis for sophisticated modern societies to function. Both teachers and students should be encouraged to become more familiar with basic science in general and with biotechnology in particular. Awareness and knowledge can also be promoted by making information available in brochures and through other channels, and by encouraging visits to factories operating biological processes.

But education is by no means the entire answer. Increasing familiarity does not automatically result in increasing acceptance. Dialogue should be established by as many means as possible, including the following possible actions:

- Establishment of a "science and society" strand to R&D programmes on industrial biotechnology. These should be adequately funded and supported, and fulfilment of certain outreach objectives should be mandatory.
- Carrying out at an early stage a consultative exercise (involving scientists, industrialists, politicians and other decision makers, regulators, social scientists, ethicists, NGOs and the media) to forecast likely scientific and commercial developments and the public and policy response to them. A possible model would be the Commission's consultation and conference on genetic testing (ref 24).
- Holding a major conference on industrial biotechnology, organised by the Commission, similar to those organised by the European Group on Life Sciences (ref 25).
- Producing for wide circulation to non-specialists a series of high-quality, concise, authoritative briefing papers on various aspects of white biotechnology. These should be in non-technical language and include case studies. See, for example (ref 26).
- Establishing a white biotechnology communication programme, bringing in speakers from overseas (particularly developing countries) to speak about the applications and implications of the biological sciences in their own countries (ref 27).

11. Towards a European strategy for industrial biotechnology

Considerable benefits will accrue across the whole enlarged European Union as industrial biotechnology begins to be introduced in a coordinated way. Currently only technologically-advanced Member States with some history of using biotechnology in manufacturing have begun to reap the benefits of innovation and environmental improvements. Spreading these gains to all must be done on an EU basis.

Industrial biotechnology not only has a big direct impact on manufacturing processes, it will also play a major role in rural development. At the same time, its effects cut across a range of sectors which are already subject to European framework legislation, including industry, research, the environment, agriculture and energy. To assure successful coordination at a

European level, the Commission would be well placed to bring together the various policy strands into a cohesive policy framework which takes the specific needs of white biotechnology fully into account. To support the development of a consistent set of policies, a multi-Directorate General task force could be formed, encompassing DGs Research, Industry, Environment, Trans-European Networks, Agriculture and Regional Policy. To ensure proper financing, the European Investment Bank and the European Investment Fund would be expected to be closely involved.

To complement the centralised Commission initiative, the creation of a reference group for white biotechnology with Member States would ensure greater coordination of national programmes and help to spread best practice. International cooperation on industrial biotechnology could also be fostered through existing mechanisms such as the Transatlantic Dialogue and the EU-Japanese Business Dialogue.

The Commission has established a helpful new mechanism for fostering important areas where Research, Technology and Development are key to addressing major economic, technological or societal challenges: the **Technology Platform (TP)** (ref 28). These can enable the formation of strategic alliances to foster public-private partnerships between the research community, industry and policy makers. The intention is to stimulate effective investment in R&D, accelerate innovation and remove barriers to growth. At the same time, they provide an important output to national and EU policy makers.

Participation in a Technology Platform should include the research community, industry (including SMEs, private research and technology transfer firms), public authorities (as policy makers, regulators and purchasers), the financial community, consumers, civil society groups and other relevant stakeholders. The expectation is that the Technology Platform should:

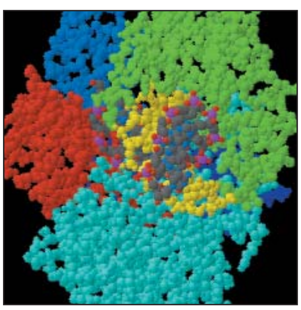
- Give a common vision which contributes to coherent policy making.
- Overcome obstacles at all levels to accelerate the market penetration of new technologies.
- Stimulate knowledge and innovation, so increasing productivity and competitiveness and making the investment climate more attractive.
- Encourage public debate on risks and benefits to facilitate technology acceptance.

In June 2004, the **Technology Platform for Sustainable Chemistry** was set up (ref 29), with three pillars:

i. Industrial Biotechnology
ii. Materials Technology
iii. Reaction and Process Design

Within this framework, the Industrial Biotechnology section will ensure a coherent policy framework and the most effective use of R&D resources. Being part of the broader Sustainable Chemistry Platform will guarantee that biotechnology will be properly integrated in the chemical industry. Importantly, the Technology Platform goes beyond merely fostering cooperation at the research stage, but also encourages downstream collaboration to bring technology to full commercialisation. The Platform includes:

- A **strategic alliance of stakeholders**. There is an incentive for stakeholder groups to overcome internal divisions and present united views in order to interact most effectively with political institutions and other interest groups.
- A flexible, **comprehensive governance structure** taking full account of the roles of different stakeholder groups and range of activities both at national and European level.
- A **coherent strategic research agenda** for the technology.
- An **action plan** including policy measures to provide incentives and reduce barriers to the introduction of industrial biotechnology and to raise public awareness and encourage public acceptance of its increasing role.



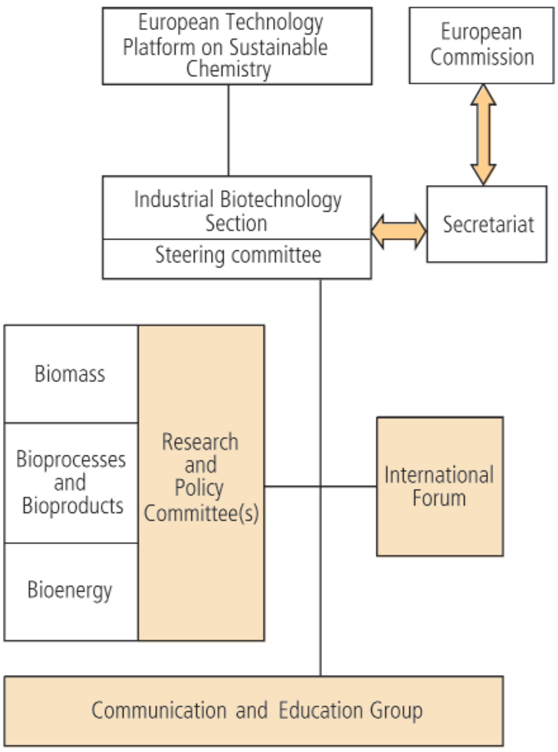
12. Structure of the Industrial Biotechnology Section of the Sustainable Chemistry Technology Platform

Since industrial biotechnology covers such a range of policy areas, governance of the Technology Platform will inevitably be complex.

The **Steering Committee** is the main coordination and decision-making body of the Industrial Biotechnology Section. This body will develop an action programme for the short term and plan a strategic approach for the longer term, consistent with the vision of the Sustainable Chemistry Technology Platform, especially with the Industrial Biotechnology of it. It also approves the composition of the research and policy committees.

The following groups will be represented in the Steering Committee:

- **Academics** working on industrial biotechnology.
- **Industry**: Representatives of companies (including SMEs) with direct interests in the technology, either as users or providers. Also representatives of the various industry sectors interested in biological processing (biotechnology, chemistry, paper/pulp, textile, detergents, pharma, and food and feed in particular).
- **National Technology Platforms (NTPs)**: Representatives of member states having a national industrial biotechnology programme.
- **Other interest groups**: Representing, for example, environmental concerns, agriculture and power generation.
- **European Commission**: Representatives of the various Directorates General covering the relevant policy areas.



The **Research and Policy Committees** are charged with developing and implementing a detailed Strategic Research Agenda and developing policy instruments and incentives. The research committees will also work with the European Science Foundation on the possibility of setting up a European Research Area (ERA), and ensure that the basic science base of white biotechnology is properly supported. The committees' role includes setting up Public-Private Partnerships in pre-competitive research. Focussed around a theme, these allow partners to contribute towards a long-term research agenda rather than run a series of short-term projects. The policy committees will find constructive policy solutions to promote industrial biotechnology and suggest ways to accelerate its introduction by overcoming regulatory and other barriers and providing incentives. Investigating the social effects within their policy field also falls within their remit.

The **Communication and Education Group** should be able to ensure that industrial biotechnology remains accepted by society. They will run communication campaigns and address all new issues as soon as possible to ensure they are properly controlled. This group will work in close collaboration with the Horizontal Issues group of the Sustainable Chemistry Technology Platform.

An **International Forum for Industrial Biotechnology** would enhance international cooperation by discussing research, innovation and policy with representatives of third countries. This would transform existing collaborations via the Transatlantic Dialogue, EU-Japan Business Dialogue and EU-China EFBIC programme into a coherent policy network, to which other partners could be invited as appropriate.

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